



Product Catalogue 2021

Quality is our passion



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MediHerb was born out of my desire for efficacious herbal therapy. This continues to underpin every aspect of our company from raw material sourcing, manufacturing, quality assurance and research through to our world-class education programs.

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Professor Kerry Bone
MediHerb Co-Founder and Director of Research & Development



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Exclusive Canadian Distributor for MediHerb®

MediHerb is extremely proud to partner with ProMedics as our exclusive Canadian distributor for the MediHerb line of quality herbal products. With a mutual commitment to product quality, a strictly monitored manufacturing process and rigorous product testing, ProMedics mirrors our devotion to providing solutions for good health. Like us, ProMedics also recognizes the importance of patient education, and that is why our products are available exclusively through qualified health care professionals. Together we strive to uphold our belief that whole food supplements and herbal products are natural complements for optimal health.

How we go beyond

The MediHerb Philosophy

MediHerb® was co-founded in 1986 by Professor Kerry Bone, an inspiring herbal practitioner, scientist and academic. Kerry's reputation is cemented by his significant world-wide contribution to education, research and advocacy of the profession.

At MediHerb we have redefined quality in natural medicines and our commitment to exceeding this means we are the first choice for many health care professionals in Canada, Australia, USA, New Zealand, South Africa and the United Kingdom. We have engaged the right mix of passionate people to meet the challenge of addressing quality and understanding the key phytochemicals in each herb and how they work in the body in a complex, interactive way. It is a philosophy that we have always stood by, remains integral to our future focus, and is always supported by our values and commitments.



Our values

We proudly come to work every day to provide high-quality treatment solutions that deliver on the needs of our patients and yours. We are continually motivated and energized to help empower people to be healthier in the most natural way. This is emphasised through our knowledge, our relationships and our vision.

Our knowledge

From discovering adulteration in Skullcap raw materials and developing a method to identify the correct species, to undertaking research with herb growers and agronomists for the best growing, harvesting and drying requirements for herbs; we are always investing in our knowledge base to share the latest developments with the industry in our quest for quality, safety and efficacy. We are a team of practicing natural health care professionals and scientists whose thought leadership has seen us partner with like-minded groups to drive herbal research, innovation, authenticity and safety.

Our relationships

The long-term relationships we have fostered with reputable growers ensure we always obtain optimal quality materials. Since the beginning, we have actively supported herb growers, and provide them with technical support and information on varietal selection, climatic and soil requirements, time of harvest, harvesting techniques, drying parameters, storage requirements, post-drying and feedback on herb quality. In addition, we collaborate closely on groundbreaking research projects to support our quest for quality, safety and efficacy. Our research partners (current and past) are part of leading Australian and international institutions, including the University of Queensland, Griffith University, Southern Cross University, the University of New

England, Swinburne University of Technology, the University of Western Sydney, the University of Wisconsin, Oregon Health and Science University, the University of Pisa and the University of Modena and Reggio Emilia.

Our vision

MediHerb was established by practitioners for practitioners, and from day one we have been passionate about investing in the future of natural medicine and delivering innovative health care solutions. We will continue to facilitate the mainstream acceptance of the professional natural medicine industry as a significant contributor to health globally. We are excited about the discoveries to come and to continue to advance knowledge and excellence through the latest scientific evidence and centuries of traditional wisdom. Most of all, we look forward to continuing to partner with you, our network of passionate practitioners, to give your patients natural health care solutions that work and make a difference in their lives.



Our commitment

MediHerb was co-founded in 1986 by Professor Kerry Bone; one of the world's most inspiring herbal practitioners, scientists and academics whose reputation is cemented by his significant contribution to education, research and advocacy for the profession.

Today the genuine passion of our team continually upholds the values and commitment of our founder and drives our benchmark of quality, safety and efficacy in natural health care. This is supported by our focus to combine the time-honored wisdom of traditional knowledge with sound clinical experience, the rigor of scientific research and power of education to ensure we continue to deliver unparalleled quality in our products.

Every day patients worldwide will experience the MediHerb way in natural health—our unique manufacturing processes, unrivalled testing regimes, focus on research; and commitment to our practitioners, growers and suppliers; herb sourcing expertise, clinical formulations and of course, the passion of our people.

Skullcap: championing authenticity in herbs

Our stringent testing regimes are renowned for guarding against substitution of species, adulteration of herbs and poor quality. It is of paramount importance to us that the herbs approved for use in MediHerb products are of the correct species and plant part, have the legitimate active constituent profile and are free from contamination. Due to our rigorous testing processes, we have found many issues relating to quality over the years.

One of our most notable discoveries was the substitution of *Scutellaria lateriflora* (Skullcap) with other *Scutellaria* spp. and *Teucrium* spp. We also identified that the substitution of *Stephania tetrandra* by *Aristolochia* spp. has the potential to cause kidney failure. Amongst many other examples we also found that *Crataegus monogyna* (Hawthorn), *Vitex agnus-castus* (Chaste Tree) and *Turnera diffusa* (Damiana) extracts were adulterated with rutin, and samples of *Vaccinium myrtillus* (Bilberry) contained a colouring agent used to imitate anthocyanins (the compounds responsible for the ripe blue colour of the berries).



To quality

Our unique approach to quality is unsurpassed in the world today. It is paramount to everything we do and evident across our entire business. Herbal products in Australia are regulated by the Australian government's Therapeutic Goods Administration (TGA), a body similar to Health Canada.

At MediHerb, we rigorously source and test all raw materials in our TGA-certified laboratories, and research and develop herb active constituents and therapeutic applications. Our unique manufacturing and extraction processes are revolutionary while our unique "Quantified Activity" (QA) system ensures consistent quality extracts with guaranteed minimum levels of active constituents. Only when all quality aspects of raw materials are confirmed does the manufacturing process begin.

Bilberry: changing global safety standards

In 2003, we received samples of *Vaccinium myrtillus* (Bilberry fruit extracts), which showed differing behaviors. Using the industry standard method (spectrophotometric assay) to determine the anthocyanin (colour quality marker) content, we found that two extracts had 25% levels as claimed by the manufacturers, but when we applied our high-performance liquid chromatography (HPLC) testing, one extract was found to contain just 9%.

Further testing identified the addition of an adulterant—amaranth, which is a synthetic dark red dye. The testing also revealed that when deliberate adulteration occurs in an extract, a spectrophotometric assay is inadequate to accurately determine the levels of compounds such as anthocyanins. One of our proudest achievements is that this work was published and led to a change in global regulatory testing standards for Bilberry.



Our commitment

To safety

Safety is paramount in every aspect of our operations and stringent testing regimes to guard against substitution, adulteration and poor quality. Our quality assurance process may test herbs for species identity, plant part, colour, aroma, texture, content of specified actives, microbial levels, amount of extraneous matter, pesticides and herbicides, heavy metals and aflatoxins. Strict standards are predetermined to ensure only quality materials from reputable sources are used and every ingredient goes through thorough assessment for safety and toxicology.

To efficacy

As practicing health care professionals ourselves, we fully understand the necessity for efficacious products that meet a genuine health need. This is reflected by our diligence towards research and ability to select herbs phytochemically as nature intended. Based on the latest credible evidence, our team of naturopaths, scientists and herbal experts carefully collaborate to formulate every product with the highest quality ingredients. We are committed to the development of efficacious herbal therapies with a focus on meeting patient needs, validating the efficacy of herbal formulas through researching published clinical trials and *in vitro* research and researching the phytochemistry of medicinal plants. By combining phytochemical, biochemical, clinical and traditional herbal knowledge, we can continue to produce high-quality products to meet changing health care needs.

Echinacea: the MediHerb "Quantified Activity" (QA) Program

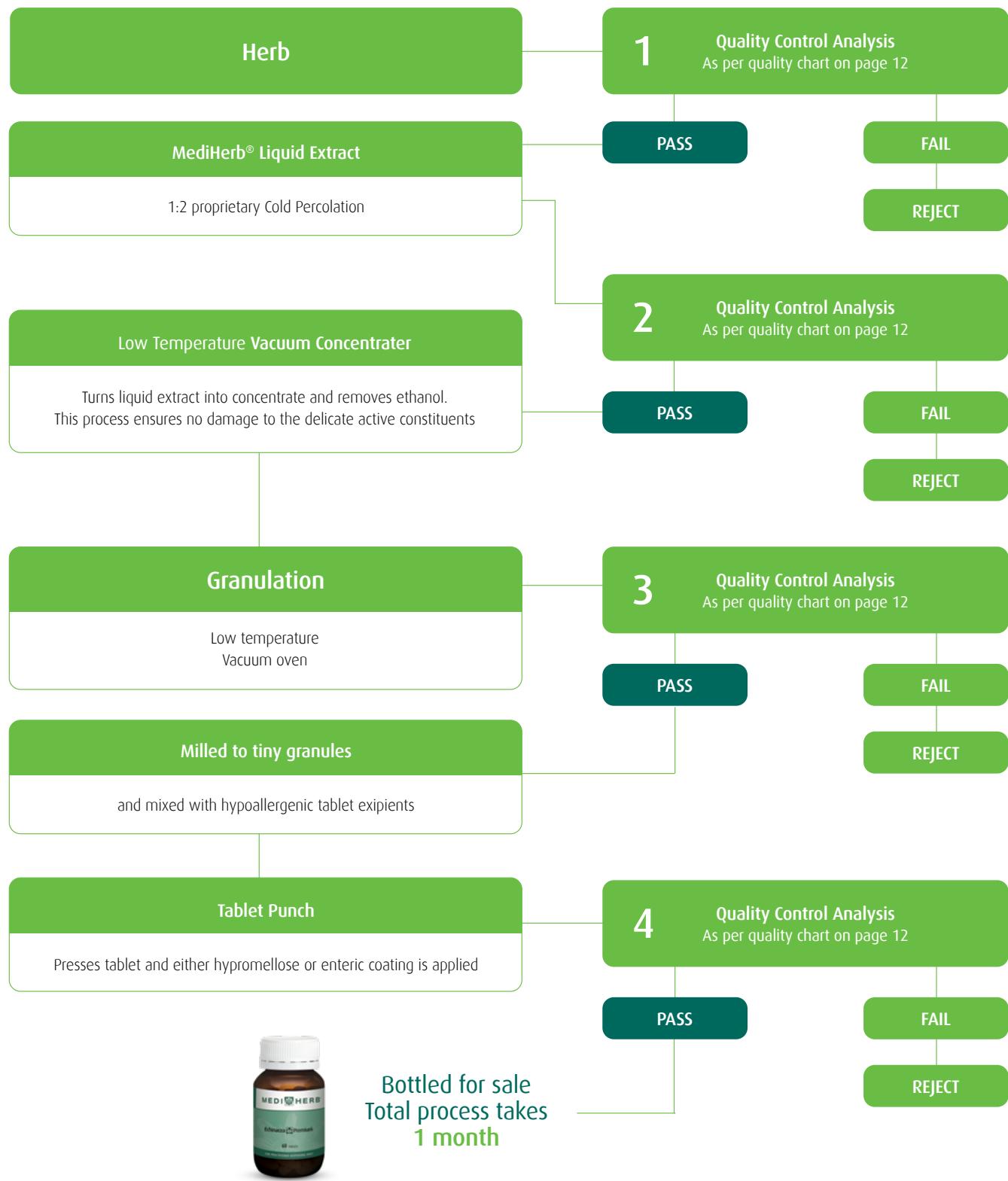
Our QA program is unique to MediHerb and uses the latest research and clinical experience underpinned by batch consistency to define stringent guidelines to produce consistent quality extracts with guaranteed minimum levels of active constituents. To date we have quantified the activity of over 70 herbs through this program — a world first.

Representing the most up-to-date scientific knowledge available, the process of developing QA extracts is complex, however, once constituents are selected and QA levels are set, we focus on ensuring the supply of consistent quality raw materials and the retention of the constituents throughout the manufacturing process. QA extracts are carefully selected whole herbs manufactured using our 1:2 Cold Percolation process to contain the active constituents from the raw herb. Our program links together all possible parameters that can affect product and extract quality, guaranteeing a high quality, efficacious extract every time.

Our commitment to guarantee supply of authentic Echinacea led to the development of our QA program, as the herb was suffering from global confusion over what constituted authentic Echinacea. This was due to another herb's uncanny physical root similarity. We adopted sophisticated analyses to compare Echinacea's chemical fingerprint with a certified reference sample from the correct species. We also investigated methods to quantify the herb's alkylamides and other important compounds, resulting in our high performance liquid chromatography (HPLC) methodology. Armed with these stringent testing processes, we worked with Echinacea growers to determine appropriate growing conditions and handling parameters, and internally we established protocols to ensure optimum retention and stability of alkylamides during all phases of the production process. This allowed us to establish our standard for acceptance of Echinacea raw material based on alkylamide content.



MediHerb's unique tabling process when using our liquid extracts



Our commitment

To manufacturing

After testing, all herbs are transferred to our temperature-controlled warehouse to preserve the herbs before undertaking our unique 1:2 Cold Percolation manufacturing process. Extensive scientific testing proves that this is unlike any other herbal extraction method and is the benchmark for producing the highest quality extracts using no heat or concentration. It ensures herbal constituents remain intact with only ethanol or purified water (and occasionally glycerol).

Each liquid variety is processed using specific ethanol percentages for optimum extraction. Our extraction equipment is built from stainless steel, and we use pharmaceutical-grade filtering units. All process water is purified by reverse osmosis, and our experience with developing specific ethanol percentages for each herb helps us maximize quality. Our internal benchmarks for each herb must be met or exceeded for acceptance into manufacturing.

Our unique tablet manufacturing process also uses our 1:2 Cold Percolation liquid extracts to ensure potency equivalent to the original galenical liquid extract. It has also been subject to extensive research and development to ensure that the finished tablet is as efficacious as the liquid extract, and that the full phytochemical profile has been retained.

See diagram on page 13

To testing

Herbs are naturally complex and not all are grown, harvested, dried or stored in the same way. We use the latest technology, invest in the best equipment, and employ and train the best scientific talent who understand the complexities of phytochemistry in order to undertake highly detailed testing throughout all stages of the sourcing and manufacturing process. This guarantees validation of species and plant parts and efficacy of active ingredients and phytochemical profiles.

Our tests include:

- **High Performance Thin Layer Chromatography (HPTLC)** is a high resolution thin layer chromatography separation technique where liquid extract is precisely spotted onto a high-resolution silica gel plate and exposed to solvent to separate the extract into a series of molecules characteristic to the plant based on sample interactions with the plate and the solvent. HPTLC is the next generation of thin layer chromatography (TLC) as it is quicker and more sensitive. This means that the separation provides more detailed information allowing lower levels of adulteration to be detected. HPTLC may also be able to quantify compounds whereas TLC can only identify presence. HPTLC also features an auto sampler to eliminate any variation from different technicians setting up the sampling manually, which can happen under the TLC process.
- **Gas Chromatography (GC)** is a separation technique performed in the gas phase for volatile components such as essential oils. Samples can be introduced either as a liquid or a gas (headspace injector) using an inert carrier gas into a hot injector block. The volatilised constituents then pass onto a heated capillary column separating the gaseous constituents based predominately on their boiling point and the interaction with the column chemistry. The constituents are moved into a flame and the resultant by-products pass through electrodes to generate a signal (detection can also be done by Mass Spectrometry).
- **Ultra High Performance Liquid Chromatography (UHPLC)** is a separation technique performed in the liquid phase. Liquid samples are injected into a solvent stream under high pressure at an extremely rapid flow rate, which is carried onto a high resolution packed column and separated into individual constituents based on the interaction between the solvent and column chemistry. Constituents are detected and quantified by Photo-Diode Array (PDA), which measures the absorption spectrum of each chemical constituent at an extremely rapid acquisition rate (Mass Spectrometry can also be used). UHPLC offers

Tableting: benchmarking quality

Our research has proven that the optimal method of herb processing for tableting involves the evaporation of the ethanol and water at low temperatures under vacuum. This important step minimises the exposure of the delicate chemicals in the herbal matrix to the damaging effects of heat and oxidation.

Our tableting process takes this one step further to actually specify the optimal parameters employed during the evaporation and drying processes for each of the active constituents of the final tablet. As with our liquid herbal extracts, our tablets are manufactured to pharmaceutical standards. Each batch is tested for disintegration, friability, weight uniformity and for active constituents (if applicable). Our tablets are required by the TGA to disintegrate in less than 30 minutes for maximum efficacy.





a three times higher pressure rate than HPLC and is much faster and more sensitive. Notably, it allows us to gain more detailed information about the breakdown of various peaks and marker compounds for a more accurate identification. In addition, the use of less solvent is a great environmental benefit. UHPLC allows us to establish our own test methods for compounds creating a greater understanding of phytochemistry.

- **Mass Spectrometry (MS)** is an extremely specific and sensitive technique that volatilises, ionises and filters molecules in complex mixtures. It can be used to identify molecular weights of molecules or for quantification purposes. They can be connected to most separation techniques to detect the eluting molecules from the column. MS is used routinely with GS and UHPLC testing.
- **Ultraviolet/Visible Detector (UV-vis)** is a quantitative technique that exposes the sample to light and measures how the molecule interacts in the Ultraviolet/Visible region (electron excitation spectra). It can also be useful in elucidating molecular structure and can be attached to a UHPLC as a detection technique (i.e. photo diode array). UV-vis is a sensitive technique used to measure the spectrum of each phytochemical as it passes the detector (diode array) and depending on the herb being tested, is connected to UHPLC.

▪ **Fourier Transform Infrared Spectrometry (FTIR)** is an identification technique that exposes the sample to light and measures how the molecule interacts in the infrared region (molecule vibrational spectra). This testing is useful in elucidating molecular structural information by identifying samples and quantification. FTIR is the next generation UV-vis. It is more sensitive and more detailed and useful for delivering unknown compounds as it gives detailed information about the functional groups attached to the molecule.

We hold all our suppliers to our benchmark testing standards, and before any herb is purchased, we analyze a batch sample to ensure compliance with our strict quality criteria. The purchased batch is also sampled and subjected to the same battery of tests. Only if the herb passes this second set of tests is the batch accepted into the factory for further processing. Our stringent testing processes reveal any quality issues from substitution of species to adulteration or simply a poor quality plant. All herbs approved for use in our products are the correct species, plant part, active constituent profile and are free from contamination.

See diagram on page 12

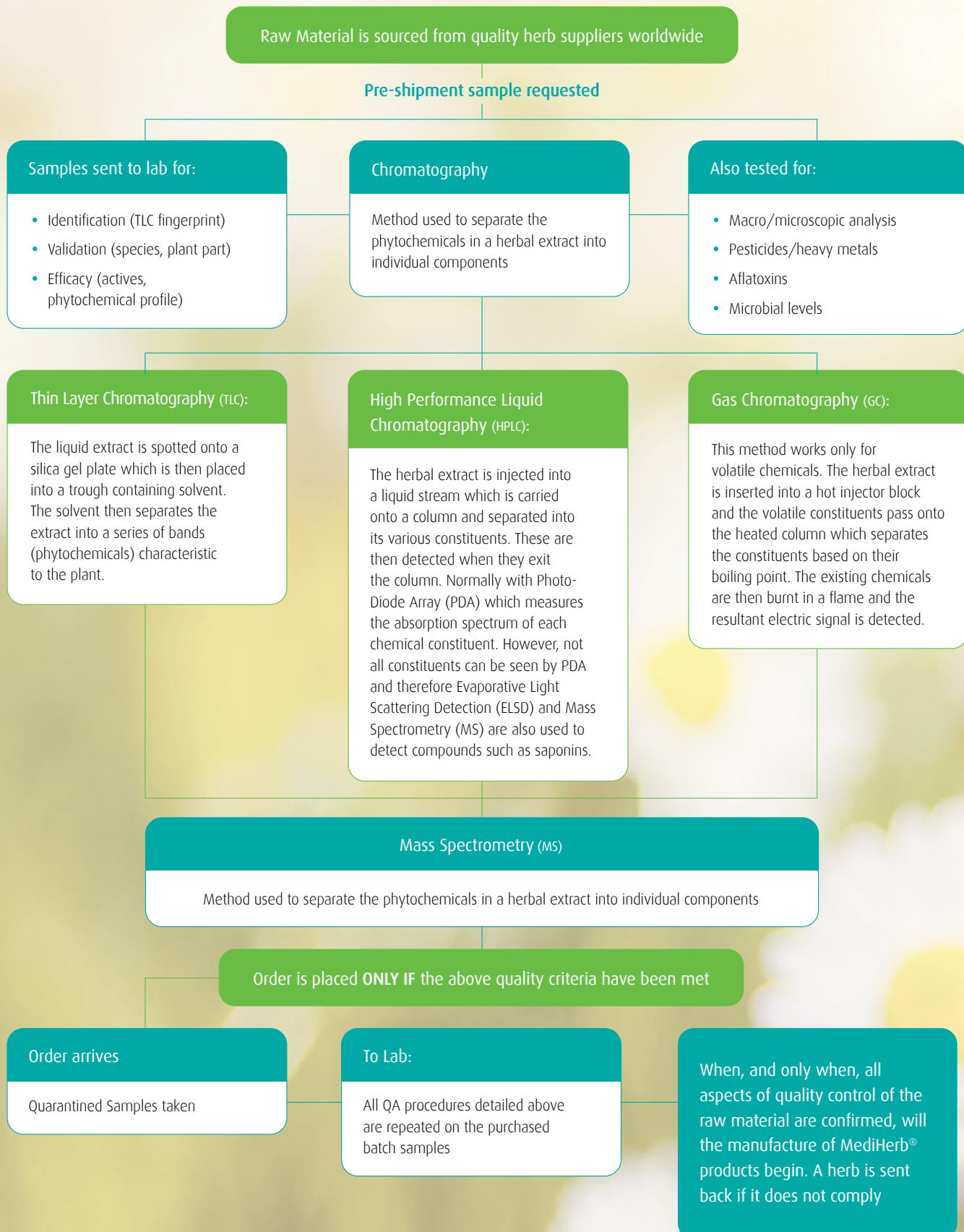
Golden Seal: identifying substitution issues

Golden Seal (*Hydrastis canadensis*) is very expensive and has always been in short supply; thus it is commonly substituted with cheaper herbs that greatly affect efficacy. These cheaper species do not contain hydrastine; rather they contain only berberine and berberine-related compounds. They do, however, produce an extract of the same colour as Golden Seal. Berberine is a potent antibacterial agent, but it is the hydrastine that is believed responsible for the unique trophorestorative effects of Golden Seal upon mucous membranes.

Similarly, the hair roots of Golden Seal, which have lower levels of hydrastine than the rhizome, are sold as the root and rhizome, which provides lower efficacy. The presence of hydrastine and the differentiation of adulterants are easily determined by UHPLC, and, therefore, we only purchase cultivated Golden Seal as it is now considered endangered.



Quality Assurance of Herbs (Identity And Purity)



MediHerb manufacturing processes & quality control for herbs

Cool room storage of herbs for quality assurance

Ideal cool room storage conditions are used for raw materials to minimise degradation of actives, control insects and contamination.



Raw material milled under cryogenic conditions so no heat can affect the phytochemicals



Proprietary Cold Percolation

A unique slow process over 7-10 days, developed by Kerry Bone, to extract the full spectrum of compounds of the herb without causing damage or degradation.



Liquid Extracts

The majority of our liquid extracts are made as 1:2 liquid extracts as this is the most effective method to extract the full phytochemical profile in a convenient dosage unit. However we also make liquid extracts with other ratios depending on the optimum extraction of the individual herb.



Samples sent to the QA Laboratory where they are analysed for phytochemical profile, level of actives, consistency, verification of original herb with no deterioration or degradation.
This is the third round of testing performed. When the extract meets all criteria.

Bottled for sale



Our commitment

To research

We are a global leader in herbal scientific knowledge and often partner on research projects to advance quality and efficacy with reputable establishments. Our outstanding team of scientists and health care professionals drive our research, development and quality control practices. We also collaborate with health care professionals for real-time patient feedback. Significant innovations include our revolutionary process of manufacturing herbal tablets from liquid extracts and 1:2 Cold Percolation manufacturing process. Our Research and Development team combine experience in food and herbal products, university research, drug analysis in hospitals, pharmaceuticals, quality assurance, technical writing, clinical nutrition and work *in situ* with our own herbalists and naturopaths, along with a board of leading American, Australian and other international herbalists. This ensures we can combine the best of science, traditional knowledge and current clinical knowledge to produce the most therapeutic herbal solutions.

To innovation

Innovation is the lifeblood of our business and supports our culture of excellence. We undertake a rigorous new product development process to ensure that appropriate steps are undertaken when investigating the introduction of a new product. This allows us to develop a shortlist of key herbs that are then subjected to closer analysis. This involves detailed examination of the clinical outcomes, phytochemistry and biological activity, analytical methodology, continuity of supply, economic sustainability, synergy of the final formula, cost to the patient and practicality of final dose formulation. Once the prototype formulation is agreed upon, we may then undertake a human feedback trial to prove the efficacy and safety of the product and regularly supply product to support other industry research projects.

Echinacea: the landmark research project

The most well-known herbal support for the immune system is Echinacea, yet it is both misunderstood and underestimated. There are many Echinacea products available, which differ according to plant species, plant part (root, leaves, seeds or a combination), quality markers and dosage. In 2003, MediHerb began an extensive research project designed to identify the bioavailable components of Echinacea Premium and how they exert an effect on the immune system. MediHerb's research results made a substantial contribution to a new understanding of lipophilic extracts of Echinacea, which conclude that alkylamides must be used as the markers of quality and activity, the root of Echinacea is the preferred plant part given its high levels of alkylamides and the preferred species of Echinacea are *E. angustifolia* and *E. purpurea* since they contain high levels of alkylamides. In addition, our research has proven that Echinacea must be extracted using an alcohol percentage sufficiently high to efficiently extract the alkylamides.*



To professional medicine

We are committed to actively support natural health care professionals and passionately advocate for quality, efficacy and safety to benchmark natural medicines to the highest of standards. In particular, our founder, Kerry Bone, was integral in establishing professional standards of the industry, including leading MediHerb's discovery of the adulteration of a commonly available Bilberry extract—the catalyst for a global change in testing regulations. We invest significantly in our profession by funding clinical trials. Our reputation for scientific knowledge means we often collaborate on projects investigating herbal therapies, so we apply stringent criteria to assess viability. The trial must fit with our philosophy of superior quality, innovative, and holistic herbal solutions, and must be conducted at a reputable research establishment. We do not fund or involve ourselves with research that utilizes animals as human models. As practicing clinicians, we also regularly conduct professional seminars for health care professionals and are dedicated to being a key source of knowledge for the natural health care profession. Through our website, mediherb.ca we also provide extensive clinic and reference tools, library resources and webinars.

To ingredients

We handle and process raw materials with the utmost of care. As the largest purchaser and processing plant of herbs in Australia, we assist growers with support on varietal selection, climatic and soil requirements, time of harvest, harvesting techniques, drying parameters and storage requirements. Where possible, we source organically grown and wild-crafted herbs, including internationally where conditions and handling requirements are the optimum. For example, Cat's Claw from Peru. We work with growers to help cultivate endangered species and our unique system of identifying and classifying any threat allows us to immediately find alternatives or reduce that threat. Our commitment to efficacy has also uncovered examples of substitution including Echinacea, commercial Wild Yam, Cat's Claw and Golden Seal. If any herb does not meet our standards, we go out of stock rather than supply an inferior product, so you can always be confident in consistent results with patients from batch to batch.

Wild Yam: identifying quality issues

There are around 600 species of Yam, many of them wild species that flourish in damp woodlands and thickets. *Dioscorea villosa* (also known as Colic Root or Wild Yam) is a twining, tuberous vine native to eastern North America. The roots initially taste starchy, but soon after are bitter and acrid—nothing like the taste of Yam or Sweet Potato. Commercial Wild Yam extracts available for use as raw materials are often from *Dioscorea opposita* (Chinese Yam Root), which has a different phytochemical profile. It is widely misconstrued that *Dioscorea villosa* contains diosgenin and many products have this as a statement on their labels. However it does not contain diosgenin, but rather the diosgenin precursors. Unfortunately, the phytochemical profile of Wild Yam is poorly defined and based on outdated scientific literature, so we undertook a project in conjunction with Associate Professor James De Voss from the University of Queensland Australia to investigate its phytochemistry.

Commercially available *Dioscorea villosa* is in the form of dried roots, usually harvested at the end of summer or fall when the plant is dying back to its rootstock. It was found that these roots contained only very small amounts of dioscin, not the predominance as previously thought. The major saponin found in the fall-harvested roots were in fact the furostanol-based saponins, methylparvifloside, and methylprotodeltonin,

while the spirostanol-based saponins, Zingiberensis saponin I and deltonin, were the major saponins for samples harvested in summer. The storage saponins from the fall differ from the summer saponins by the presence of an extra glucose molecule. The two main compounds found in commercial material—harvested in the fall—are significantly different as they contain extra glucose residues.



Our commitment

To sustainability

In addition to working with domestic growers, we also source herbs from abroad and recognize the importance of supporting indigenous communities in quality and sustainability standards. As these communities depend on the income of the herb crops for their well-being, it is particularly important that they understand quality issues and are educated as to how to best grow or sustainably harvest the herb. Working together, we can ensure that they will sell their crops and provide income for their community. In addition, we have a documented process to avoid using medicinal plants that are on the brink of becoming classified as endangered species. We have developed a system of identifying and classifying the "threat" to particular herbs. "Threatened" is not an official classification; rather it is determined by us based on information received from independent, reliable sources such as CITES (Convention on International Trade in Endangered Species of Wild Fauna and Flora), TRAFFIC (Wildlife Trade Monitoring Network) and United Plant Savers. When a wild-crafted herb is classified as "threatened" by us, steps are taken immediately to find alternatives to overcome or reduce the threat.

Guidelines: MediHerb's commitment to endangered species

1. Where the threatened status of an herb is specific to a region or country, we do not acquire the herb from that region or country.
2. We use cultivated herb sources of threatened herbs.
3. Where no cultivated source is available, we seek to establish cultivation in conjunction with herb growers.
4. If 2 and 3 are not options, we then investigate the wild crafting techniques and protocols to ensure they are conducted sustainably and ethically.
5. In certain cases, substitution of the threatened herb with a medicinally interchangeable species will be possible. This option requires technical and Research and Development involvement.
6. We actively promote the use of alternate herbs in place of endangered herbs by educating health care professionals.
7. Where a threatened or endangered herb is part of a tablet or liquid formulation, we will reformulate the product to include a different herb.
8. When an herb is listed in the CITES Appendix II and a cultivated source is not available, we cease to use that herb and delete the product from the range, for example Pygeum.



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Our mission always
remains to provide
high-quality
herbal solutions
to health care
professionals

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Our people

Our passionate team includes practicing natural health care professionals and scientists. We have a proud history of seeking out people with the right expertise to further our mission of providing you with the best possible products that deliver on the needs of you and your patients.

Meet our leaders



Kerry Bone

BSc (Hons), Dip Phyto FNIMH,
FNHAA, AHG, MCPP, FANTA

Kerry is recognised internationally as a pre-eminent herbal practitioner, scientist and academic with a reputation cemented by his significant contribution to excellence in education, research and advocacy. Kerry's passionate commitment to product development, research, writing, education and clinical practice positions him as a pioneer in the international herbal industry. He is the founder of MediHerb, author of six books, contributor to over 100 articles on herbal therapy to peer-reviewed journals around the world and has remained dedicated to his practice for over 30 years.



Hans Wohlmuth

PhD (Pharmacognosy),
BSc (Biology)

Hans is MediHerb's Research and Development Manager. During his 16 years at Southern Cross University, Hans taught pharmacognosy and complementary medicine. He also established the Medicinal Plant Herbarium and co-founded the Herbal Authentication Service. Hans is an active researcher and has published more than 50 scientific articles on medicinal plants, natural products and complementary medicine. He is a member of the TGA Advisory Committee on Complementary Medicines and serves on the Advisory Board of the American Botanical Council. He also has editorial roles with several journals including the "Australian Journal of Herbal Medicine" and "Advances in Integrative Medicine".



David Leach

BSC (Hon), PhD, MRACI, CChem

David is MediHerb's Senior Research and Development Chemist, an Adjunct Professor at the University of Western Sydney and one of Australia's most respected phytochemists. David has more than 30 years experience in the field of medicinal plant and natural product chemistry. His far-ranging expertise includes herbal medicines, native Australian plants and natural, plant-derived insecticides. David has also co-authored more than 100 scientific publications in international peer-reviewed journals and is an inventor of three patents on phytochemicals. He has given numerous presentations at conferences around the world and is a member of the Australian Standards Association's Essential Oil Committee.



Michelle Morgan

BSc (Chemistry), DHM

Michelle is a qualified herbalist and has worked in the scientific field as a laboratory technician for many years including more than three as a Quality Assurance Chemist. Since 1995, Michelle has worked at MediHerb as a Technical Writer responsible for information gathering and organizing technical publications. Michelle assisted in the research and writing of several herbal medicine textbooks including the award-winning "The Essential Guide to Herbal Safety" published by Elsevier in 2005.



Amanda Williams

BBus, Adv Dip Nat, Dip Bot Med

Amanda is an experienced naturopath with more than 18 years clinical experience. Since 2000, Amanda has worked with MediHerb in international business development and was instrumental in the U.S. partnership with Standard Process. A popular speaker who can convey the technical complexity of herbal medicine in an easy to understand and clinically relevant manner, Amanda has traveled across the U.S. delivering seminars to health care professionals and in Australia to the general public.



Angela Hywood

BHSc(Naturopathy), DipBotMed, DipHom, DipCN, DipNFM, MANTA, MNHAA

Angela Hywood is an experienced naturopathic clinician with over 20 years of clinical experience, specializing in integrative endocrinology, fertility, and pregnancy care. Prior to Angela's career in naturopathy, she studied at the School of Pharmacy, Curtin University of Technology in Perth, Western Australia and has a strong interest in herbal safety, particularly herb-drug interactions and pharmacology. Angela is a well-known speaker at complementary and integrative medicine conferences both in Australia and internationally; and has published articles in complementary medicine journals in Australia and the U.S. Angela's clinical passion in the art and science of herbal medicine, clinical nutrition, homoeopathy, whole food nutrition and lifestyle medicines are tailored into dynamic clinical programs for her patients.



Berris Burgoyne

BHSc, ND, Dip Herb

Berris is a renowned naturopathic clinician with more than 26 years of clinical experience. She owns and runs a highly successful naturopathic clinic in Brisbane, Australia and is a senior member of the MediHerb team as a technical writer and educator. Berris was one of Kerry Bone's first herbal students and regularly lectures alongside him in Australia and New Zealand. She has also lectured extensively in the U.S., Canada, the UK and South Africa.



Joanne Boyd

Adv Dip HSc (Nat), Adv Dip HSc (HerbMed), Dip (Nut)

Joanne is an Australian-trained naturopath who has worked in various areas of the complementary medicine industry for over 18 years. She has lectured at several colleges in Australia teaching herbal medicine, nutrition, and naturopathic clinical skills. Joanne has been a part of the MediHerb team for more than 14 years and provided education and support for sales representatives and clinicians in Australia, the U.S., Canada and the UK.

Core Products & Body Systems

Body Systems Legend

QA = Quantified Activity S = Standardised

 Musculoskeletal	 Respiratory	 Female Endocrine	 Endocrine General
 Skin	 Cardiovascular & Circulation	 Immune	 Male Endocrine
 Nervous System	 Digestive System		

Core Products

AdrenoCo	Licorice & Rehmannia Formulation	 
Andrographis Complex	Short-Term Immune System Support	 
Boswellia Complex	Joint Support	
DiGest Forte	Core Digestive Support	
Echinacea Premium	Immune System Support	 
Garlic	Cardiovascular Support	  
Ginkgo Forte	Enhance Cognitive Function	 
Gymnema	Blood Sugar Metabolism	
Kava Forte	Relieve Restlessness & Aid Sleep	
LivCo	Liver Function Support	 
Nevaton Forte	Core Nervous System Support	 
Rhodiola & Ginseng Complex	Enhance Vitality & Stamina	 
Turmeric Forte	Standardised for Bioavailable Curcumin	
Vitanox	Antioxidant Cellular Defense	  

Digestive System



Upper GIT

DiGest Forte	Core Digestive Support
LivCo	Liver Function Support
Livton Complex	Digestive Liver Support
Silymarin	Core Liver Support

Lower GIT

Golden Seal	GIT Immune System Support
Vitanox	Antioxidant Cellular Defense

Cardiovascular System



Heart Health

Garlic	Support Healthy Normal Cholesterol
Ginkgo Forte	Circulation Support
Vitanox	Antioxidant Cellular Defense

Circulation

Bilberry	Venous Eye Support
Garlic	Support Healthy Normal Cholesterol
Ginkgo Forte	Circulation Support
Horsechestnut Complex	Varicose Veins Support
Vitanox	Antioxidant Cellular Defense

Endocrine



Adrenal

Bacopa Complex	Nervous System & Memory Support
Rhodiola & Ginseng Complex	Enhance Vitality & Stamina
Withania Complex	Calming Stress Support

Pancreas

Ginkgo Forte	Circulation Support
Gymnema	Blood Sugar Metabolism
Silymarin	Core Liver Support



Core Products & Body Systems

Female Health



Menstruation/PMS

Chaste Tree	Natural Hormone Balance
FemCo	Female Vitality
Nevaton Forte	Core Nervous System Support

Child Bearing Years

Chaste Tree	Natural Hormone Balance
FemCo	Female Vitality
Tribulus Forte	Tonic Support

Menopause

Chaste Tree	Natural Hormone Balance
Tribulus Forte	Tonic Support
Wild Yam Complex	Core Menopause Support

Respiratory System



Broncafект

Immune Supporting Cough Formula

Nervous System



Ginkgo Forte	Enhance Cognitive Function
Kava Forte	Relieve Restlessness & Aid Sleep
Nevaton Forte	Core Nervous System Support
Rhodiola & Ginseng Complex	Enhance Vitality & Stamina
St John's Wort	Healthy Mood Balance
Valerian Complex	Sleep Support
Withania Complex	Calming Stress Support

Male Health



<50

Rhodiola & Ginseng Complex	Enhance Vitality & Stamina
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50+

Rhodiola & Ginseng Complex	Enhance Vitality & Stamina
Tribulus Forte	Tonic Support

Musculoskeletal



Boswellia Complex	Joint Support
Horsechestnut Complex	Venous Integrity
Kava Forte	Relieve Restlessness & Aid Sleep
St John's Wort	Nerve Function Support

Skin



Vitanox

Antioxidant Cellular Defense

Beyond Comparison

Our Products

As a health care professional, you have invested a great deal of time and energy into earning your qualifications. At MediHerb we believe you should protect that investment by using only the highest quality herbal products supported by authoritative technical and clinical information. This document is a detailed reference of all MediHerb herbal products, indexed by herb (botanical and common names) and set out in an easy to use format.

Please take the time to read the MediHerb Philosophy so that you may understand the depth of our passion for superior quality, efficacious herbal remedies. MediHerb has a total commitment to quality, which covers every aspect of our approach from research and development right through to manufacturing. Like so many decisions you will make in your clinical practice, you need to evaluate the increasing number of herbal products and suppliers by certain criteria. It is vital to your success as a health care professional that you consider these criteria closely and carefully.

The MediHerb Product Catalogue is an essential resource for any health care professional seeking to make an informed choice.

AdrenoCo

Glycyrrhiza glabra



AdrenoCo contains Licorice and Rehmannia, a combination that contains many compounds including triterpenoid saponins (especially glycyrrhizin), other saponins, iridoid glycosides and many flavonoids.

Indications

- ✓ Licorice is traditionally used in Herbal Medicine as an expectorant to help relieve chest complaints, such as catarrhs, coughs and bronchitis
- ✓ Helps relieve inflammatory conditions of the gastrointestinal tract, such as gastritis in adults

Additional Therapies

- Nevaton Forte
- St John's Wort
- Valerian Complex
- Withania Complex
- Withania 2:1
- Licorice High Grade 1:1

Dosage and Administration

Adults: 1 tablet 3 times daily or as directed by your health care practitioner. Consult a health care practitioner for use beyond 4 to 6 weeks.

Each tablet contains:

<i>Glycyrrhiza glabra</i> (Licorice) root 7:1 extract	250 mg
Dried herb equivalent of Licorice root	1.75 g
Contains glycyrrhizin 25 mg	
<i>Rehmannia glutinosa</i> (Rehmannia) rhizome 5:1 extract	150 mg
Dried herb equivalent of Rehmannia rhizome	750 mg

Contraindications and Cautions: Consult a health care practitioner if symptoms persist or worsen and prior to use if you have a liver disorder. Do not use if you are pregnant or breastfeeding. Do not use if you are taking thiazide diuretics, cardiac glycosides, corticosteroids, stimulant laxatives or other medications which may aggravate electrolyte imbalance or if you have hypokalemia, high blood pressure, or a kidney or cardiovascular disorder.

Please consult the product packaging label for the most accurate product information.
Not for public distribution. For professional use only.

Andrographis Complex

Ocimum tenuiflorum



Andrographis Complex contains a blend of herbs to support the immune system.

Andrographis, *Echinacea angustifolia* root, *Echinacea purpurea* root and Holy Basil provide a unique range of phytochemicals including diterpenoid lactones (collectively referred to as andrographolide), flavonoids, alkylamides, caffeic acid derivatives (especially echinacoside and cynarin), and polyphenols. The blending of *E. angustifolia* and *E. purpurea* roots ensures that a spectrum of constituents (especially the alkylamides) are present in the optimal form and quantity. This tablet contains herbs with standardised levels of key phytochemicals to ensure optimal strength and quality: 50 mg of andrographolide and 2.0 mg of alkylamides per tablet.

Indications

- ✓ Helps to relieve the symptoms and shorten the duration of upper respiratory tract infections
- ✓ *Echinacea purpurea* is used in Herbal Medicine to help fight off infections, especially of the upper respiratory tract.

Additional Therapies

- Echinacea Premium tablets
- Sinus Forte tablets

Dosage and Administration

Adults: 1 tablet 3 times daily. Take at the first sign of infection. For use beyond 8 weeks, consult a health care practitioner.

Each tablet contains:

<i>Andrographis paniculata</i> (Andrographis) leaf 14:1 extract	142.9 mg
Dried herb equivalent of Andrographis leaf	2 g
Contains andrographolides 50 mg	
<i>Echinacea angustifolia</i> (Echinacea) root 1:2 extract	400 mcL
Dried herb equivalent of Echinacea root	200 mg
Contains alkylamides 0.8 mg	
<i>Echinacea purpurea</i> (Echinacea) root 1:2 extract	600 mcL
Dried herb equivalent of Echinacea root	300 mg
Contains alkylamides 1.2 mg	
<i>Ocimum tenuiflorum</i> (Holy Basil) leaf 5:1 extract	100 mg
Dried herb equivalent of Holy Basil leaf	500 mg

Contraindications and Cautions: If symptoms worsen, consult a health care practitioner. If you are breastfeeding, are taking heart or blood pressure medication or immunosuppressants, or have a heart condition, diabetes, an autoimmune disorder, a progressive systemic disease such as tuberculosis, collagenosis, multiple sclerosis, AIDS and/or HIV infection, consult a health care practitioner prior to use. Do not use if you are pregnant or attempting to conceive. Rare cases of severe allergic reactions have been known to occur; use caution if you are allergic to plants of the Daisy family.

See Echinacea information on page 36 for Echinacea Quality Issues

Please consult the product packaging label for the most accurate product information.

Not for public distribution. For professional use only.



Astragalus Complex

Astragalus membranaceus



Astragalus Complex contains Astragalus, *Echinacea purpurea* root and Siberian Ginseng.

This combination of herbs contains many compounds including triterpenoid saponins, flavonoids, sterols, caffeic acid derivatives (especially cichoric acid), alkylamides and a diverse group of constituents called eleutherosides. The Siberian Ginseng component of this tablet is standardised to contain 600 mcg of eleutheroside E per tablet to ensure optimal strength and quality.

Indications

- ✓ Helps to relieve the symptoms and shorten the duration of upper respiratory tract infections
- ✓ Supportive therapy in the treatment of upper respiratory tract infections (e.g. common colds)

Additional Therapies

- Withania Complex tablets
- Withania 2:1 liquid extract
- Echinacea Premium tablets or Echinacea Premium 1:2 liquid extract

Dosage and Administration

Adults: 1 tablet 2 to 4 times daily. Take at the first sign of infection or as directed by your health care practitioner. Avoid using two hours prior to or after taking mineral supplements. Consult a health care practitioner for use beyond 8 weeks.

Each tablet contains:

<i>Astragalus membranaceus</i> (Astragalus) root 1:2 extract	1.7 mL
Dried herb equivalent of Astragalus root	850 mg
<i>Echinacea purpurea</i> (Echinacea) root 1:2 extract	1.3 mL
Dried herb equivalent of Echinacea root	650 mg
<i>Eleutherococcus senticosus</i> (Siberian Ginseng) root 10:1 extract	75 mg
Dried herb equivalent of Siberian Ginseng root	750 mg
Contains eleutheroside E 0.6 mg	

Contraindications and Cautions: Consult a health care practitioner if symptoms persist or worsen prior to use if you have stomach ulcers or inflammation, if you are taking immunosuppressants, or if you have a progressive systemic disease such as tuberculosis, leukemia, collagenosis or multiple sclerosis, if you have a kidney disorder or if you have blood pressure problems. Do not use if you are allergic to plants of the Asteraceae/Compositae/Daisy family or if you are pregnant or breastfeeding. Hypersensitivity (e.g. allergy) has been known to occur, in which case, discontinue use. Consumption of Golden Seal with alcohol, other medications and/or natural health products with sedative properties is not recommended.

See *Echinacea* information on page 36 for *Echinacea Quality Issues*

Please consult the product packaging label for the most accurate product information. Not for public distribution. For professional use only.

Bacopa Complex

Bacopa monnieri



Bacopa Complex combines the herbs **Bacopa**, **Schisandra**, **Siberian Ginseng** and the essential oil of **Rosemary**.

These herbs contribute key phytochemicals to the blend such as dammarane saponins, other saponins, flavonoids, sterols, dibenzocyclooctene lignans, a diverse group of constituents called eleutherosides, monoterpenes and sesquiterpenes. This tablet contains two herbs with standardised levels of key phytochemicals to ensure optimal strength and quality.

Indications

- ✓ Siberian Ginseng is used in Herbal medicine as a tonic to help relieve general debility

Additional Therapies

- Ginkgo Forte tablets
- St John's Wort tablets
- Withania Complex tablets

Dosage and Administration

Adults: 1 tablet 3 to 4 times daily or as directed by your health care practitioner. Consult a health care practitioner for use beyond 1 month.

Each tablet contains:

<i>Bacopa monnieri</i> (Bacopa) herb top 50:1 extract	75 mg
Dried herb equivalent of Bacopa herb top	3.75 g
<i>Schisandra chinensis</i> (Schisandra) fruit 6:1 extract	110 mg
Dried herb equivalent of Schisandra fruit	650 mg
<i>Eleutherococcus senticosus</i> (Siberian Ginseng) root 10:1 extract	50 mg
Dried herb equivalent of Siberian Ginseng root	500 mg
Contains eleutheroside E 0.4 mg	
<i>Rosmarinus officinalis</i> (Rosemary) herb top flowering essential oil	10 mg

Contraindications and Cautions: Discontinue during the treatment of any acute infectious illness. Do not use if pregnant or breastfeeding. Discontinue use 7 days prior to general anesthesia. Consult a health care practitioner if symptoms persist or worsen. Do not use if you have high blood pressure. Digestive upset has been known to occur. Discontinue use and consult a health care practitioner if digestive symptoms persist or worsen. Hypersensitivity (allergy) may occur. Use with caution if you have allergies to members of the Scrophulariaceae (figwort) family or Lamiaceae (mint) family. May cause nausea, dry mouth and fatigue.

See the LivCo information on page 47 for Schisandra Quality Issues

Please consult the product packaging label for the most accurate product information. Not for public distribution. For professional use only.

Bilberry

Vaccinium myrtillus



During World War II, bilberry jam was reportedly consumed by RAF pilots to improve their night vision. Bilberry has antioxidant properties.

Indications

- ✓ Used in Herbal Medicine to help slow the progression of disorders of the eye, such as diabetic and hypertensive retinopathy, and macular degeneration
- ✓ Helps relieve symptoms related to non-complicated chronic venous insufficiency (CVI), such as sensation of swelling, heaviness and tingling of the legs

Additional Therapies

- Ginkgo Forte
- Vitanox

Bilberry Quality Issues

In 2003 MediHerb received samples of *Vaccinium myrtillus* or bilberry fruit extracts which differed in behaviour to that normally received.

The standard method of determining the anthocyanin content at this time was a spectrophotometric assay. Using this method, anthocyanin levels of two extracts were found to be 25% as claimed by the manufacturers. When high-performance liquid chromatography (HPLC) was used, however, one extract was found to contain 9% anthocyanins probably not derived from *V. myrtillus* but from another species as well as an adulterant chemical. This adulterant was subsequently identified, using HPLC, mass spectroscopy, and nuclear magnetic resonance, as amaranth (3-hydroxy-4-[$(4$ -sulfo-1-naphthalenyl)azo]-2,7-naphthalenedisulfonic acid trisodium salts) a synthetic dark red dye. It was evident that when deliberate adulteration occurs in an extract, a spectrophotometric assay is inadequate to accurately determine the levels of compounds such as anthocyanins. This has led to a change in the standard method of analysis for bilberry extracts to a more sophisticated method of analysis, (HPLC with photodiode array detection) to counter this form of adulteration. The results of this discovery by the MediHerb team were published (*Journal of Agricultural Chemistry and Food Science* 2006; 54: 7378-7382) and led to regulators around the world to review accepted test methods for Bilberry. The British Pharmacopoeia also changed the method of analysis for Bilberry as a result of this discovery.

Dosage and Administration

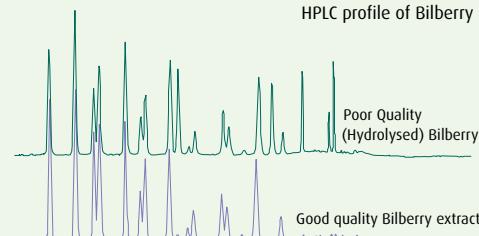
Adults: 1 tablet 3-4 times daily or as directed by your health care practitioner.

Each tablet contains:

<i>Vaccinium myrtillus</i> (Bilberry) fruit 100:1 extract	60 mg
Dried herb equivalent of Bilberry fruit	6 g
Contains anthocyanosides 36%	

Contraindications and Cautions: Consult a health care practitioner if symptoms worsen.

HPLC Profile of Bilberry



Please consult the product packaging label for the most accurate product information. Not for public distribution. For professional use only.

Boswellia Complex

Boswellia serrata



Boswellia Complex contains Boswellia, Celery Seed, Ginger and Turmeric.

These herbs provide many phytochemicals including triterpene acids (especially the boswellic acids), several essential oils (one of which contains terpenes and phthalides), coumarins, flavonoids, pungent principles (including gingerols) and yellow pigments referred to as diarylheptanoids (including curcumin). This tablet contains two herbs with standardised levels of key phytochemicals to ensure optimal strength and quality. The Boswellia component is standardised to contain 180 mg of boswellic acids per tablet, and the Turmeric component contains 70.4 mg of curcuminoids per tablet.

Indications

- ✓ Provides temporary relief of the pain and inflammation of arthritis, osteoarthritis and rheumatism

Additional Therapies

- Vitanox tablets
- Rehmanna Complex tablets
- Licorice High Grade 1:1 liquid extract

Dosage and Administration

Adults: 1 tablet 2 to 4 times daily or as directed by your health care practitioner.

Each tablet contains:

<i>Zingiber officinale</i> (Ginger) rhizome 1:2 extract	600 mL
Dried herb equivalent of Ginger rhizome	300 mg
<i>Boswellia serrata</i> (Boswellia) gum oleoresin 7:1 extract	277 mg
Dried herb equivalent of Boswellia gum oleoresin	1.9 g
Contains boswellic acids 180 mg	
<i>Curcuma longa</i> (Turmeric) rhizome 25:1 extract	80 mg
Dried herb equivalent of Turmeric rhizome	2 g
Contains curcuminoids 70.4 mg	
<i>Apium graveolens</i> (Celery) seed 1:2 extract	2 mL
Dried herb equivalent of Celery Seed	1 g

Contraindications and Cautions: Consult a health care practitioner prior to use if you have a history of gallstones, biliary tract obstructions and/or stomach ulcers or excess stomach acid or if you have diabetes or are taking anti-diabetic medication, antacids, or phenprocoumon. Consult a health care practitioner prior to taking this product if you are taking blood-thinning drugs such as warfarin or aspirin or if you have increased risk of hemorrhage. Do not use if you are pregnant or breastfeeding. Discontinue use 7 days prior to general anesthesia. Consult a health care practitioner if symptoms persist or worsen.

Please consult the product packaging label for the most accurate product information. Not for public distribution. For professional use only.

Broncafect

Asclepias tuberosa



Broncafect is a unique combination of Echinacea, Licorice, Pleurisy Root, Ginger and White Horehound which work together to support the body's natural ability to fight off infections, especially of the upper respiratory tract and in the case of common colds. The pungent, warming nature of Ginger is also an anti-tussive to help relieve coughs, providing comfort during cold weather and seasonal changes.

Indications

- ✓ Traditionally used in Herbal Medicine as an expectorant to help relieve chest complaints, such as catarrhs, coughs and bronchitis.
- ✓ Helps to relieve the symptoms and shorten the duration of upper respiratory tract infections.

Additional Therapies

- Andrographis Complex tablets
- Echinacea Premium tablets

Dosage and Administration

Adults: Take 2 tablets 2-4 times daily, at the first sign of infection. Consult a health care practitioner for use beyond 4-6 weeks.

Each tablet contains:

<i>Asclepias tuberosa</i> (Pleurisy Root) root 1:2 extract	0.75 mL
Dried herb equivalent of Pleurisy root	375 mg
<i>Echinacea purpurea</i> (Echinacea) root 1:2 extract	0.75 mL
Dried herb equivalent of Echinacea root	375 mg
<i>Glycyrrhiza glabra</i> (Licorice) root 7:1 extract	107 mg
Dried herb equivalent of Licorice root	750 mg
Contains Glycyrrhizin 10.7 mg	
<i>Marrubium vulgare</i> (White Horehound) herb 1:2 extract	0.36 mL
Dried herb equivalent of White Horehound herb	180 mg
<i>Zingiber officinale</i> (Ginger) rhizome 30:1 extract	6 mg
Dried herb equivalent of Ginger rhizome	180 mg
Contains Ginger essential oil 1%	

Contraindications and Cautions: Do not use if you are pregnant or breastfeeding, or if you have hypokalemia, high blood pressure, a kidney or cardiovascular disorder or if you are taking thiazide diuretics, cardiac glycosides, corticosteroids, stimulant laxatives or other medications which may aggravate electrolyte imbalance. If symptoms persist or worsen, consult a health care practitioner. If you have diabetes, a liver disorder, a progressive systemic disease such as tuberculosis, collagenosis, multiple sclerosis, AIDS, or HIV infection, or an auto-immune disorder, or if you are taking immune-suppressants, consult a health care practitioner prior to use. Rare cases of severe allergic reactions have been known to occur; use caution if you are allergic to plants of the Daisy family. May cause diarrhea, vomiting and dizziness, in which case discontinue use.

Please consult the product packaging label for the most accurate product information. Not for public distribution. For professional use only.

Chaste Tree

Vitex agnus-castus



Chaste Tree contains flavonoids (especially methoxylated flavones), iridoid glycosides (such as aucubin), diterpenes, sesquiterpenes, essential oils and other compounds.

Indications

- ✓ Used in Herbal Medicine to help relieve premenstrual symptoms and symptoms associated with menopause

Additional Therapies

- LivCo tablets
- Wild Yam Complex tablets
- Livton Complex tablets
- Tribulus Forte tablets

Dosage and Administration

Adults and children over 12 years: 1 to 4 tablets daily or as directed by your health care practitioner. Use for a minimum of 3 months to see beneficial effects.

Each tablet contains:

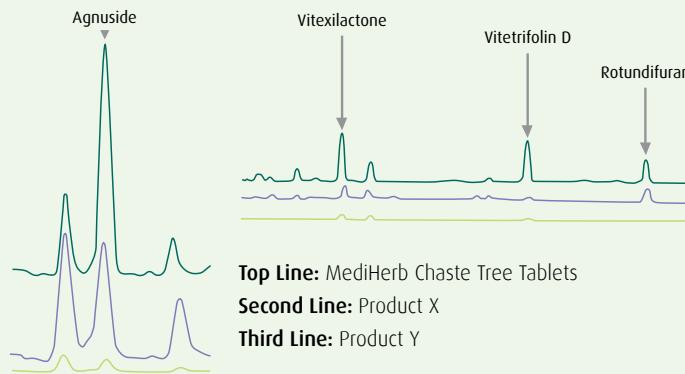
<i>Vitex agnus-castus</i> (Chaste Tree) fruit 1:2 extract	1 mL
Dried herb equivalent of Chaste Tree fruit	500 mg

Contraindications and Cautions: Consult a health care practitioner if symptoms persist or worsen. Consult a health care practitioner prior to use if you are taking hormone-containing medications such as progesterone preparations, oral contraceptives or hormone replacement therapy.

Chaste Tree Quality Issues

Chaste Tree (*Vitex agnus-castus*) contains three important classes of phytochemicals: iridoid glycosides (such as agnuside and aucubin), flavonoids (such as casticin) and diterpenoids (such as vitexilactone, rotundifuran and vitetriterfolin D).

It is believed that the diterpenoids are the more important of these constituents and therefore MediHerb has developed analytical methods for the determination of these constituents and manufactures extracts containing high levels of these diterpenoids, but not at the expense of other vital components.



Please consult the product packaging label for the most accurate product information. Not for public distribution. For professional use only.

Chaste Tree 1:2

Vitex agnus-castus



Indications

- ✓ Used in Herbal Medicine to help relieve premenstrual symptoms (PMS)

Additional Therapies

- Echinacea Premium tablets or Echinacea Premium 1:2 liquid extract
- Golden Seal tablets
- Rehmannia Complex tablets

Dosage and Administration

Adults: 1-4 mL daily. Use for a minimum of 3 months to see beneficial effects.

Each tablet contains:

<i>Vitex agnus-castus</i> (Chaste Tree) fruit 1:2 liquid extract	1 mL
Dried herb equivalent of Chaste Tree fruit	500 mg

Contraindications and Cautions: Use only as directed by a health care practitioner. Consult a health care practitioner prior to use if you are taking hormone-containing medications such as progesterone preparations, oral contraceptives or hormonal replacement therapy. Consult a health care practitioner if pain or symptoms persist. Chaste Tree may interact antagonistically with dopamine receptor antagonists. Chaste Tree is best not taken in conjunction with progesterone drugs, contraceptive pill or hormone replacement therapy (HRT). Chaste Tree may aggravate pure spasmodic dysmenorrhoea not associated with premenstrual syndrome (PMS). Use cautiously in pregnancy and only in the early stages for treatment of insufficient corpus luteal function. Discontinue use 7 days prior to general anaesthesia.

See the Chaste Tree information on page 31 for Chaste Tree Quality Issues



Please consult the product packaging label for the most accurate product information.
Not for public distribution. For professional use only.

DiGest Forte

Gentiana lutea



DiGest Forte contains Gentian, Feverfew, Ginger, Wormwood and Tangerine in order to provide a broader range of bitter principles to interact with more bitter receptors.

Indications

- ✓ Traditionally used in Herbal Medicine as a digestive tonic and bitter to aid digestion

Additional Therapies

- Astragalus Complex tablets
- Gymnema tablets
- Livton Complex tablets
- Silymarin tablets
- Withania Complex tablets

Dosage and Administration

Adults: 1 tablet once daily or as directed by your health care practitioner. Take 15 minutes before meals. Consult your health care practitioner for use beyond 4 months.

Each tablet contains:

<i>Artemisia absinthium</i> (Wormwood) herb 1:5 extract	0.5 mL
Dried herb equivalent of Wormwood root	100 mg
<i>Gentiana lutea</i> (Gentian) root 1:2 extract	0.4 mL
Dried herb equivalent of Gentian root	200 mg
<i>Tanacetum parthenium</i> (Feverfew) leaf 1:5 extract	1 mL
Dried herb equivalent of Feverfew leaf	200 mg
<i>Zingiber officinale</i> (Ginger) rhizome 1:2 extract	0.5 mL
Dried herb equivalent of Ginger rhizome	250 mg
<i>Citrus reticulata</i> (Tangerine) fruit peel 5:1 extract	100 mg
Dried herb equivalent of Tangerine fruit peel	500 mg

Contraindications and Cautions: Do not use if you are allergic to plants of the Asteraceae/Compositae/Daisy family or if you are pregnant, or if you have acute stomach irritation, inflammation, and stomach or duodenal ulcers, or if you have obstruction of the bile duct, cholangitis or liver disease. Consult a health care practitioner if symptoms persist or worsen and prior to use if you are breastfeeding or if you are taking blood thinners, or if you have gallstones or other biliary disorders. Exercise caution if operating heavy machinery, driving a motor vehicle or involved in activities requiring mental alertness. Hypersensitivity, such as an allergy, has been known to occur; in which case, discontinue use. Some people may experience headaches, sore mouth, mouth ulcers and/or gastrointestinal discomfort.

Please consult the product packaging label for the most accurate product information. Not for public distribution. For professional use only.

Echinacea Premium

Echinacea angustifolia



Echinacea Premium combines the roots of *Echinacea angustifolia* and *Echinacea purpurea* to enlist properties unique to each. The blending of these two plant species ensures that the specific caffeic acid derivatives (cichoric acid, echinacoside, cynarin) and the lipophilic components (especially alkylamides) are present in appropriate quantities. This product contains 4 mg of alkylamides per tablet to ensure optimal strength and quality.

Indications

- ✓ Used in Herbal Medicine to help fight off infections
- ✓ Helps relieve the symptoms and shorten the duration of upper respiratory tract infections
- ✓ Supportive therapy in the treatment of upper respiratory tract infections (e.g. common colds)

Additional Therapies

- Andrographis Complex tablets
- Rehmannia Complex tablets
- Astragalus Complex tablets

Dosage and Administration

Adults and adolescents >15 years: 2 tablets once daily at first sign of infection or as directed by your health care practitioner. Consult your health care practitioner for use beyond 8 weeks.

Each tablet contains:

<i>Echinacea purpurea</i> (Echinacea) root 1:2 extract	1.35 mL
Dried herb equivalent of Echinacea root	675 mg
Contains alkylamides 1.74 mg	
<i>Echinacea angustifolia</i> (Echinacea) root 1:2 extract	1.2 mL
Dried herb equivalent of Echinacea root	600 mg
Contains alkylamides 2.26 mg	

Contraindications and Cautions: Do not use if you are pregnant. Consult a health care practitioner if symptoms persist or worsen or prior to use if you are taking immunosuppressants, if you have an autoimmune disorder, or a progressive systemic disease such as tuberculosis, leucosis, collagenosis, multiple sclerosis, AIDS and/or HIV infection. Rare cases of severe allergic reactions have been known to occur; use with caution if you are allergic to plants of the Daisy family.

Please consult the product packaging label for the most accurate product information. Not for public distribution. For professional use only.

Echinacea Premium 1:2

Echinacea angustifolia



Indications

- ✓ Used to fight off colds and infections, especially of the upper respiratory tract

Dosage and Administration

Adults: 3 to 4 mL daily with water at first sign of infection or as directed by your health care practitioner. For use beyond 8 weeks, consult a health care practitioner.

Each tablet contains:

<i>Echinacea purpurea</i> (Echinacea) root 1:2 extract	0.6 mL
Dried herb equivalent of Echinacea root	300 mg
<i>Echinacea angustifolia</i> (Echinacea) root 1:2 extract	0.4 mL
Dried herb equivalent of Echinacea root	200 mg
(Combined total alkylamides 1.5 mg – 3 mg)	

Contraindications and Cautions: Echinacea is contraindicated in persons taking immunosuppressant medication (eg transplant patients). Short term therapy only is suggested in this instance. Consult a health care practitioner prior to use if you have an autoimmune disorder or progressive systemic disease such as tuberculosis, leukosis, collagenosis, multiple sclerosis, AIDS and/or HIV infection. Discontinue 7 days prior to general anesthesia.

See the Echinacea Premium information on page 36 for Echinacea Quality Issues



Echinacea Premium®

Leading Echinacea liquid, used by practitioners worldwide

Please consult the product packaging label for the most accurate product information. Not for public distribution. For professional use only.

MediHerb has developed specialised knowledge in the manufacture and testing of Echinacea products over the past 20 years. This includes a PhD study, extensive analytical method development, development of harvesting, drying and storage protocols to maximise retention of actives and a successful clinical trial.

MediHerb Echinacea products are market leaders based on the most up-to-date science and the best of traditional wisdom.

In November 2014, independent testing of nine Australian Echinacea liquids and 4 tablet products showed that MediHerb Echinacea Premium tablets and liquid extracts are higher in alkylamides (both 2-ene and 2,4-diene alkylamides), which are clinically relevant

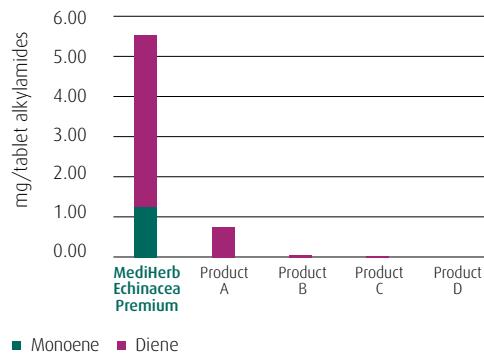
active constituents. The testing was conducted by an independent analytical laboratory holding a licence issued by the Therapeutic Goods Administration.

2-ene alkylamides are only found in *Echinacea angustifolia* and are an important measure of quality. MediHerb's research has found that 2-ene alkylamides improve the bioavailability of 2,4-diene alkylamides in *Echinacea purpurea*. This means that the alkylamides in MediHerb's unique blend, Echinacea Premium, are available to the body, resulting in a better effect on the immune system.

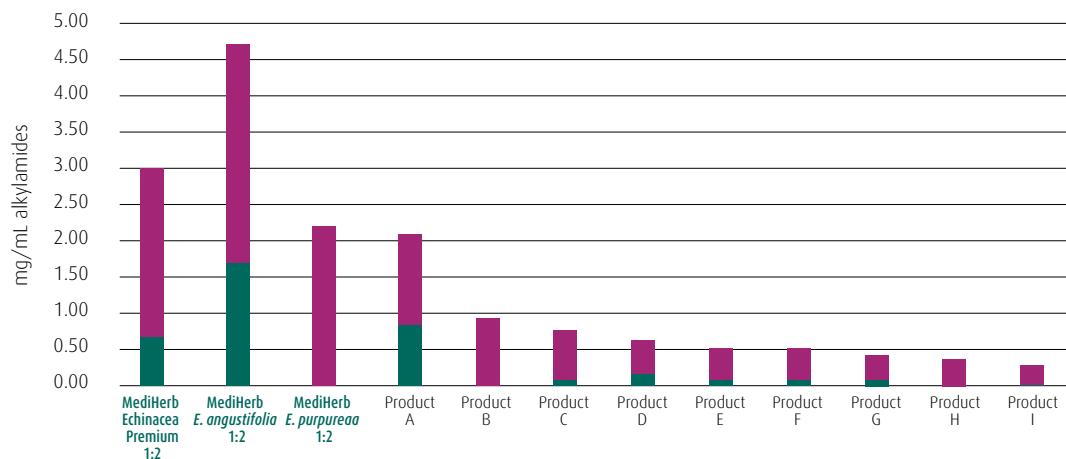
MediHerb's Echinacea Premium formula is patented in Australia, New Zealand, USA and the UK to protect this important finding.

Echinacea Tablet Product Comparison

Product	Monoene	Diene	Total Alkylamides	Tablets required to meet 1 Echinacea Premium
MediHerb Echinacea Premium	1.22	4.40	5.62 (Label Claim 4.6mg)	1
Product A	0.00	0.69	0.69	8
Product B	0.00	0.02	0.02	314
Product C	0.00	0.01	0.01	668
Product D	0.00	0.00	0.00	n/a



Echinacea Liquid Product Comparison



Alkylamides

- Monoene = protects against degradation
- Diene = immune active

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The Science of Echinacea – MediHerb's Research

Kerry Bone has always believed that a key aspect of modern phytotherapy is a respect for traditionally-generated knowledge. *E. angustifolia* root however is very expensive and was cost prohibitive for many of his patients. To overcome this, Kerry developed **Echinacea Premium**, a particular blend of *E. angustifolia* and *E. purpurea* roots. In 2003 MediHerb began an extensive research project which was designed to identify the bioavailable components of Echinacea Premium and how they exert an effect on the immune system.

What is Active Must First Be Absorbed

Which of the key phytochemicals in Echinacea Premium are absorbed and therefore bioavailable? From MediHerb's *in vitro* and pharmacokinetic research we know:

- **ONLY alkylamides** could be **detected in the blood** after taking Echinacea Premium. No caffeic acid conjugates, degradation products of these or the alkylamides were found¹
- The alkylamides mainly in *E. purpurea* were found to be rapidly degraded by human liver microsomes
- In contrast the alkylamides mainly in *E. angustifolia* were much more slowly degraded
- Interestingly, the alkylamides from *E. angustifolia* actually **slowed down the rate of degradation** of the alkylamides from *E. purpurea*
- The presence of only relatively small proportions of the *E. angustifolia* alkylamides will result in a product with **enhanced bioavailability** due to their protective effect

A New Understanding of Echinacea

The research on Echinacea Premium by the MediHerb scientists has made a substantial contribution to a new understanding of lipophilic extracts of Echinacea. It can be concluded from this research that:

- Alkylamides must be used as the markers of **quality and activity**
- The **root of Echinacea** is the preferred plant part, since it is highest in alkylamides
- The **preferred species** of Echinacea are *E. angustifolia* and *E. purpurea* since they contain high levels of alkylamides (compared to *E. pallida*)
- Echinacea must be extracted using an **alcohol percentage sufficiently high** to efficiently extract the alkylamides

For more information on the Echinacea Research Project see page 8

- This is a strong justification for the combination of *E. angustifolia* root with *E. purpurea* root, as in the Echinacea Premium. A **patent has been applied for to protect this very important finding**²
- The total amount of alkylamides absorbed into the bloodstream was **essentially the same** for both Echinacea Premium tablets and Echinacea Premium 1:2 liquid³

Once Absorbed is it Active?

The key findings of recent studies on Echinacea and alkylamide's effects on the immune system are that:

- Echinacea does not activate the immune response in the absence of any immunological challenge (*in vitro* research)⁴
- The Echinacea alkylamides tended to **modulate the immune response** of macrophages and T cells *in vitro*, toning the response down in the face of a strong stimulus^{4,5}
- These results, combined with the fact that alkylamides are the only phytochemicals which are bioavailable from traditional lipophilic extracts of Echinacea root (such as ethanolic liquid extracts)¹, suggests that the alkylamides are **largely responsible** for the systemic immune effects of Echinacea lipophilic extracts
- This immune modulating activity may (at least in part) due to the **interaction of alkylamides with cannabinoid receptors, specifically CB2** (*in vitro* research)⁶⁻⁸
- Echinacea Premium alters the expression of **heat shock protein 70** (hsp70) in leucocytes and increased white cell count in healthy volunteers.⁸ *E. purpurea* root boosted the number and function of **natural killer (NK) cells** (a class of white blood cell) in mice¹⁰

- The synergistic blend of *E. angustifolia* and *E. purpurea* alkylamides in Echinacea Premium **potentiate each other** for greater therapeutic potential
- One potential way in which the bioavailable **alkylamides modulate** the immune response is by interacting with CB2 receptors
- Echinacea root (rich in alkylamides) also **boosts the white cell count**
- The traditional way Echinacea was used has been validated by scientific research at the cutting edge of modern immunology



REFERENCES ¹ Matthias A et al. Life Sciences 2005; 77: 2018-2029 ² Matthias A et al. Chemico-Biological Interactions 2005, 155: 62-70 ³ Matthias A et al. Phytomedicine 2007; 14(9): 587-590 ⁴ Stevenson LM et al. Molecules 2005; 10: 1279-1285 ⁵ Matthias A et al. Fitoterapia 2008; 79(1): 53-58 ⁶ Gertsch J, Schoop R, Kuenzle U et al. Alkylamides from Echinacea purpurea potently modulate TNF-alpha gene expression: Possible role of cannabinoid receptor CB2, NF-κB, P38, MAPK and JNK pathways. International Congress on Natural Products Research, Phoenix, Arizona USA, July 31-August 4, 2004, Lecture O: 9 ⁷ Woelkart K, Xu W, Makriyannis A et al. The endocannabinoid system as a target for alkylamides from Echinacea roots. International Congress on Natural Products Research, Phoenix, Arizona USA, July 31-August 4, 2004, Poster P:342 ⁸ Matthias A, Lehmann RP, Bone KM. Echinacea in Health - Risks and Benefits. In: Watson, R, Preedy V (eds). Botanical Medicine in Clinical Practice. CABI, Wallingford, UK, 2008, pp 683-689. ⁹ Agnew LL et al. Journal of Clinical Pharmacy and Therapeutics 2005; 30: 363-369 ¹⁰ Miller SC. eCAM 2005; 2(3): 309-314

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Paeonia lactiflora



Indications

- ✓ Schisandra and Shatavari are used in Herbal Medicine as an adaptogen to help increase energy and resistance to stress (e.g. in case of mental and physical fatigue related to stress)

Additional Therapies

- Tribulus Forte tablets
- Chaste Tree tablets
- AdrenoCo tablets
- St John's Wort tablets
- Nevaton Forte tablets

Dosage and Administration

Adults: 1 tablet 3 times a day. For prolonged use, consult your health care practitioner.

Each tablet contains:

<i>Schisandra chinensis</i> (Schisandra) fruit 6:1 extract	166.7 mg
Dried herb equivalent of Schisandra fruit	1 g
<i>Paeonia lactiflora</i> (Chinese Peony) root 4:1 extract	187.5 mg
Dried herb equivalent of Chinese Peony root	750 mg
<i>Asparagus racemosus</i> (Shatavari) root 6:1 extract	100 mg
Dried herb equivalent of Shatavari root	600 mg

Contraindications and Cautions: Consult a health care practitioner prior to use if you are taking prescription medications or if you have serious or major conditions, any type of acute infection, deficiency or excess. Discontinue use and consult a health care practitioner if symptoms persist or worsen or if new symptoms develop. Do not use if you are pregnant or breastfeeding.

See the LivCo information on page 47 for Schisandra Quality Issues



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Garlic



Garlic contains sulfur compounds (particularly alliin) and other compounds.

Indications

- ✓ Used in Herbal Medicine to help reduce hyperlipidemia in adults

Additional Therapies

- Slippery Elm 400mg capsules
- Echinacea Premium tablets or Echinacea Premium 1:2 liquid extract
- Andrographis Complex tablets

Garlic Quality Issues

Alliin (an odourless amino acid) is naturally found in garlic cloves but is rapidly converted to allicin (a strong smelling volatile sulfide) when exposed to the enzyme alliinase in the presence of water or when the garlic clove is crushed – as shown below by the absence of the alliin peak in the HPLC trace on the right hand side.

Alliin is rather unstable and is the precursor to a range of sulfur containing compounds including, diallylsulfides, ajoenes and vinylidithiins. It is important that quality products take this enzymatic process into account since the strongest published evidence to date is for garlic preparations standardised this way. Therefore alliin must be present together with the correct amount of alliinase in the tablet to allow full conversion to allicin. Furthermore, because stomach acid can degrade the activity of alliinase, quality products should be enterically coated to protect the enzyme. That is why all MediHerb Garlic tablets are enterically coated and tested not only for the level of alliin but for its conversion into allicin, “its allicin releasing ability”.

Dosage and Administration

Adults and adolescents (14 years old and over): 1 to 2 tablets daily or as directed by your health care practitioner.

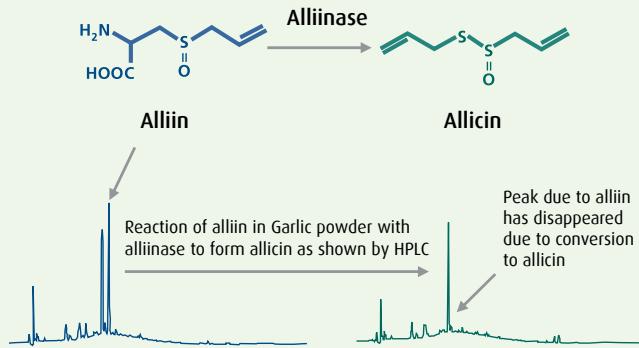
Adolescents (10-13 years old): 1 tablet daily or as directed by your health care practitioner. Enteric coated tablets. Do not crush.

Each tablet contains:

<i>Allium sativum</i> (Garlic) root 12:1 extract	300 mg
Fresh herb equivalent of Garlic bulb	3.6 g
<i>Allium sativum</i> (Garlic) bulb powder	45 mg

Contraindications and Cautions: Consult a health care practitioner if symptoms persist or worsen and prior to use if you are pregnant, have diabetes, or if you are taking blood thinners or protease inhibitors. Hypersensitivity (e.g. allergy) has been known to occur; in which case discontinue use.

Formation of Allicin from Alliin



Ginkgo Forte

Ginkgo biloba



Ginkgo contains flavonoids, terpene lactones and other phytochemicals. This product is standardised to contain 24% flavonoid glycosides and 6% terpene lactones per tablet to ensure optimal strength and quality.

Indications

- ✓ Helps to enhance cognitive function and memory in adults
- ✓ Helps to support peripheral circulation

Additional Therapies

- Bacopa Complex tablets
- Vitanox tablets

Dosage and Administration

Adults: 1 tablet 3 times daily or as directed by your health care practitioner. Consult a health care practitioner for use beyond 6 weeks.

Each tablet contains:

<i>Ginkgo biloba</i> (Ginkgo) leaf 50:1 extract	0.06 g
Dried herb equivalent of Ginkgo leaf	3 g
(24% flavonoid glycosides, 6% terpene lactones)	

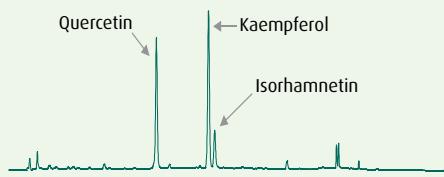
Contraindications and Cautions: Consult a health care practitioner prior to use if you are pregnant or breastfeeding or taking medications for diabetes, high blood pressure, or seizures. Do not use if you are taking health products that affect blood coagulation (e.g. blood thinners, clotting factor replacements, acetylsalicylic acid, ibuprofen, fish oils, vitamin E) as this may increase the risk of spontaneous bleeding.

Ginkgo Quality Issues

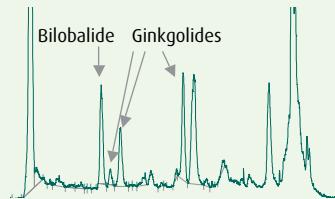
The ginkgo flavonglycosides (*ginkgo flavone glycosides*) of *Ginkgo biloba*, comprising quercetin, kaempferol and isorhamnetin are the phytochemicals most often referred to as indicators of quality and efficacy.

However, these compounds are mainly marker compounds which are used to identify the extract. The therapeutically active ingredients are believed to include the ginkgolides and bilobalide, which cannot be tested by normal HPLC methods. They require more sophisticated methods of detection such as Refractive Index (RI), Evaporative Light Scattering Detectors (ELSDs) or Mass Spectrometry (MS). MediHerb uses ELSD detection to accurately quantify the levels of these therapeutically important phytochemicals. The other important group of phytochemicals from Ginkgo are the ginkgolic acids (C13:0, C15:1 and C17:1 on the third figure). These compounds have been identified as contact allergens. The maximum level of ginkgolic acids in *Ginkgo biloba* extracts has been set by the European authorities at 5 ppm. Many poor quality extracts contain levels of ginkgolic acids many orders of magnitude higher than this recommended maximum.

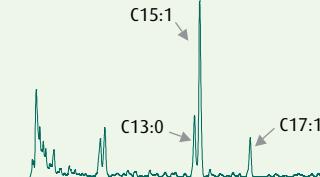
HPLC Detection of Ginkgo Flavonglycosides (Ginkgo Flavone Glycosides)



LC - ELSD Detection of Bilobalide and Ginkgolide



Ginkgolic Acids by HPLC



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Golden Seal

Hydrastis canadensis



Golden Seal contains alkaloids (especially hydrastine and berberine) and other phytochemicals.

MediHerb Golden Seal tablets are made from a cultivated source of Golden Seal.

Indications

- ✓ Traditionally used in Herbal Medicine to help alleviate infectious and inflammatory conditions of the digestive tract such as gastritis

Additional Therapies

- Sinus Forte tablets
- Slippery Elm 400mg capsules

Dosage and Administration

Adults: 1 to 2 tablets 3 times daily or as directed by your health care practitioner. May take up to one week to produce beneficial effects.

Each tablet contains:

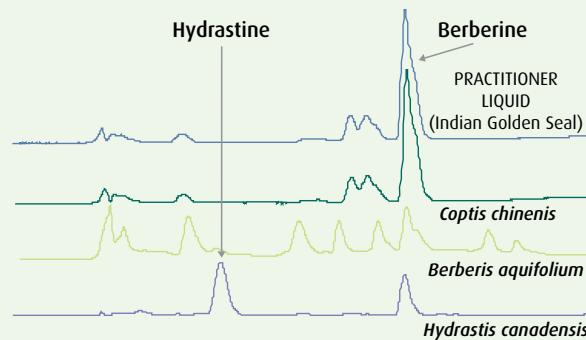
<i>Hydrastis canadensis</i> (Golden Seal) root and rhizome 1:3 extract	1.5 mL
Dried herb equivalent of Golden Seal root and rhizome	500 mg

Contraindications and Cautions: Consult a health care practitioner if symptoms persist or worsen and prior to use if you have blood pressure problems or a kidney disorder. Consumption with alcohol, other medications and/or natural health products with sedative properties is not recommended. Do not use if you are pregnant or breastfeeding.

Golden Seal Quality Issues

Golden Seal (*Hydrastis canadensis*) is an endangered herb and as a result is very expensive and often substituted by other herbs.

The substituted herbs usually contain the substance berberine which provides the yellow colour, but they do not contain hydrastine which is unique to Golden Seal. Only HPLC enables this differentiation to be made. MediHerb only buys cultivated Golden Seal to ensure sustainability of the herb long term. MediHerb tests each batch of Golden Seal raw material and finished product to ensure the claimed levels of hydrastine and berberine are present. Using HPLC, MediHerb is able to clearly differentiate true Golden Seal from other berberine containing herbs. The table demonstrates the difference between the various berberine containing species. The top trace is an example of substitution where a professional product being sold in Australia as Indian Golden Seal matched the trace of *Coptis chinensis*.



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Gymnema

Gymnema sylvestre



Gymnema contains a complex mixture of saponins (gymnemic acids) and other compounds. This product is standardised to contain 100 mg of gymnemic acids per tablet to ensure optimal strength and quality.

Indications

- ✓ Helps to support healthy blood glucose levels

Additional Therapies

- Livton Complex tablets
- Vitanox tablets
- Slippery Elm 400mg capsules

Dosage and Administration

Adults: 1 tablet daily or as directed by your health care practitioner.

Each tablet contains:

<i>Gymnema sylvestre</i> (Gymnema) leaf 16:1 extract	400 mg
Dried herb equivalent of Gymnema leaf	6.4 g
Contains gymnemic acids	100 mg

Contraindications and Cautions: Consult a health care practitioner prior to use if you have diabetes, low blood sugar, or if you are taking insulin or oral hypoglycemic medication, if you have intestinal disorders, or symptoms such as abdominal pain, nausea, vomiting or fever. Discontinue use and consult a health care practitioner if you experience symptoms of hypoglycemia including feelings of anxiety, dizziness, tremor, sweating, nausea or headache. Do not use if you are pregnant or breastfeeding.



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Hawthorn Berries 1:2

Crataegus monogyna



Hawthorn Berries 1:2 has cardiotonic and cardioprotective properties.

Indication

- ✓ Used in Herbal Medicine to help maintain and/or support cardiovascular health in adults

Additional Therapies

- Boswellia Complex tablets
- DiGest Forte tablets
- Horsechestnut Complex tablets
- LivCo tablets
- Vitanox tablets

Dosage and Administration

Adults: 2 to 4 mL daily or as directed by your health care practitioner. Use for a minimum of 2 months to see beneficial effects.

Each tablet contains:

<i>Crataegus monogyna</i> (Hawthorn) berries 1:2 extract	1 mL
Dried herb equivalent of Hawthorn berries	500 mg

Contraindications and Cautions: Consult a health care practitioner prior to use if you are taking cardiac glycosides such as digitalis/digoxin, or blood pressure medication. Consult a health care practitioner if symptoms persist or worsen. Discontinue 7 days prior to general anesthesia.

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Horsechestnut Complex

Aesculus hippocastanum



Horsechestnut Complex is a combination of Horsechestnut, Butcher's Broom and Ginkgo. These herbs contain steroidal saponins, other saponins (a complex mixture known as aescin), flavonoids, lipids, sterols, terpene lactones and other phytochemicals. The Horsechestnut component is standardised to contain 40 mg of aescin per tablet, and the Ginkgo component contains 7.3 mg of flavonoid glycosides per tablet.

Indications

- ✓ Used in Herbal Medicine to help treat chronic venous insufficiency and associated symptoms
- ✓ Used in Herbal Medicine to help treat varicose veins

Additional Therapies

- Garlic tablets
- Vitanox tablets
- Ginkgo Forte tablets

Dosage and Administration

Adults: 1 tablet 2 times daily with food or as directed by your health care practitioner. Enteric coated tablets. Do not break or crush.

Each tablet contains:

<i>Ruscus aculeatus</i> (Butcher's Broom) root and rhizome 4:1 extract	200 mg
Dried herb equivalent of Butcher's Broom root and rhizome	800 mg
<i>Aesculus hippocastanum</i> (Horsechestnut) seed 6:1 extract	200 mg
Dried herb equivalent of Horsechestnut seed	1.2 g
Contains aescin 40 mg	
<i>Ginkgo biloba</i> (Ginkgo) leaf 50:1 extract	30 mg
Dried herb equivalent of Ginkgo leaf	1.5 g
Contains flavonoid glycosides 7.3 mg	

Contraindications and Cautions: Consult a health care practitioner prior to use if you are taking medications for diabetes, high blood pressure, or seizures or if you are pregnant or breastfeeding or if you suffer from gastrointestinal disorders such as irritation, ulcers, gastric reflex, celiac disease, etc. Consult a health care practitioner if symptoms persist or worsen. Some people may experience headaches, dizziness, gastric irritation, or itchiness. If inflammation of the skin or subcutaneous induration, ulcers, sudden swelling of leg(s), cardiac or renal insufficiency occurs, discontinue use and consult a health care practitioner. Do not use if you are taking health products that affect blood coagulation as this may increase the risk of spontaneous bleeding.

See the Ginkgo biloba information on page 40 for Ginkgo Quality Issues

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Kava Forte

Piper methysticum



This tablet contains Kava root extracted with 100% water, which provides an extract with a full spectrum of compounds including the kavalactones. This product is standardised to contain 50 mg of kavalactones per tablet to ensure optimal strength and quality.

Indications

- ✓ Used in Herbal Medicine as a calmative to help relieve restlessness and/or to aid sleep

Additional Therapies

- Valerian Complex tablets
- Nevaton Forte tablets or St John's Wort tablets
- AdrenoCo tablets

Kava Quality Issues

Kava is derived from the rootstock of the sterile cultivated species of *Piper methysticum*.

The psychosedative property of Kava has been attributed to the kavalactones, a group of structurally related lipophilic lactones. These compounds can represent 3 to 20% by weight of the dried rootstock, depending on the age of the plant and the specific cultivar. The majority of the Kava used commercially in the world is in the form of a high ethanol or other organic solvent extract, which extracts little more than the kavalactones and has reported potential hepatotoxicity concerns. The Therapeutic Goods Administration (Australian Regulatory Authority) allows water extracted or plain unextracted root to be sold in Australia. Traditionally Kava beverages are prepared by chewing or pounding the root to produce a cloudy, milky mash, which is then consumed orally. It is known that extraction with different solvents affects the phytochemical profile of the extract.

MediHerb investigated the difference in bioavailability of the water extract of Kava and the 96% ethanol extract using the Caco-2 monolayer model. The kavalactones (as kawain) were found to be potentially bioavailable as they all crossed the membrane quite readily with the exception of one kavalactone (yangonin). The water extract of Kava was only slightly less bioavailable than the ethanol extract. Therefore the clinical effect of the water extract of Kava would be similar to that of an ethanol extract, without the hepatotoxicity concerns.

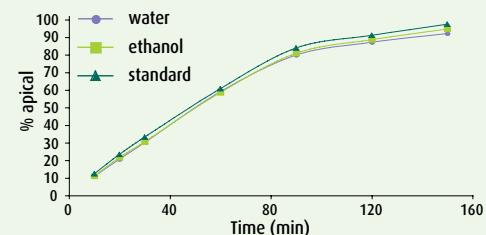
Dosage and Administration

Adults: 1 tablet 3 times daily. For use beyond 6 months, consult your health care practitioner.

Each tablet contains:

<i>Piper methysticum</i> (Kava) root 7:1 extract	455 mg
Dried herb equivalent of Kava root	3.2 g
Contains kavalactones 50 mg	

Contraindications and Cautions: Consult a health care practitioner if symptoms persist or worsen. Consult a health care practitioner prior to use if you have a liver disease, epilepsy or if you are using conventional sedative-hypnotics or natural health products with similar effects, anxiolytics, MAO inhibitors and other psychopharmacologic agents, levodopa or other drugs for Parkinson's disease, or antiplatelet agents. Consumption with alcohol or anti-convulsants is not recommended. Do not use if you are pregnant or breastfeeding. Discontinue use and consult a health care practitioner if you develop signs of liver trouble. Excessive use, or use with products that cause drowsiness, may impair your ability to operate a vehicle or use heavy machinery.



Kawain % apical average data

Time	water	ethanol	standard
10	11	11	12
20	21	22	23
30	30	31	33
60	59	59	61
90	80	81	84
120	87	89	91
150	92	95	97

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Licorice High Grade 1:1



Indications

- ✓ Traditionally used in Herbal Medicine as an expectorant to help relieve chest complaints

Additional Therapies

- Echinacea Premium tablets or Echinacea Premium 1:2 liquid extract
- Golden Seal tablets
- Rehmannia Complex tablets

Dosage and Administration

Adults: 2-4 mL daily. May be used up to 4-6 weeks or as directed by health care practitioner.

Each tablet contains:

Glycyrrhiza glabra (Licorice) root 1:1 extract	1 mL
Dried herb equivalent of Licorice root	1 g
Glycyrrhiza glabra (Licorice) root 7:1 extract	170 mg
Dried herb equivalent of Licorice root	1190 mg
Contains glycyrrhetic acid	30 mg

Contraindications and Cautions: Consult a health care practitioner if symptoms persist or worsen and prior to use if you are pregnant or have a liver disorder. Do not use if you are taking thiazide diuretics, cardiac glycosides, corticosteroids, stimulant laxatives or other medications which may aggravate electrolyte imbalance. Do not use if you have hypokalemia, high blood pressure, or a kidney or cardiovascular disorder.



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Schisandra chinensis

The combination of Schisandra, Rosemary and St Mary's Thistle (Milk Thistle) provides a range of compounds including dibenzocyclooctene lignans, phenolic diterpenes (including carnosol and rosmarinic acid), other terpenes, flavonoids and flavanolignans (collectively known as silybin or silymarin). The St Mary's Thistle component of this tablet is standardised to contain 24 mg of flavanolignans per tablet to ensure optimal strength and quality.

Indications

- ✓ Helps to support liver function
- ✓ Used in Herbal Medicine to help relieve digestive disturbances/dyspepsia
- ✓ Traditionally used in Herbal Medicine as a liver protectant

Additional Therapies

- Vitanox tablets
- Silymarin tablets

Schisandra Quality Issues

Schisandra is a well-known Chinese herb, however it is not well known that two species of Schisandra are used in TCM, the phytochemical profile of each being very different. *Schisandra chinensis* (northern Schisandra) is the preferred species in TCM and by Western health care professionals.

It contains compounds called schisandrin (schisandrin, gomisin A, deoxyschisandrin, gomisin N and wuweizizi C) which are believed responsible for the therapeutic effects. Southern Schisandra, *Schisandra spenanthera*, (see Product X in the trace) is considered inferior due to lower levels of schisandrin, however it is often used interchangeably with *Schisandra chinensis*. Manufacturers therefore need to be very careful to avoid substitution with *Schisandra spenanthera*. The species are readily distinguishable morphologically and by HPLC. MediHerb routinely uses HPLC to ensure the correct identity and guarantee consistent levels of schisandrin.

Dosage and Administration

Adults: 1 tablet 3 to 4 times a day or as directed by a health care practitioner. Use for a minimum of 3 weeks to see beneficial effects in liver function/protection.

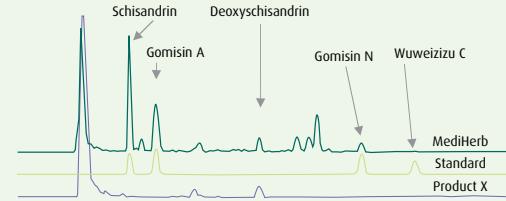
Each tablet contains:

<i>Schisandra chinensis</i> (Schisandra) fruit 6:1 extract	167 mg
Dried herb equivalent of Schisandra fruit	1 g
<i>Rosmarinus officinalis</i> (Rosemary) leaf 5:1 extract	100 mg
Dried herb equivalent of Rosemary leaf	500 mg
<i>Silybum marianum</i> (St Mary's Thistle) seed 70:1 extract	34 mg
Dried herb equivalent of St Mary's Thistle seed	2.38 g

Contraindications and Cautions: your health care practitioner if symptoms persist or worsen. Do not use if you are pregnant or breastfeeding. Hypersensitivity, such as allergy, has been known to occur; in which case, discontinue use.

See the Silymarin information on page 53 for St Mary's Thistle Quality Issues

Schisandra HPLC Comparison of Good Quality Product with Poor Quality Product



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Livton Complex

Taraxacum officinale



Livton Complex contains Globe Artichoke, Bupleurum, Dandelion Root, St Mary's Thistle (Milk Thistle) and Fringe Tree. These herbs contribute key phytochemicals to the blend such as sesquiterpene lactones, caffeic acid derivatives, flavonoids, phenolic acids, triterpenes, sterols, flavanolignans (collectively known as silybin or silymarin) and triterpenoid saponins (called saikosaponins). The St Mary's Thistle component of this tablet is standardised to contain 80 mg of flavanolignans per tablet to ensure optimal strength and quality.

Indications

- ✓ Used in Herbal Medicine to help relieve digestive disturbances (such as dyspepsia) and increase bile flow

Additional Therapies

- Silymarin tablets

Dosage and Administration

Adults: 1 tablet 3-4 times daily or as directed by your health care practitioner

Each tablet contains:

<i>Taraxacum officinale</i> (Dandelion) root 1:2 extract	800 mCL
Dried herb equivalent of Dandelion root	400 mg
<i>Bupleurum falcatum</i> (False Bupleurum) root 1:2 extract	600 mCL
Dried herb equivalent of False Bupleurum root	300 mg
<i>Chionanthus virginica</i> (Fringe Tree) stem bark 1:2 extract	320 mCL
Dried herb equivalent of Fringe Tree stem bark	160 mg
<i>Cynara scolymus</i> (Globe Artichoke) leaf 4:1 extract	200 mg
Dried herb equivalent of Globe Artichoke leaf	800 mg
<i>Silybum marianum</i> (St Mary's Thistle) seed 70:1 extract	114.29 mg
Dried herb equivalent of St Mary's Thistle seed	8.0 g
Contains silymarin 80 mg	

Contraindications and Cautions: Consult a health care practitioner if symptoms persist or worsen and prior to use if you are pregnant, or if you are taking metronidazole. In anemia and cases where iron supplementation is required, do not take simultaneously with meals or iron supplements. Do not use if you have a bile duct obstruction, liver or gall bladder disorders and/or bowel obstruction or if you are allergic to plants of Asteraceae/Compositae/ Daisy family. Hypersensitivity (e.g. allergy) has been known to occur, in which case, discontinue use. Discontinue use if you develop symptoms of liver trouble. Discontinue 7 days prior to general anesthesia.

See Silymarin information on page 53 for St Mary's Thistle Quality Issues



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Nevaton Forte

Crocus sativus



Nevaton Forte contains St John's Wort, Schisandra, Skullcap and Saffron. These herbs provide a wide range of phytochemicals including the naphthodianthrones hypericin and pseudohypericin (hypericin), flavonoids, phenolics, dibenzocyclooctene lignans, sesquiterpenes, monoterpenes and other compounds. The St John's Wort component of this tablet is standardised to contain 375 mcg of hypericin tablet to ensure optimal strength and quality.

Indications

- ✓ Used in Herbal Medicine as an adaptogen to help increase resistance to stress

Additional Therapies

- Valerian Complex tablets
- Withania Complex tablets

Dosage and Administration

Adults: 1 tablet 3-4 times daily or as directed by your health care practitioner. Use for a minimum of 1 week to see beneficial effects. Consult a health care practitioner for use beyond 18 weeks.

Each tablet contains:

<i>Hypericum perforatum</i> (St John's Wort) herb top 6:1 extract	125 mg
Dried herb equivalent of St John's Wort herb top	750 mg
<i>Schisandra chinensis</i> (Schisandra) fruit 6:1 extract	112.5 mg
Dried herb equivalent of Schisandra fruit	675 mg
<i>Scutellaria lateriflora</i> (Skullcap) herb top 1:2 extract	1 mL
Dried herb equivalent of Skullcap herb top	500 mg
<i>Crocus sativus</i> (Saffron) stigma 3:1 extract	7.5 mg
Dried herb equivalent of Saffron stigma	22.5 mg

Contraindications and Cautions: Do not use if you are pregnant or breastfeeding, taking anti-cancer medications, blood thinners, antidepressant medications, anti-HIV agents, cardiovascular medications, immunosuppressants, and/or contraceptive medications. Consult a health care practitioner prior to use if you are taking prescription medications, anti-anxiety medications, seizure medications, antihistamines, bronchodilators, muscle relaxants and/or opiates. Consult a health care practitioner if symptoms persist or worsen or if new symptoms develop or if sleeplessness persists continuously for more than 3 weeks. Avoid prolonged exposure to sunlight, ultraviolet light (UV) or UV therapy. Consumption with alcohol, drugs and/or other natural health products with sedative properties is not recommended. Hypersensitivity, such as an allergy, has been known to occur; in which case, discontinue use. Some people may experience mild gastrointestinal disturbances, nausea, restlessness, drowsiness and/or headaches. Exercise caution if operating heavy machinery, driving a motor vehicle or involved in activities requiring mental alertness.

See St John's Wort information on page 56 for St John's Wort Quality Issues

See LivCo information on page 47 for Schisandra Quality Issues

Please consult the product packaging label for the most accurate product information.

Not for public distribution. For professional use only.

Rehmannia Complex



The combination of herbs in Rehmannia Complex contain many compounds including iridoid glycosides, triterpenoid saponins (called saikosaponins), other saponins, sterols, sesquiterpene lactones of the germacranolide type, particularly parthenolide and other terpenes.

Indications

- ✓ Traditionally used in Herbal Medicine to help relieve headaches

Additional Therapies

- Echinacea Premium tablets or Echinacea Premium 1:2 liquid extract
- Boswellia Complex tablets
- Astragalus Complex tablets
- Vitanox tablets
- Licorice High Grade 1:1 liquid extract

Dosage and Administration

Adults: 1 tablet 2-4 times daily. Reduce the dosage gradually if treatment is to be paused or discontinued. Take with or after food. Consult a health care practitioner for use beyond 4 months.

Each tablet contains:

<i>Rehmannia glutinosa</i> (Rehmannia) root 1:5 extract	1.75 mL
Dried herb equivalent of Rehmannia root	350 mg
<i>Bupleurum falcatum</i> (False Bupleurum) root 1:2 extract	1.4 mL
Dried herb equivalent of False Bupleurum root	700 mg
<i>Hemidesmus indicus</i> (Indian-sarsaparilla) root 5:1 extract	100 mg
Dried herb equivalent of Indian-sarsaparilla root	500 mg
<i>Tanacetum parthenium</i> (Feverfew) herb top 5:1 extract	33 mg
Dried herb equivalent of Feverfew herb top	165 mg

Contraindications and Cautions: Consult a health care practitioner if symptoms persist or worsen. Consult a health care practitioner prior to use if you are breastfeeding, or if you are taking blood thinners. Do not use if you are allergic to plants of the Asteraceae/Daisy family, or if you are pregnant. Hypersensitivity, such as an allergy, has been known to occur; in which case discontinue use. Some people may experience sore mouth, mouth ulcers and/or gastrointestinal discomfort.



Please consult the product packaging label for the most accurate product information.
Not for public distribution. For professional use only.

Rhodiola & Ginseng



Rhodiola rosea

Rhodiola & Ginseng contains Rhodiola and Korean Ginseng, a combination which contains many compounds including phenylpropanoids such as rosarin, rosavin and rosin (rosavins), salidroside (a hydroxyphenethyl glucoside), and a complex mixture of steroidal saponins (called ginsenosides).

Indications

Used in Herbal Medicine as supportive therapy for:

- ✓ The promotion of healthy glucose levels
- ✓ To help support cognitive function and/or reduce mental fatigue (in cases of mental stress)
- ✓ To help enhance physical capacity/performance (in cases of physical stress)

Additional Therapies

- Valerian Complex
- Withania Complex
- Nevanon Forte
- Bacopa Complex

Rhodiola Quality Issues

Rhodiola rosea is commonly referred to as Golden Root or Roseroot and grows in dry sandy ground at high altitudes in the arctic regions of Europe and Asia.

The freshly cut root has a rose-like odour that has led to its botanical name and one of its common names. The root has been used for centuries in the traditional medicines of Russia and Scandinavia. There are however 16 common species of Rhodiola growing in the Eurasian area. Of these, 11 have been tested in animal studies, but only *R. rosea* (17 studies) and *R. crenulata* (1) have been assessed in human trials.

Most of the Rhodiola species have been reported to contain the marker compound salidroside and this was originally used to standardise extracts of *Rhodiola rosea*. After more than a decade of research, however, it was

Dosage and Administration

Adults: 1 tablet daily or as directed by your health care practitioner.
Not to be taken immediately before bedtime.
Consult a health practitioner for use beyond 3 months.

Each tablet contains:

<i>Rhodiola rosea</i> (Rhodiola) root extract	180 mg
Contains rosavins 5.4 mg	
<i>Panax ginseng</i> (Korean Ginseng) root 5:1 extract	100 mg
Dried herb equivalent of Korean Ginseng root	500 mg
Contains total ginsenosides 8.4 mg	

Contraindications and Cautions: Consult a health care practitioner if symptoms persist or worsen and prior to use if you have diabetes or if you are pregnant or breastfeeding, or if you are taking antidepressant medication, blood thinners, or digoxin or hormone replacement therapy (HRT) or birth control pills. Do not use if you have bipolar disorder or bipolar spectrum disorder. If you experience irritability, insomnia, anxiety, or headaches, discontinue use.

shown that the chemical composition of *R. rosea* root is, in fact, different to the other species of the genus Rhodiola. Using newly developed methods of analysis, it was shown that *R. rosea* root contains three cinnamyl alcohol-vicianosides: rosavin, rosin, and rosarin that are specific to this species. They are collectively termed rosavins. HPLC offers a ready method to differentiate true *Rhodiola rosea* from the other species offered on the market. The two major rosavins found are rosavin and rosarin, with only very low quantities of rosin.

Please consult the product packaging label for the most accurate product information. Not for public distribution. For professional use only.



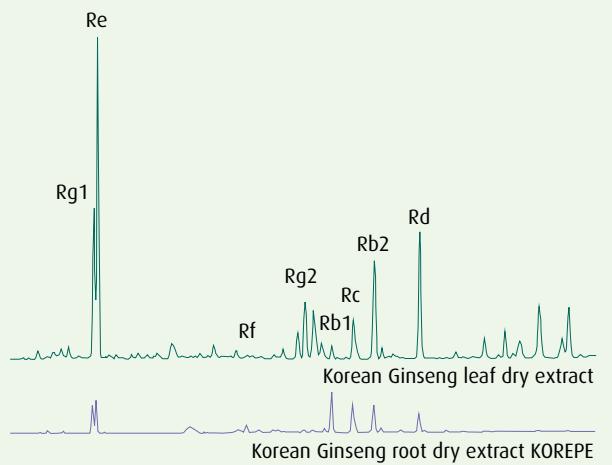
Rhodiola rosea

Korean Ginseng Quality Issues

Panax ginseng is a widely used and misunderstood herb. Traditionally the main root of the plant has been preferred for therapeutic use.

The other parts of the plant such as the root hairs, leaves, leafstalks, etc are considered inferior and are never used medicinally in the East. However, many herb traders will sell the other plant parts as they are substantially cheaper than the main root. The major marker compounds used to characterise *Panax ginseng* are the ginsenosides which occur in all parts of the plant and if you were to only consider total ginsenosides the main root is not the highest in content. The importance is in the ratio of specific ginsenosides. The European clinical studies were undertaken on extracts manufactured from the main root of *Panax ginseng* which have a particular ratio of ginsenosides. To achieve the clinical results obtained traditionally and supported by clinical trials it is important to use raw material from the correct plant part and the correct species. This is readily achievable using HPLC which easily distinguishes the different preparations.

	% Content								
	Rg ₁	Re	Rf	Rg ₂	Rb ₁	Rc	Rb ₂	Rd	Total
Leaves	1.078	1.524	—	—	0.184	0.736	0.553	1.113	5.188
Leafstalks	0.327	0.141	—	—	—	0.190	—	0.107	0.765
Stem	0.292	0.070	—	—	—	—	0.397	—	0.759
Main root	0.379	0.153	0.092	0.023	0.342	0.190	0.131	0.038	1.348
Lateral roots	0.406	0.668	0.203	0.090	0.850	0.738	0.434	0.143	3.532
Root hairs	0.376	1.512	0.150	0.249	1.351	1.349	0.780	0.381	6.148
Main root dry extract	1.4	2.1	0.6	0.6	2.9	1.9	2.4	1.5	13.4



Please consult the product packaging label for the most accurate product information. Not for public distribution. For professional use only.

Silymarin

Silybum marianum



St Mary's Thistle (Milk Thistle) contains Silymarin calculated as silibin/silybin, flavonoids and other compounds. This product is standardised to contain 168 mg of silymarin per tablet to ensure optimal strength and quality.

Indication

- ✓ Promotion of a healthy liver

Additional Therapies

- LivCo tablets or Livton Complex tablets
- Garlic tablets
- Vitanox tablets

Dosage and Administration

Adults: 1 tablet 2 times daily or as directed by your health care practitioner. Use for a minimum of 3 weeks to see beneficial effects.

Each tablet contains:

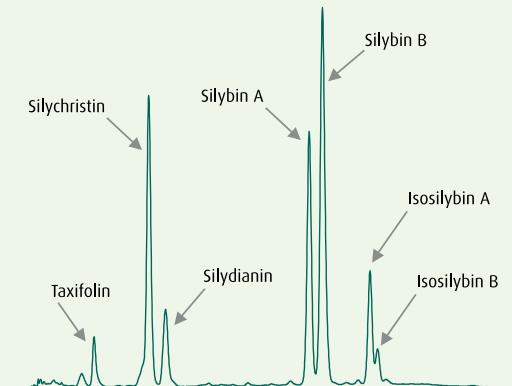
<i>Silybum marianum</i> (St Mary's Thistle) fruit 70:1 extract	240 mg
Dried herb equivalent of St Mary's Thistle fruit	16.8 g
Contains silymarin 168 mg	

Contraindications and Cautions: Consult a health care practitioner if symptoms persist or worsen or prior to use if you have a liver disease or impaired liver function. Do not use if you are pregnant or breastfeeding. Hypersensitivity/allergy is known to occur, in which case, discontinue use. Discontinue use 7 days prior to general anesthesia.

St Mary's Thistle Quality Issues

St Mary's Thistle (*Silybum marianum*) contains a range of flavanolignans (silybin A and B, silychristin, silydianin, isosilybin and 2, 3-dehydro derivatives) collectively called silybin or silymarin, as well as simple flavonoids such as taxifolin.

St Mary's Thistle (*Silybum marianum*) contains a range of flavanolignans (silybin A and B, silychristin, silydianin, isosilybin and 2, 3-dehydro derivatives) collectively called silybin or silymarin, as well as simple flavonoids such as taxifolin. Flavanolignans are important indicators of quality and efficacy. The flavanolignans are often measured analytically by the non-specific and less accurate 2, 4-dinitrophenylhydrazine colourimetric method, which also reacts with any ketonic compounds, which includes the flavonoid taxifolin. MediHerb has developed a High Performance Liquid Chromatographic method to allow the individual levels of the flavanolignans to be accurately measured, and determine a value for these which is not inflated by the presence of simple flavonoids.



Please consult the product packaging label for the most accurate product information. Not for public distribution. For professional use only.

Sinus Forte

Hydrastis canadensis



Sinus Forte combines the herbs Eyebright, Golden Rod, Echinacea root, Golden Seal and Cayenne. These five powerful herbs contain iridoid glycosides (especially aucubin), saponins, flavonoids, diterpenoid lactones, caffeic acid derivatives (especially chichoric acid), alkylamides, alkaloids (especially hydrastine and berberine), pungent principles (particularly capsaicin), carotenoids and other compounds.

Indications

- ✓ Used in Herbal Medicine to help fight off infections, especially of the upper respiratory tract
- ✓ Supportive therapy in the treatment of upper respiratory tract infections (e.g. common colds)
- ✓ Helps to relieve the symptoms and shorten the duration of upper respiratory tract infections

Additional Therapies

- Echinacea Premium tablets or Echinacea Premium 1:2 liquid extract
- Golden Seal tablets
- Rehmannia Complex tablets

Dosage and Administration

Adults: 1 tablet 3 to 4 times daily or as directed by your health care practitioner. Take at the first sign of infection. Consult a health care practitioner for use beyond 4 weeks.

Each tablet contains:

<i>Solidago virgaurea</i> (Golden Rod) herb 1:2 extract	1.3 mL
Dried herb equivalent of Golden Rod herb	650 mg
<i>Euphrasia officinalis</i> (Eyebright) herb 1:2 extract	1.3 mL
Dried herb equivalent of Eyebright herb	650 mg
<i>Echinacea purpurea</i> (Echinacea) root 1:2 extract	0.74 mL
Dried herb equivalent of Echinacea root	370 mg
<i>Hydrastis canadensis</i> (Golden Seal) root and rhizome 1:3 extract	375 mcL
Dried herb equivalent of Golden Seal root and rhizome	125 mg
<i>Capsicum annuum</i> (Cayenne) fruit 1:3 extract	30 mcL
Dried herb equivalent of Cayenne fruit	10 mg

Contraindications and Cautions: Consult a health care practitioner if symptoms persist or worsen prior to use if you have stomach ulcers or inflammation, if you are taking immunosuppressants, or if you have a progressive systemic disease such as tuberculosis, leukemia, collagenosis or multiple sclerosis, if you have a kidney disorder or if you have blood pressure problems. Do not use if you are allergic to plants of the Asteraceae/Compositae/Daisy family or if you are pregnant or breastfeeding. Hypersensitivity (e.g. allergy) has been known to occur, in which case, discontinue use. Consumption of Golden Seal with alcohol, other medications and/or natural health products with sedative properties is not recommended.

See the Golden Seal information on page 41 for Golden Seal Quality Issues

See the Echinacea Premium information on page 36 for Echinacea Quality Issues

Please consult the product packaging label for the most accurate product information.
Not for public distribution. For professional use only.

Slippery Elm 400mg

Ulmus rubra



The key constituents of Slippery Elm stem bark are water-soluble polysaccharides. This product is a vegetarian capsule and is suitable for vegetarians.

Indications

- ✓ Traditionally used in Herbal Medicine for maintaining a healthy lower gastrointestinal tract

Additional Therapies

- Golden Seal tablets
- Vitanox tablets

Dosage and Administration

Adults: 1 capsule up to 5 times a day or as directed by your health care practitioner. Take with plenty of water. Avoid using until two hours after taking other medications.

Each tablet contains:

<i>Ulmus rubra</i> (Slippery Elm) inner stem bark	400 mg
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Contraindications and Cautions: Consult a health care practitioner if symptoms persist or worsen. Contraindicated in intestinal obstruction. Discontinue 7 days prior to general anesthesia.



St John's Wort

Hypericum perforatum



St John's Wort contains the naphthodianthrones hypericin and pseudohypericin (hypericin), flavonoids, phenolics and other compounds. This product is standardised to contain 990 mcg of hypericin per tablet to ensure optimal strength and quality.

Indications

- ✓ Used in Herbal Medicine to help relieve restlessness and/or nervousness (sedative and/or calmative)
- ✓ Used in Herbal Medicine to help promote healthy mood balance and relieve sleep disturbances associated with mood imbalance

Additional Therapies

- Echinacea Premium tablets or 1:2 liquid extract, or Andrographis Complex tablets
- Valerian Complex tablets
- Withania Complex tablets

Dosage and Administration

Adults: 1 tablet 2 times daily or as directed by a health care practitioner. Use for a minimum of 1 week to see beneficial effects. Consult a health care practitioner for use beyond 18 weeks.

Each tablet contains:

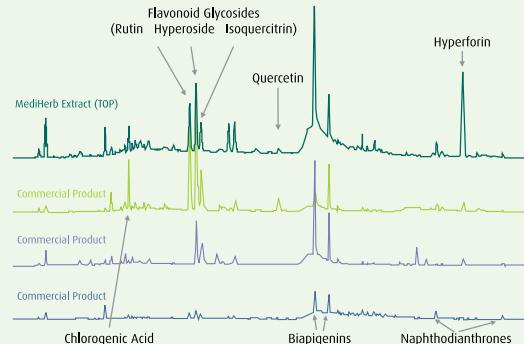
<i>Hypericum perforatum</i> (St John's Wort) aerial parts 6:1 extract	300 mg
Dried herb equivalent of St John's Wort aerial parts	1.8 g
Contains hypericin 990 mcg	

Contraindications and Cautions: Avoid prolonged exposure to sunlight, ultraviolet light (UV) or UV therapy. Consult a health care practitioner if symptoms persist or worsen. Consult a health care practitioner prior to use if you are pregnant or breastfeeding or if you are taking anti-anxiety medications, seizure medications, antihistamines, bronchodilators, muscle relaxants and/or oplates. Do not use if you are taking anti-cancer medications, blood thinners, antidepressant medications (e.g. selective serotonin reuptake inhibitors (SSRI)), anti-HIV agents, cardiovascular medications, immunosuppressants, and/or contraceptive medications. Hypersensitivity, such as allergy, has been known to occur; in which case, discontinue use. Some people may experience mild gastrointestinal disturbances, nausea, restlessness and/or headaches.

St John's Wort Quality Issues

St John's Wort is comprised of a wide range of phytochemicals of which the naphthodianthrones (consisting mainly of hypericin and psuedohypericin) are characteristic, while several other constituents are found across a very wide variety of plant species: eg chlorogenic acid, flavonoids and biapigenins.

Studies have shown that hypericin administered with flavonoid glycosides caused an increase in the bioavailability of hypericin. St John's Wort extracts containing the flavonoid glycosides but devoid of hypericin and hyperforin have been shown to be pharmacologically active in model systems. Additionally extracts devoid of hyperforin have been proven effective in clinical trials as have extracts containing hyperforin. In the graph, all extracts contained the same level of naphthodianthrones (hypericins), however a wide range of variation was shown for the other constituents when analyzed by HPLC – Some extracts having very low levels of all the phytochemicals you would expect in a good quality extract of *Hypericum perforatum*. MediHerb recognises the importance of all the other constituents, particularly the OPCs and flavonoids and tests all of its products using the techniques which allow the identification of these components.



Please consult the product packaging label for the most accurate product information. Not for public distribution. For professional use only.

Tribulus Forte

Tribulus terrestris



Tribulus Forte contains an extract of *Tribulus terrestris* herb (aerial parts - leaves and stems) and contains steroid saponins, mainly furostanol glycosides (including protodioscin and protogracillin) and small quantities of spirostanol glycosides, sterols and other compounds. This product is standardised to contain 110 mg of furostanol saponins as protodioscin per tablet to ensure optimal strength and quality.

Indications

- ✓ Source of saponins with tonic properties

Additional Therapies

- Withania Complex tablets
- Wild Yam Complex tablets
- Chaste Tree tablets or 1:2 liquid extract

Dosage and Administration

Adults: 1-2 tablets daily or as directed by your health care practitioner. Consult your health care practitioner for use beyond 4 weeks.

Each tablet contains:

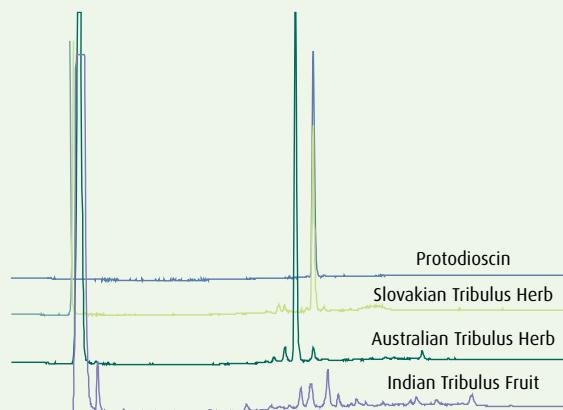
<i>Tribulus terrestris</i> (Tribulus) aerial parts 55:1 extract	245 mg
Dried herb equivalent of <i>Tribulus</i> aerial parts	13.5 g
Contains furostanol saponins as protodioscin 110 mg	

Contraindications and Cautions: Consult a health care practitioner prior to use if you have benign prostate hyperplasia or prostate cancer (due to possible androgenic effects). Discontinue use if you experience breast pain, discomfort and/or tenderness. Do not use if you are pregnant or breastfeeding. Diuretic effects may occur. If this is the case, discontinue use. Hypersensitivity/allergy has been known to occur. If this is the case, discontinue use.

Tribulus Quality Issues

Tribulus terrestris is an herb which is endemic to many different geographical zones, from the Mediterranean regions, India, China, South Africa and Australia.

Research undertaken by MediHerb has shown that the phytochemical profile of the herb varies depending upon the geographical origin and the plant part utilized. Only herb sourced from the Central European regions of Bulgaria and Slovakia have been found to contain protodioscin, which is an important indicator of quality and efficacy. Additionally only the leaves and stem of the plant contain protodioscin, the fruit does not contain this phytochemical. MediHerb has undertaken this research to ensure that our Tribulus product is of the correct phytochemical profile to ensure phytoequivalence with the Bulgarian clinical trials and therefore optimal therapeutic outcome.



Please consult the product packaging label for the most accurate product information. Not for public distribution. For professional use only.

Turmeric Forte

Curcuma longa



Turmeric Forte contains the curcuminoids-galactomannan complex, a combination of Fenugreek seed dietary fibre and Turmeric rhizome extract to enhance absorption* and improve bioavailability of curcuminoids, the active constituents of Turmeric.

Indications

- ✓ Provides antioxidant for the maintenance of good health

Additional Therapies

- Boswellia Complex tablets
- DiGest Forte tablets
- Horsechestnut Complex tablets
- LivCo tablets
- Vitanox tablets

Dosage and Administration

Adults: 1 tablet 2 times daily. Consult a health care practitioner for use beyond 4 weeks.

Each tablet contains:

Curcuminoid-galactomannan complex (<i>Curcuma longa</i> rhizome, <i>Trigonella foenum-graecum</i> seed)	270 mg
Contains Curcumin 33%	

Contraindications and Cautions: Consult a health care practitioner prior to use if you are pregnant or breastfeeding. Consult a health care practitioner prior to use if you are taking antiplatelet medication or blood thinners. Consult a health care practitioner prior to use if you have gallstones, stomach ulcers, excess stomach acid or a bile duct obstruction.

*Contains dietary ingredient (curcuminoids-galactomannan complex), found to have enhanced bioavailability of curcuminoids than unformulated curcumin.



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Valerian Complex



Valerian Complex contains Valerian, Passionflower and *Zizyphus spinosa*. This combination of herbs contains many compounds including iridoids (known as valepotriates), an essential oil, cyclopentane sesquiterpenes (including valerenic acid), flavonoids and dammarane-type saponins called jujubosides.

Indications

- ✓ Helps promote sleep

Additional Therapies

- Nevaton Forte tablets
- St John's Wort tablets
- Withania Complex tablets
- Withania 2:1 liquid extract

Valerian Quality Issues

Valerian (*Valeriana officinalis*) contains Valerenic acids (predominantly acetoxyvalerenic and valerenic acids and low levels of hydroxyvalerenic acid) and valepotriates (valtrate and isovaltrate).

While other species of Valerian may contain the valepotriates only true Valerian contains the valerenic acids. MediHerb has developed a unique High Performance Liquid Chromatography analytical method to determine the levels of valerenic acids and valepotriates in Valerian. This method can also determine the level of the baldrinals (valtrate degradation products) which are an indicator of poor quality herb. By using this analytical method on all its Valerian products, MediHerb assures that these products contain high levels of valerenic acids and valepotriates, with no baldrinals.

Dosage and Administration

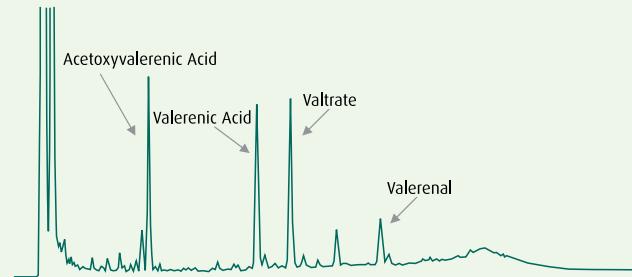
Adults: 1 tablet 4 times daily or as directed by your health care practitioner

Each tablet contains:

<i>Zizyphus spinosa</i> (<i>Zizyphus</i>) seed 10:1 extract	90 mg
Dried herb equivalent of <i>Zizyphus</i> seed	900 mg
<i>Valeriana officinalis</i> (<i>Valerian</i>) root and rhizome 5:1 extract	140 mg
Dried herb equivalent of Valerian root and rhizome	700 mg
Contains valerenic acids 1.12 mg	
<i>Passiflora incarnata</i> (<i>Passionflower</i>) aerial parts 5:1 extract	100 mg
Dried herb equivalent of Passionflower aerial parts	500 mg

Contraindications and Cautions: Consult a health care practitioner if symptoms persist, prior to use if you are pregnant or breastfeeding or if you are taking other sedatives, CNS depressants, or if you experience severe drowsiness and/or withdrawal symptoms upon abrupt discontinuation following chronic use. Consumption of alcohol, other drugs or natural health products with sedative properties is not recommended. Some people may experience drowsiness. Exercise caution if operating heavy machinery, driving a motor vehicle or involved in activities requiring mental alertness. Hypersensitivity (e.g. allergy) has been known to occur, in which case, discontinue use. Discontinue 7 days prior to general anesthesia.

See the Valerian Complex information on page 60 for Passionflower Quality Issues



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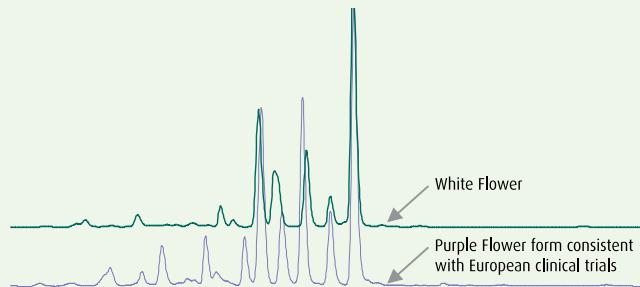
Valerian Complex



Passionflower Quality Issues

There are over 500 species of Passionflower, which includes the edible passionfruit and varieties grown for their characteristic flowers. The preferred medicinal species is *Passiflora incarnata* which is native to the Americas and has many common names, including 'Maypop' and 'Purple Passionflower'.

The original forms of this plant have flowers varying in colour from pale lavender through to dark violet. There is also a white-flowered form which appears in the wild, as well as in cultivation, and is sold as *P. incarnata* "Alba". During routine analysis in the MediHerb Research Laboratory it became evident that there were two different phytochemical profiles of Passionflower being encountered. The samples varied in the flavonoid constituents which are among the proposed therapeutically active components. In conjunction with Southern Cross University, Australia it was determined that the different flavonoid profiles were related to the colour of the flowers (purple or white). The clinical evidence for Passionflower is derived from European clinical trials and the corresponding phytochemical profiles have been published. By using LC/MS it was determined that these profiles matched that of the purple-flowered form. Two of the peaks are consistent between the two different forms, however, the remaining 8 or more flavonoids are different. Without using at least HPLC, or ideally LC/MS, this differentiation is easily missed and the inappropriate form of herb might be used. Products contain high levels of valerenic acids and valepotriates, with no baldrinols.



Please consult the product packaging label for the most accurate product information. Not for public distribution. For professional use only.

Vitanox

Rosmarinus officinalis



Vitanox contains a synergistic blend of herbs which provide strong antioxidant protection. The herbs Rosemary, Green Tea, Turmeric and Grape Seed provide phenolic diterpenes (including carnosol and rosmarinic acid), polyphenols including epigallocatechin gallate, essential oils containing sesquiterpenes, yellow pigments referred to as diarylheptanoids (including curcumin), flavonoids, triterpenoids and oligomeric procyandins. This product contains three herbs with standardised levels of key phytochemicals to ensure optimal strength and quality.

Indications

- ✓ Provides antioxidants to protect against oxidative damage
- ✓ Used in Herbal Medicine to aid digestion
- ✓ Used in Herbal Medicine as a liver protectant to help increase bile excretion by the liver and stimulate contraction of the gallbladder
- ✓ Turmeric is traditionally used in Ayurveda to relieve pain and inflammation, and assist healing of minor wounds and as an anti-inflammatory to help relieve joint pain

Additional Therapies

- Ginkgo Forte tablets
- Horsechestnut Complex tablets
- Boswellia Complex tablets
- Silymarin tablets
- LivCo tablets

Please consult the product packaging label for the most accurate product information.
Not for public distribution. For professional use only.

Dosage and Administration

Adults: 1 tablet 2 times daily or as directed by your health care practitioner. Consult your health care practitioner for use beyond 12 weeks.

Each tablet contains:

<i>Rosmarinus officinalis</i> (Rosemary) leaf 5:1 extract	200 mg
Dried herb equivalent of Rosemary leaf	1 g
<i>Camellia sinensis</i> (Green Tea) leaf 25:1 extract	166.7 mL
Dried herb equivalent of Green Tea leaf	4.17 mg
Contains catechins 83.35 mg	
Contains caffeine 12.5 mg	
<i>Curcuma longa</i> (Turmeric) rhizome 25:1 extract	80 mg
Dried herb equivalent of Turmeric rhizome	2 mg
<i>Vitis vinifera</i> (Grape Seed) seed 120:1 extract	50 mg
Dried herb equivalent of Grape Seed seed	6 mg
Contains proanthocyanidins 42.5 mg	

Contraindications and Cautions: Consult a health care practitioner prior to use if you have an iron deficiency, gallstones or bile duct obstruction or stomach ulcers or excess stomach acid or if you have liver disorder. Stop use if you develop symptoms of liver trouble such as yellowing of the skin/eyes (jaundice), stomach pain, dark urine, sweating, nausea, unusual tiredness and/or loss of appetite and consult a health care practitioner. Rare, unpredictable cases of liver injury associated with green tea extract-containing products have been reported. Do not use if pregnant or breastfeeding.

Wild Yam Complex



Dioscorea villosa



Wild Yam Complex contains Wild Yam, Black Cohosh, Shatavari, Korean Ginseng, St John's Wort and Sage. This combination of herbs contains many compounds including several types of saponins (including ginsenosides), an essential oil (containing monoterpenes, including thujone), phenolic compounds (such as rosmarinic acid), naphthodianthrones hypericin and pseudohypericin, and flavonoids. This tablet contains two herbs with standardised levels of key phytochemicals to ensure optimal strength and quality; 333 mcg of hypericin and 1.3 mg of total ginsenosides per tablet.

Indications

- ✓ Helps relieve symptoms associated with menopause

Additional Therapies

- Chaste Tree tablets or 1:2 liquid extract
- Nevaton Forte tablets
- St John's Wort tablets
- Valerian Complex tablets

Dosage and Administration

Adult Women: 1 tablet 3 to 4 times daily or as directed by your health care practitioner. Use for a minimum of 1 week to see beneficial effects. For use beyond 2 weeks consult your health care practitioner.

Each tablet contains:

<i>Asparagus racemosus</i> (Shatavari) root 1:2 extract	0.8 mL
Dried herb equivalent of Shatavari root	400 mg
<i>Dioscorea villosa</i> (Wild Yam) root and rhizome 1:2 extract	0.8 mL
Dried herb equivalent of Wild Yam root and rhizome	400 mg
<i>Actaea racemosa</i> (Black Cohosh) root 1:2 extract	0.2 mL
Dried herb equivalent of Black Cohosh root	100 mg
<i>Hypericum perforatum</i> (St John's Wort) herb top 6:1 extract	100 mg
Dried herb equivalent of St John's Wort herb top	600 mg
<i>Panax ginseng</i> (Korean Ginseng) root 5:1 extract	15 mg
Dried herb equivalent of Korean Ginseng root	75 mg
<i>Salvia officinalis</i> (Sage) leaf 1:2 extract	0.58 mL
Dried herb equivalent of Sage leaf	290 mg

Contraindications and Cautions: Avoid prolonged exposure to sunlight, ultraviolet light (UV) or UV therapy. Consult a health care practitioner if symptoms persist or worsen. Consult a health care practitioner prior to use if you are taking digoxin or medications such as anti-anxiety and/or antidepressant, seizure, antihistamines, bronchodilators, muscle relaxants and/or opiates; if you have a liver disorder or if you have diabetes. Do not use if you are pregnant or breastfeeding, or if you are taking medications for anti-cancer, blood thinners, antidepressants (e.g. selective serotonin reuptake inhibitors (SSRI)), anti-HIV agents, cardiovascular, immunosuppressants, and/or contraceptive, if you have hormone sensitive conditions such as uterine, endometrial, breast or ovarian cancer as well as endometriosis and uterine fibroids, if you have a protein S deficiency as wild yam may increase the risk of thrombosis, or a seizure disorder (e.g. epilepsy). Hypersensitivity, such as an allergy, has been known to occur, and some people may experience mild gastrointestinal disturbances, nausea, insomnia, restlessness and/or headaches in which case, discontinue use.

Please consult the product packaging label for the most accurate product information. Not for public distribution. For professional use only.

Wild Yam Quality Issues

There are some 600 species of Yam in the genus *Dioscorea*, many of them are wild species that flourish in damp woodlands and thickets.

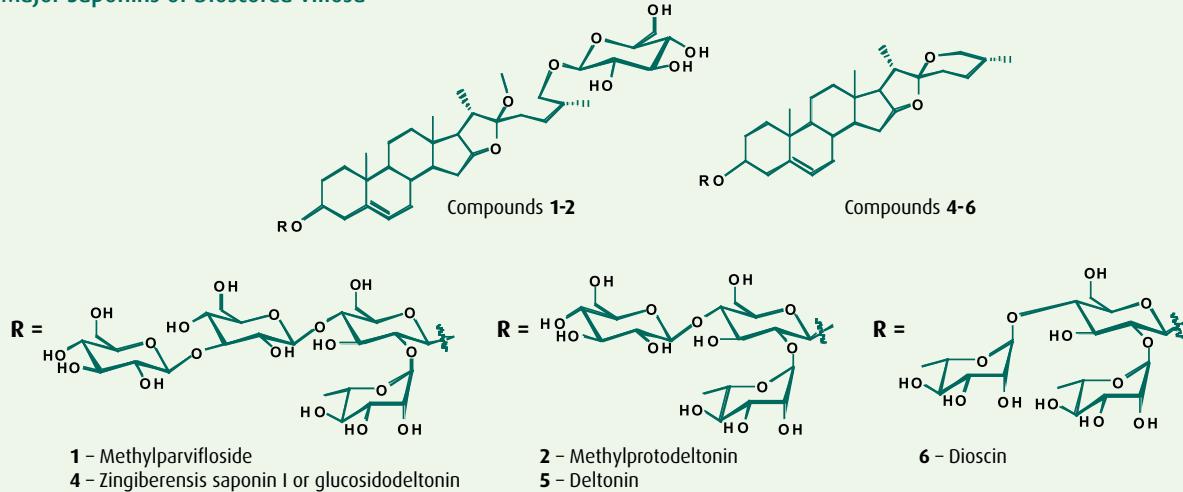
Dioscorea villosa, also known as Colic Root or Wild Yam, is a twining, tuberous vine native to eastern North America. The roots initially taste starchy, but soon after are bitter and acrid, nothing like the taste of Yam or Sweet Potato grown for the dinner table. Commercial Wild Yam extracts available for use as raw materials are often not *Dioscorea villosa* but instead *Dioscorea opposita* (Chinese Yam Root) which has a different phytochemical profile. It is widely misconstrued that *Dioscorea villosa* contains diosgenin and many products have this as a statement on their labels. However it does not contain diosgenin, but rather the diosgenin precursors. Traditionally *Dioscorea villosa* was believed to contain predominantly dioscin, however, the origin of this assignment is unclear (dioscin is a steroid glycoside precursor of diosgenin). The phytochemical profile of Wild Yam is poorly-defined and based on scientific literature from the 1940s. MediHerb undertook a project in conjunction with Associate Professor James De Voss, Chemistry Department, University of Queensland to investigate the phytochemistry. Commercially available *Dioscorea villosa* is in the form of dried roots, usually harvested at the end of summer or autumn when the plant is dying back to its rootstock. It was found that these roots contained only very small amounts of dioscin, not the predominance as previously

thought. The major saponin found in the autumn harvested roots were in fact the furostanol-based saponins, methylparvifloside and methylprotodeltonin, while the spirostanol-based saponins, Zingiberensis saponin I and deltonin were the major saponins for samples harvested in summer. The autumn storage saponins differ from the summer saponins by the presence of an extra glucose at the C-26 position of the diosgenin base structure. The two main compounds found in commercial material – harvested in autumn – are significantly different from dioscin by having an extra one or two glucose residues in methylprotodeltonin and methylparvifloside respectively. All of these compounds have been reported from other *Dioscorea* species, however, the profile of saponins was different in the other species.

See *St John's Wort information on page 56 for St John's Wort Quality Issues*

See *Rhodiola & Ginseng information on page 52 for Korean Ginseng Quality Issues*

Major Saponins of *Dioscorea villosa*



Withania 2:1

Withania somnifera



Indications

- ✓ Traditionally used in Ayurveda as Rasayana (rejuvenative tonic), a sleep aid, for memory enhancement, to balance aggravated Vata (nervine tonic, sedative) and to relieve general debility, especially during convalescence or old age

Dosage and Administration

2 to 3 mL daily or as directed by your health care practitioner.

Each tablet contains:

<i>Withania somnifera</i> (Withania) root 10:1 extract	200 mg
Dried herb equivalent of Withania root	2 g

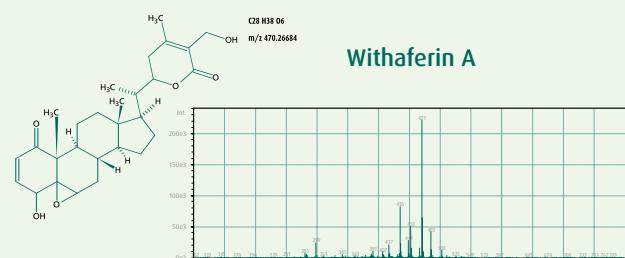
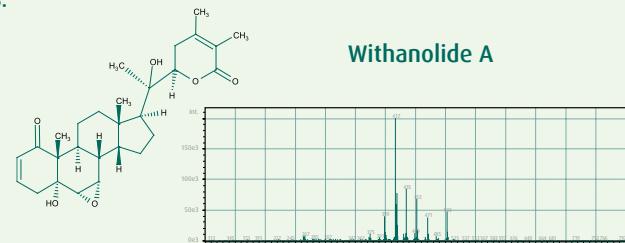
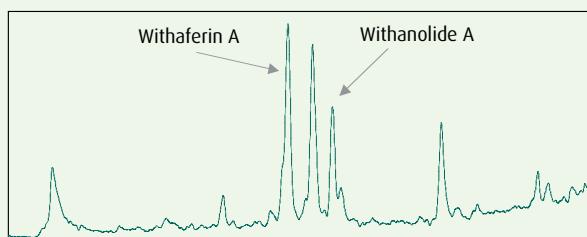
Contraindications and Cautions: Consult a health care practitioner prior to use if you are pregnant or breastfeeding. Consumption with alcohol, other drugs or natural products with sedative properties is not recommended.

Withania Quality Issues

Withania (*Withania somnifera*) is an Indian (Ayurvedic) herb which contains a group of therapeutically important steroidal compounds referred to collectively as withanolides.

Withania contains more than fifty withanolides which vary greatly depending upon the geographic location and plant part. The withanolide profile and content is a key determinant of Withania quality and efficacy. Liquid Chromatography/Mass Spectrometry (LC/MS) is the method of choice for characterizing such a wide range of similar compounds and unequivocally identifying key major components such as withaferin A and withanolide D. This technique is used routinely in the MediHerb Laboratories to identify and analyze Withania and other saponin-containing herbs.

HPLC detection of Withanolides



Please consult the product packaging label for the most accurate product information. Not for public distribution. For professional use only.

Withania Complex

Withania somnifera



Withania Complex contains Withania, Licorice, Skullcap and Korean Ginseng. This combination of herbs contains many compounds including steroidal compounds (including the complex mixture of steroidal saponins called ginsenosides), alkaloids, triterpenoid saponins (especially glycyrrhizin), other saponins and many flavonoids. The Korean Ginseng component of this tablet is standardised to contain 1.68 mg of total ginsenosides per tablet to ensure optimal strength and quality.

Indications

- ✓ Helps support cognitive functions and/or reduce mental fatigue
- ✓ Used in Herbal Medicine to help enhance physical capacity/performance

Additional Therapies

- Nevanon Forte tablets
- Valerian Complex tablets
- St John's Wort tablets
- Tribulus Forte tablets

Dosage and Administration

Adults: 6 tablets daily or as directed by your health care practitioner. Consult a health care practitioner for use beyond 4-6 weeks.

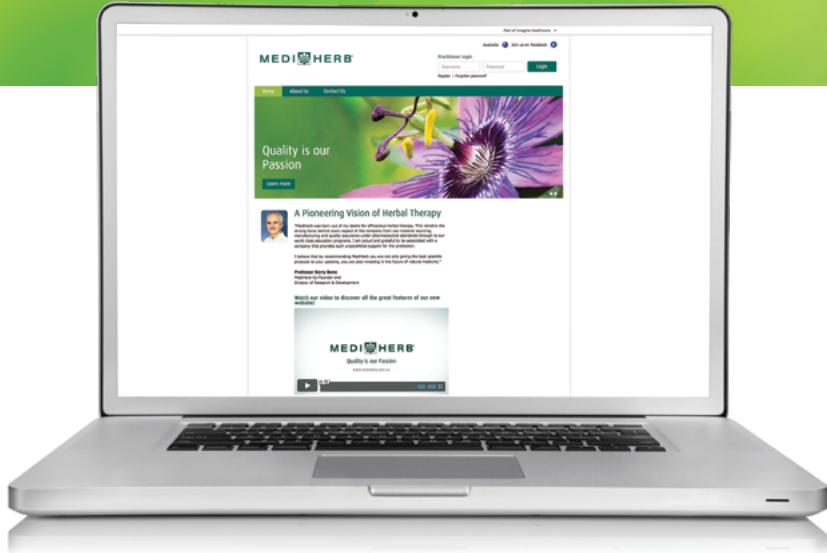
Each tablet contains:

<i>Scutellaria lateriflora</i> (Skullcap) herb top 1:2 extract	0.94 mL
Dried herb equivalent of Skullcap herb top	470 mg
<i>Glycyrrhiza glabra</i> (Licorice) root 7:1 extract	107.15 mg
Dried herb equivalent of Licorice root	750 mg
<i>Withania somnifera</i> (Withania) root 10:1 extract	95 mg
Dried herb equivalent of Withania root	950 mg
<i>Panax ginseng</i> (Korean Ginseng) root 5:1 extract	20 mg
Dried herb equivalent of Korean Ginseng root	100 mg
Contains total ginsenosides 1.68 mg	

Contraindications and Cautions: Do not use if you are pregnant or breastfeeding. Consult a health care practitioner prior to use if you have a liver disorder or diabetes, or if you are taking antidepressant medications or blood thinners or digoxin. When used as a sleep aid, consult a health care practitioner if sleeplessness persists continuously for more than 3 weeks (chronic insomnia). Consumption with alcohol, other drugs or natural health products with sedative properties is not recommended. Do not use if you are taking thiazide diuretics, cardiac glycosides, corticosteroids, stimulant laxatives or other medications which may aggravate electrolyte imbalance; or if you have hypokalemia, high blood pressure, or a kidney or cardiovascular disorder. Consult a health care practitioner if symptoms persist or worsen. Some people may experience insomnia, anxiety or headaches, in which case, discontinue use. Some people may experience drowsiness. Exercise caution if operating heavy machinery, driving a motor vehicle or involved in activities requiring mental alertness.

Please consult the product packaging label for the most accurate product information. Not for public distribution. For professional use only.

Practitioner Resources



MediHerb Website

Our website, www.mediherb.ca is the most comprehensive website on natural medicine and an invaluable resource for practitioners and students. www.mediherb.ca features both public and member only information.

Public Area

Contains information on the MediHerb philosophy and the quality processes that deliver the world's finest herbal products.

Members Only Area

This is where the site gets really interesting! You can go into the different areas to view comprehensive information on:

MediHerb Professional Library: use the dynamic search engine to discover all the herbal information we have produced dating back to 1987. You can search and view the *Phytotherapist's Perspective* by herb, phytochemical, condition or topic. It is a fantastic reference tool for all health professionals!

Products: view the most up-to-date information on new and existing products and search products by ingredient.

Clinical Research Review: by registering your details on the MediHerb website, you will automatically receive a free subscription to our popular Clinical Research Review articles, which contain the latest research on herbal therapy curated by the MediHerb team.



MEDI+HERB
a phytotherapist's perspective



www.mediherb.com | 800.333.8000 | 100% Natural | 100% Organic | 100% Safe

Bitter Herbs: Improve Digestive Function & Potentially More

Key Points at a Glance

- Bitter herbs have been used for thousands of years to stimulate the digestive system.
- Many bitter herbs contain bioactive compounds that have been shown to exert positive effects on the digestive system.
- Medicinal use of bitter herbs dates back to ancient Egypt, Greece, and Rome.
- Bitter herbs are known to stimulate the liver and gallbladder, increase bile production, and improve the absorption of nutrients.
- Bitter herbs may help to reduce H. pylori, which can contribute to related intestinal problems.
- Bitter herbs may have anti-inflammatory properties that reduce pain and inflammation.
- Bitter herbs may have antioxidant properties that reduce oxidative stress and related damage.
- Bitter herbs may have antimicrobial properties that reduce the growth of bacteria that infect the digestive system.
- Bitter herbs may have immunomodulatory, anti-inflammatory, and analgesic effects.
- Bitter herbs may have other beneficial effects in addition to those mentioned.

The Choice of Bitters

• Bitter herbs contain low levels of alkaloids, usually by weight.

• Bitter herbs are often combined with other herbs to create synergistic effects.

• Individualized combinations of bitters and other herbs are often recommended for best effect.

Gentian & Wormwood

- Well-known classic herbs, well as the demands, some newer research suggests they may have additional health benefits.
- Gentian has been used for centuries to treat digestive problems, diarrhea, abdominal spasms, and liver and gallbladder disorders.
- Wormwood has also been used extensively as a liver and gallbladder herb.

Ginger & Curcumin (Turmeric)

- Used primarily as an anti-nauseant, digestive aid, and anti-inflammatory agent.
- Used as an analgesic, a sedative that relieves anxiety and stress.

Conclusion

• Bitter herbs have been used for thousands of years to stimulate the digestive system.

• Many bitter herbs contain bioactive compounds that have been shown to exert positive effects on the digestive system.

• Medicinal use of bitter herbs dates back to ancient Egypt, Greece, and Rome.

• Bitter herbs are known to stimulate the liver and gallbladder, increase bile production, and improve the absorption of nutrients.

• Bitter herbs may help to reduce H. pylori, which can contribute to related intestinal problems.

• Bitter herbs may have anti-inflammatory properties that reduce pain and inflammation.

• Bitter herbs may have antioxidant properties that reduce oxidative stress and related damage.

• Bitter herbs may have antimicrobial properties that reduce the growth of bacteria that infect the digestive system.

• Bitter herbs may have immunomodulatory, anti-inflammatory, and analgesic effects.

• Bitter herbs may have other beneficial effects in addition to those mentioned.

Phytotherapist's Perspectives

These publications provide website users with more clinical and technical information in a concise format. Like the rest of our Professional Library, the *Phytotherapist's Perspective* can be searched by:

- **Herb** – common or botanical name (eg ‘green tea’ or *‘Camellia sinensis’*)
 - **Phytochemical** (eg ‘resveratrol’ or ‘flavonoids’)
 - **Condition** (eg ‘fatigue’)
 - **Topic** (eg ‘quality issues’)
 - **Activity** (eg ‘anti-inflammatory’ or ‘joint support’)

The ***Phytotherapist's Perspective*** features phytotherapy articles written by Kerry Bone and Michelle Morgan, and includes:

- Selected articles written by Kerry Bone for the *Townsend Letter for Doctors and Patients*.
 - Monographs detailing technical and clinical information on specific herbs written by Kerry Bone and Michelle Morgan.
 - An assortment of other articles outlining herbs suitable for use in specific conditions. Key constituents, quality issues, therapeutic activity and clinical studies are often a feature of these articles.

Clinical Research Review

The latest clinical research on herbal therapy, covering research about the efficacy, safety and quality of herbs prepared by MediHerb herbal experts. These findings shed light on how herbs may be used to improve health and support wellbeing. These documents are shared quarterly in digital format and can be downloaded from the MediHerb website under the Professional Library section.

Seminars & Webinars for Qualified Health Care Professionals

MediHerb conducts professional seminars and webinars throughout the world with experienced speakers including Professor Kerry Bone, Berris Burgoyne, ND, Angela Hywood, ND, Joanne Boyd, ND and Amanda Williams, ND. These educational forums combine the best of traditional knowledge with the latest scientific research.

Excipient Glossary

Tablet Excipients

MediHerb uses a range of low allergenic and pharmaceutical grade excipients in the manufacture of its tablet range. These excipients are carefully chosen using experience gained from over 10 years of manufacturing herbal tablets and are necessary to aid the manufacturing process, stability, disintegration and to allow ease of swallowing.

Calcium Hydrogen Phosphate

Calcium hydrogen phosphate is the binder or filler which actually holds the tablet together and allows it to be compressed to form a tablet. It also assists in formulation flow and resists the uptake of moisture, thus reducing the risk of poor stability.

Cellulose

Cellulose acts with calcium hydrogen phosphate as the binder that holds the tablet together. It also works to assist with tablet disintegration.

Silica

Silica is used as a glidant to assist with the flow properties of the tablet powder as it travels through the tablet machine. Good flow characteristics are crucial to the manufacture of tablets with consistent weight and active content. Silica is also used to increase the hardness of the tablet to ensure they are robust enough to handle coating, packaging and transport.

Sodium Starch Glycollate

Due to the high proportion of herb used in the MediHerb tablets, an aid to disintegration is required to ensure that the tablets disintegrate in less than 30 minutes. Sodium starch glycollate performs this function best for the high potency tablets manufactured by MediHerb.

Magnesium Stearate – Vegetable Origin

Most tablets need some form of lubrication to assist in the removal of the tablet from the tableting machine die. Magnesium stearate of vegetable origin is the most effective ingredient for this purpose.

Orange Oil

Pressed oil from orange peel is used as a flavour masker.

Hypromellose (Cellulose Derivative)

Hypromellose is used as a film coating agent on most MediHerb tablets. It is applied as a thin inert layer and has four important actions:

1. The thin layer makes the tablet much more resistant to dust formation in the packaging.
2. When the tablet surface is wetted in the mouth a lubricant, mucilaginous layer is formed on the tablet which facilitates swallowing.
3. The inert layer acts to hide any unpleasant odours or tastes that are found in many herbal tablets.
4. It aids in enhancing the stability of the product by forming a barrier to the external environment.

Enteric Coating

Some MediHerb tablets may have a specialised enteric coating which makes the tablets acid resistant. This is important for some herbs which can cause gastric discomfort and for herbs whose actives are damaged by stomach acid. Enterically coated tablets pass through the high acid environment of the stomach safely and then dissolve once they reach the pH neutral environment of the small intestine.

Solubility Test

Enterically coated tablets must be stable for 2 hours in dilute hydrochloric acid and then dissolve within 1 hour when placed in pH 7 buffer.

Effervescent Factors

The following ingredients are used in effervescent powders to adjust the pH and give the product fizz.

- **Calcium carbonate** is a naturally occurring mineral, found as the following minerals and rocks: aragonite, calcite, chalk, limestone, marble and travertine.
- **Citric acid (anhydrous)** is naturally occurring in plants and animals.
- **Potassium and sodium bicarbonates** are naturally occurring inorganic minerals.

Herbal Medicine Text Books



Principles and Practice of Phytotherapy – Second Edition Modern Herbal Medicine

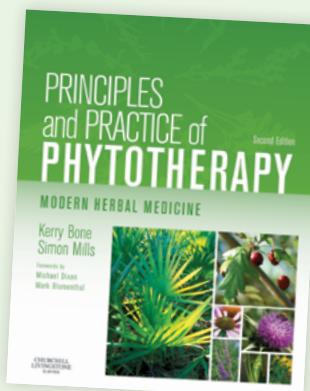
By Kerry Bone and Simon Mills



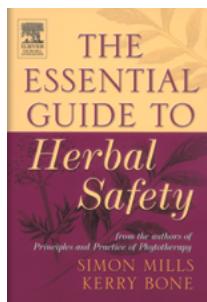
The first edition of *Principles and Practice of Phytotherapy* is well known as the leading text of herbal medicine in naturopathic and herbal colleges throughout the world. Now the long-awaited second edition brings a complete revision of the material in the first text including:

- 50 fully up-to-date evidence-based monographs including 7 new herbs: Gotu Kola, Willow Bark, Bugleweed, Butcher's Broom, Boswellia, Myrrh and Tribulus.
- New insights on herbal management of approximately 100 modern disease states.
- A comprehensive revision of vital safety data, including an extensive herb-drug interaction chart addressing key safety issues to help the reader differentiate between false and real concerns.
- Extensive coverage of vital new topics such as asthma, atopic dermatitis, acne, fibromyalgia, inflammatory bowel disease, insulin resistance, migraine headaches and prostate cancer, to name a few.

This valued text was exhaustively researched and carefully compiled by Kerry Bone and Simon Mills, who have more than 60 years of combined experience in clinical practice, education, manufacturing and research. This text is a must-have resource for any herbal medicine practitioner or student.



Winner of the 2013 James A Duke Excellence in Botanical Literature Award



Winner of the 2005
James A. Duke Botanical
Literature Award

The Essential Guide to Herbal Safety

Edited by Kerry Bone and Simon Mills

The first accurate and comprehensive book on herbal safety – a must for all health care professionals!

This innovative new book presents an extensive discussion of the principles of herbal safety and the current major issues relating to this important area. Leading international experts contribute to the book providing a wealth of information on issues such as quality, interactions, adverse reactions, toxicity, allergy, contact sensitivity and idiosyncratic reactions. In March 2006, the American Botanical Council (ABC) announced that *The Essential Guide to Herbal Safety* was the recipient of the James A. Duke Botanical Literature Award which honours the singular, outstanding contribution by a book to the knowledge and understanding of medicinal and aromatic plants.



Phytotherapy Essentials: Healthy Children

By Rob Santich and Kerry Bone

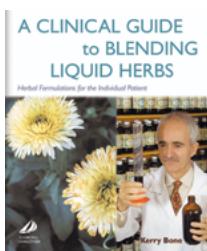
Healthy Children has been written with the special needs of children in mind. The benefits, risks and requirements for herbal therapy in children differ from those in adults. This book outlines the key principles that govern herbal practice for this special patient group. A well-researched text, written by Rob Santich and Kerry Bone who together have almost 50 years of clinical practice, this book provides a comprehensive treatise on the common health problems encountered by children. Sound, practical information based on clinical experience as well as evidence-based research, provides a balanced and authoritative approach to children's health.

The Ultimate Herbal Compendium

By Kerry Bone

A Desktop Guide for Herbal Prescribers

The Ultimate Herbal Compendium is a reliable ready reference designed for the busy health practitioner. It contains up-to-date easily found information on a wide range of herbs and conditions, including doses for herbs in tablet form as well as liquids. Careful research of all the available herbal information combined with Kerry Bone's 25 years of clinical practice ensures that all valid herbal treatment options can be considered.



A Clinical Guide to Blending Liquid Herbs:

Herbal Formulations for the Individual Patient

By Kerry Bone

This highly practical guide explains in-depth how to use and blend liquid extracts for optimum results making it a must for all herbal medicine practitioners and students.

Monographs of 125 popular herbs used in the form of liquid extracts provide the herbal clinician with accessible and clinically relevant information. The monographs have been specifically designed for use in the clinic with an emphasis on providing the essential information in an easy to read format and outlines traditional use and the most up-to-date pharmacological and clinical studies. This guide is comprehensively referenced and contains appendices for thorough explanations, indices of herb and herb action as well as complete glossaries and a table of recommended dosages.

If you would like to order any of the books listed above, contact:

Canada - ProMedics Toll Free: 877-268-5057 Fax: 604-730-7186 Email: order@promedics.ca

Ingredient Index

The ingredient index lists all active ingredients used in MediHerb products.

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Bladderwrack	<i>Fucus vesiculosus</i>
Boswellia	<i>Boswellia serrata</i>
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H	
Hawthorn	<i>Crataegus monogyna</i>
Hemidesmus, Indian-sarsaparilla	<i>Hemidesmus indicus</i>
Holy Basil	<i>Ocimum tenuiflorum</i>
Horsechestnut	<i>Aesculus hippocastanum</i>
I	
Indian-sarsaparilla, Hemidesmus	<i>Hemidesmus indicus</i>

Common Name	Botanical Name
K	
Kava	<i>Piper methysticum</i>
Korean Ginseng	<i>Panax ginseng</i>
L	
Licorice	<i>Glycyrrhiza glabra</i>
M	
Milk Thistle, St Mary's Thistle	<i>Silybum marianum</i>
P	
Paeonia, Chinese Peony	<i>Paeonia lactiflora</i>
Passionflower	<i>Passiflora incarnata</i>
Pleurisy Root	<i>Asclepias tuberosa</i>
R	
Rehmannia	<i>Rehmannia glutinosa</i>
Rhodiola	<i>Rhodiola rosea</i>
Rosemary	<i>Rosmarinus officinalis</i>
S	
Saffron	<i>Crocus sativus</i>
Sage	<i>Salvia officinalis</i>
Schisandra	<i>Schisandra chinensis</i>
Shatavari	<i>Asparagus racemosus</i>
Siberian Ginseng	<i>Eleutherococcus senticosus</i>
Skullcap	<i>Scutellaria lateriflora</i>
Slippery Elm	<i>Ulmus rubra</i>
St John's Wort	<i>Hypericum perforatum</i>
St Mary's Thistle, Milk Thistle	<i>Silybum marianum</i>
T	
Tangerine	<i>Citrus reticulata</i>
Three-leaf caper, Crateva	<i>Crateva magna, Crateva nurvala</i>
Tribulus	<i>Tribulus terrestris</i>
Turmeric	<i>Curcuma longa</i>
U	
Uva Ursi	<i>Arctostaphylos uva-ursi</i>
V	
Valerian	<i>Valeriana officinalis</i>
W	
White Horehound	<i>Marrubium vulgare</i>
Wild Yam	<i>Dioscorea villosa</i>
Withania	<i>Withania somnifera</i>
Wormwood	<i>Artemisia absinthium</i>
Y	
Yellow Dock	<i>Rumex crispus</i>
Z	
Zizyphus	<i>Zizyphus spinosa</i>

Index of Herb Botanical Names

Botanical Name	Common Name
A	
<i>Actaea racemosa, Cimicifuga racemosa</i>	Black Cohosh
<i>Aesculus hippocastanum</i>	Horsechestnut
<i>Allium sativum</i>	Garlic
<i>Andrographis paniculata</i>	Andrographis
<i>Apium graveolens</i>	Celery
<i>Arctostaphylos uva-ursi</i>	Uva Ursi
<i>Artemisia absinthium</i>	Wormwood
<i>Asclepias tuberosa</i>	Pleurisy Root
<i>Asparagus racemosus</i>	Shatavari
<i>Astragalus membranaceus</i>	Astragalus
B	
<i>Bacopa monniera, Bacopa monnierii</i>	Bacopa
<i>Boswellia serrata</i>	Boswellia
<i>Bupleurum falcatum</i>	False Bupleurum
C	
<i>Camellia sinensis</i>	Green Tea
<i>Capsicum annuum, Capsicum spp.</i>	Cayenne
<i>Chionanthus virginica</i>	Fringe Tree
<i>Cimicifuga racemosa, Actaea racemosa</i>	Black Cohosh
<i>Citrus reticulata</i>	Tangerine
<i>Crataegus monogyna</i>	Hawthorn
<i>Crateva magna, Crateva unguifera</i>	Three-leaf caper, Crateva
<i>Crocus sativus</i>	Saffron
<i>Curcuma longa</i>	Turmeric
<i>Cynara scolymus</i>	Globe Artichoke
D	
<i>Dioscorea villosa</i>	Wild Yam
E	
<i>Echinacea angustifolia, Echinacea purpurea</i>	Echinacea
<i>Eleutherococcus senticosus</i>	Siberian Ginseng
<i>Euphrasia officinalis</i>	Eyebright
F	
<i>Frangula purshiana, Rhamnus purshianus</i>	Cascara
<i>Fucus vesiculosus</i>	Bladderwrack
G	
<i>Gentiana lutea</i>	Gentian
<i>Ginkgo biloba</i>	Ginkgo
<i>Glycyrrhiza glabra</i>	Licorice
<i>Gymnema sylvestre</i>	Gymnema
H	
<i>Hemidesmus indicus</i>	Indian-sarsaparilla, Hemidesmus
<i>Hydrastis canadensis</i>	Golden Seal
<i>Hypericum perforatum</i>	St John's Wort

Botanical Name	Common Name
M	
<i>Marrubium vulgare</i>	White Horehound
O	
<i>Ocimum tenuiflorum</i>	Holy Basil
P	
<i>Paeonia lactiflora</i>	Chinese Peony, Paeonia
<i>Panax ginseng</i>	Korean Ginseng
<i>Passiflora incarnata</i>	Passionflower
<i>Piper methysticum</i>	Kava
R	
<i>Rehmannia glutinosa</i>	Rehmannia
<i>Rhamnus purshianus, Frangula purshiana</i>	Cascara
<i>Rhodiola rosea</i>	Rhodiola
<i>Rosmarinus officinalis</i>	Rosemary
<i>Rumex crispus</i>	Yellow Dock
<i>Ruscus aculeatus</i>	Butcher's Broom
S	
<i>Salvia officinalis</i>	Sage
<i>Schisandra chinensis</i>	Schisandra
<i>Scutellaria lateriflora</i>	Skullcap
<i>Silybum marianum</i>	St Mary's Thistle, Milk Thistle
<i>Solidago virgaurea</i>	Golden Rod
T	
<i>Tanacetum parthenium</i>	Feverfew
<i>Taraxacum officinale</i>	Dandelion
<i>Tribulus terrestris</i>	Tribulus
<i>Trigonella foenum-graecum</i>	Fenugreek
U	
<i>Ulmus rubra</i>	Slippery Elm
V	
<i>Vaccinium macrocarpon</i>	Cranberry
<i>Vaccinium myrtillus</i>	Bilberry
<i>Valeriana officinalis</i>	Valerian
<i>Vitex agnus-castus</i>	Chaste Tree
<i>Vitis vinifera</i>	Grape seed
W	
<i>Withania somnifera</i>	Withania
Z	
<i>Zingiber officinale</i>	Ginger
<i>Ziziphus spinosa</i>	Ziziphus

Potential Herb-Drug Interactions for Commonly Used Herbs*

How to Read the Chart

The chart is read from left to right. The information in the Basis of Concern column provides the evidence for the information in the Potential Interaction column. For example, *clinical studies* found that administration of St John's Wort resulted in *decreased levels* of cancer chemotherapeutic drugs. (Italized words represent the information in the Herb-Drug Interaction chart below.)

More details may be provided in the Basis of Concern column. For example, in a *clinical study with healthy volunteers* administration of St John's Wort resulted in *increased clearance* of the hypoglycemic drug gliclazide, and so *may reduce the drug's efficacy*; however, *glucose and insulin response to glucose loading were unchanged*.

Health care professionals please note: When a patient presents using any of the drugs listed below and there is a potential interaction with the herb you intend to dispense, it is important that you or your patient discuss the potential interaction with their prescribing physician before you dispense the herb to the patient.

Drug	Potential Interaction	Basis of Concern	Recommended Action
Andrographis <i>Andrographis paniculata</i>			
Immunosuppressant medication	May decrease effectiveness of drug. ¹	Theoretical concern based on immune-enhancing activity of Andrographis.	Contraindicated
Midazolam	May potentiate effects of drug.	Clinical study with healthy volunteers (providing 100 mg/day of andrographolide): pulse rate and blood pressure decreased. ² See note A.	Monitor (medium level of risk).
Ashwagandha <i>Withania somnifera</i>			
Thyroxine	May potentiate effects of drug.	Theoretical concern based on stimulating effect on thyroid hormones. Case report (increased serum T4 level). ³ Clinical study: improved serum T4 level in subclinical hypothyroid patients, ⁴ three bipolar patients in a clinical trial experienced small increases in serum T4 from baseline (one subclinical hypothyroid patient); ⁵ although the extract was made from leaf and root and provided a high concentration of withanolides (50 mg/day). ⁶	Monitor (low level of risk).
Bilberry <i>Vaccinium myrtillus</i>			
Warfarin	Potentiation of bleeding.	Herb Alone Antiplatelet activity observed in healthy volunteers (173 mg/day of bilberry anthocyanins). ⁷ Case report of postoperative bleeding (bilberry extract undefined). ⁸ Herb or Constituent and Drug Uncontrolled trial (600 mg/day of bilberry anthocyanins + 30 mg/day of vitamin C for 2 months then reduced maintenance dose) of 9 patients taking anticoagulant drugs – treatment reduced retinal hemorrhages without impairing coagulation. ⁹ Case report (retinal bleeding and hematuria with elevated INR; patient reported to consume "large amounts of bilberry fruits every day for five years"). ¹⁰	Monitor at high doses (> 100 mg/day anthocyanins, low level of risk).
Black Cohosh <i>Actaea racemosa</i> (<i>Cimicifuga racemosa</i>)		Case report (decreased INR, 200 mL/day of "concentrate" juice, causality rated as possible (score 4) ¹¹).	Monitor (low level of risk).
Statin drugs eg atorvastatin	May potentially increase in liver enzymes, specifically ALT.	Case report; ¹²	Monitor (low level of risk).

Drug	Potential Interaction	Basis of Concern	Recommended Action
Bladderwrack <i>Fucus vesiculosus</i>	May decrease effectiveness of drug. eg carbimazole	Theoretical concern due to natural iodine content.	Contraindicated unless under close supervision.
Hypothyroid medication eg thyroxine	May add to effect of drug.	Theoretical concern linked to a case report where "kelp" caused hypothyroidism in a person not taking thyroxine. ¹³	Monitor (low level of risk).
Thyroid replacement therapies eg thyroxine	May increase effectiveness of drug.	Two case reports (increased INR; concentrated extract (95%; 1.2–1.5 g/day), causality rated as probable (score 6) ¹¹)	Monitor (low level of risk).
Boswellia <i>Boswellia serrata</i>	May interfere with administration of diagnostic procedures using radioactive isotopes. ¹⁴	Case report.	Contraindicated.
Bugleweed <i>Lycopus virginicus</i> , <i>Lycopus europaeus</i>	May interfere with administration of radioactive isotopes. ¹⁴	Case report.	Contraindicated.
Radiactive iodine	Should not be administered concurrently with preparations containing thyroid hormone. ¹⁵	Theoretical concern based on deliberations of German Commission E.	Contraindicated.
Thyroid hormones	May impair absorption and drug levels. <i>L-Dopa</i> and other Parkinson's disease treatments	Case report. ¹⁶	Monitor (low level of risk).
Cat's Claw <i>Uncaria tomentosa</i>	May increase drug level.	Case report, in a patient with cirrhosis being evaluated for liver transplant. ¹⁷	Monitor (low level of risk).
HIV protease inhibitors	May cause drug-induced cough.	Case report (topical capsaicin). Theoretical concern since capsaicin depletes substance P. ¹⁸	Monitor (very low level of risk).
Cayenne (Chili Pepper) <i>Capsicum</i> spp. (See also Polyphenol-containing and/or Tannin-containing herbs)	May increase absorption and drug level.	Clinical study (healthy volunteers, chili-spiced meal). ¹⁹	Monitor (low level of risk).
ACE inhibitor	May reduce serum levels of thyroxine.	Case reports. ²⁰	Monitor (very low level of risk).
Theophylline	May reduce serum levels of thyroxine.	Case reports. ²¹	Monitor (very low level of risk).
Celery Seed <i>Apium graveolens</i>	May affect hormone levels and/or alter efficacy of hormone-containing medications	Case report of unwanted pregnancy in Australia (herb and concurrent use of progesterone-only OCP) and one other similar case reported internationally. ²¹ There are several trials published in which the herb has been administered to women using OCP without causing unwanted pregnancy – see note C.	Monitor (low level of risk).
Thyroxine	May decrease drug levels.	Clinical study with healthy volunteers using 150 mg/day of isolated constituent (baicalin). ²²	Monitor (low level of risk).
Chaste Tree <i>Vitex agnus-castus</i>			
Hormone-related medications eg progesterone drugs, hormonal contraceptive or HRT		Theoretical concern initially based on <i>in vitro</i> antiplatelet activity of active constituent forskolin, and <i>in vivo</i> antiplatelet activity in an animal model (oral doses: standardised Coleus extract and forskolin). ²³ More recent <i>in vivo</i> animal research: standardised Coleus extract reduced the anticoagulant activity of warfarin. ²⁴	Monitor (low level of risk).
Chinese Skullcap <i>Scutellaria baicalensis</i>			
Rosuvastatin		Theoretical concern based on ability of high doses of forskolin and standardised Coleus extract to lower blood pressure in normotensive and hypertensive animals. ^{25,26} Clinical data from weight management trials: no effect on blood pressure in three trials, trend toward lower blood pressure in one small study. ^{27,28} Clinical trial (dose-escalation in healthy volunteers): extract providing 25–100 mg/day of forskolin): no significant effect on blood pressure or heart rate. ²⁹	Monitor (low level of risk).
Coleus <i>Coleus forskohlii</i>	May alter response to drug.	Theoretical concern based on ability of forskolin and standardised Coleus extract to activate increased intracellular cyclic AMP <i>in vitro</i> . ³⁰	Monitor (low level of risk).
Antiplatelet and anticoagulant drugs			
Hypotensive medication	May potentiate effects of drug.		
Prescribed medication	May potentiate effects of drug.		

Drug	Potential Interaction	Basis of Concern	Recommended Action
Cranberry <i>Vaccinium macrocarpon</i>			
Midazolam	May increase drug levels.	Clinical trials, with healthy volunteers, effect on drug levels conflicting - increased (double-strength juice ¹ , 240 ml tds) ³¹ and no effect (cranberry juice, f. 200 ml tds). ³²	Monitor (low level of risk).
Statin drugs	May increase side effects of drug.	Two case reports (355–473 mL/day cranberry juice drink (7% juice), and 473 mL/day 'cranberry juice'). ^{33,34}	Monitor (low level of risk).
Tacrolimus	May decrease drug levels.	Case report (2 g/day 'juice extract'; causality rated as possible (score 4) ⁶). ³⁵	Monitor (medium level of risk).
Warfarin	May alter INR (most frequently increase).	Case reports (where reported the dosage was often high, up to 2000 mL/day, juice strength undefined, 1.5–2 quarts (420–1893 mL/day) of cranberry juice cocktail; 113 g/day, cranberry sauce). ^{36–44} Clinical trials: no significant effect found in atrial fibrillation patients (250 mL/day cranberry juice cocktail), ⁴⁵ in patients on warfarin for a variety of indications (8 oz (236 mL)/day cranberry juice cocktail), ⁴⁶ but increase observed in healthy volunteers (juice concentrate equivalent to 57 g of dry fruit/day). ⁴⁷ No alteration of prothrombin time in patients on stable warfarin therapy (480 mL/day cranberry juice), ⁴⁸ or of thromboplastin time in healthy volunteers (600 mL/day cranberry juice). ³² See also note E.	Monitor (low level of risk at typical doses).
Dong Quai <i>Angelica polymorpha</i>			
Antiplatelet and anticoagulant drugs	May potentiate effect of drug.	Herb Alone and with Drug Aspirin: Clinical study found inhibitory effect on arachidonic acid-induced platelet aggregation (2 of 24 healthy volunteers) and on epinephrine-induced platelet aggregation (1 of 24) after several days' consumption of dried root and rhizome (1 g/day). Bleeding was not reported in these participants. Taking with aspirin did not further suppress platelet function and prothrombin time was not impaired. Two other participants reported abnormality in platelet aggregation or thrombin generation. ⁴⁹ Warfarin: Case reports (increased INR and PT), ⁵⁰ increased INR and PT, ⁵¹ increased INR and widespread bruising). ⁵¹	Monitor (low level of risk).
Echinacea <i>Echinacea angustifolia</i> , <i>Echinacea purpurea</i>			
Antiretroviral drugs	HIV non-nucleoside transcriptase inhibitors eg etravirine: May alter drug levels.	Clinical trial (<i>E. purpurea</i> root; HIV-infected patients); no effect overall, but large interindividual variability occurred (from near 25% decreases to up to 50% increases in drug levels). All maintained an undetectable viral load. ⁵²	Monitor (low level of risk).
	HIV protease inhibitors eg darunavir: May decrease drug levels.	Clinical trial (<i>E. purpurea</i> root; HIV-infected patients); no effect overall, but some patients showed a decrease by as much as 40%. All maintained an undetectable viral load. (Patients were also taking a low dose of ritonavir). ⁵³	Monitor (low level of risk).
Dextromethorphan	May increase drug levels.	Clinical study (healthy volunteers): no effect in CYP2D6 extensive metabolizers; increase in AUC without increase in drug level in one poor metabolizer. ⁵⁴	Monitor (very low level of risk).
Immunosuppressant medication	May decrease effectiveness of drug. ^{1,55}	Theoretical concern based on immune-enhancing activity of Echinacea.	Contraindicated.
Midazolam	Decreases drug levels when drug administered intravenously. ⁶	Clinical study (<i>E. purpurea</i> root). ⁵⁴	Monitor (medium level of risk) when drug administered intravenously.
Eleuthero (Siberian Ginseng) <i>Eleutherococcus senticosus</i>			
Atorvastatin	May cause liver injury due to high elevation of liver enzymes.	Case report (combination of "Siberian ginseng" and silymarin). ⁵⁶	Monitor (low level of risk).
Digoxin	May increase plasma drug levels.	Case report: apparent increase in plasma level, but herb probably interfered with digoxin assay ⁵⁷ (patient had unchanged ECG despite apparent digoxin concentration of 5.2 nmol/L). ⁵⁷ In a later clinical trial no effect observed on plasma concentration. ⁵⁸	Monitor (very low level of risk).
Evening Primrose Oil <i>Oenothera biennis</i>			
Phenothiazines	May decrease effectiveness of drug.	Reports of worsening epilepsy in schizophrenics. No causal association demonstrated and no effect observed in later trials. ⁵⁹	Monitor (very low level of risk).

Drug	Potential Interaction	Basis of Concern	Recommended Action
Garlic <i>Allium sativum</i> (See also Hypoglycemic herbs)			
Antiplatelet and anticoagulant drugs	Aspirin: May increase bleeding time. Clopidogrel: May potentiate effect of drug. Warfarin: May potentiate effect of drug. Large doses could increase bleeding tendency.	Concern may be overstated, as antiplatelet/anticoagulant drugs are often coadministered eg aspirin and warfarin. Herb Alone Case reports of increased bleeding tendency with high garlic intake. In three of the four cases the bleeding occurred after surgery. ⁶⁰⁻⁶³ Anecdotal: garlic taken shortly before testing interferes with platelet aggregation in control subjects. ⁶⁴ Single-dose studies, and studies demonstrating a beneficial effect on disordered function, including for example, in atherosclerosis, are excluded. Clinical studies (3 g/day or less of fresh garlic): inhibited platelet aggregation in three trials ¹ (about 2.4–2.7 g/day; patients and healthy volunteers); ⁶⁵⁻⁶⁷ but no effect on platelet aggregation in one trial ¹ (about 1–1.8 g/day; patients). ⁶⁸ decreased serum thromboxane in one trial (3 g/day; healthy volunteers). ⁶⁹ † See note 1. Clinical study (1.25–3.75 g/day): no effect on platelet aggregation, but women in the highest dose group experienced menorragia (as did women receiving 80 mg/day of aspirin) and nose bleeds were also reported in 24% of those receiving the highest dose of garlic. ⁷⁰ See note K. Clinical studies (4.2–5 g/day of fresh garlic; patients and healthy volunteers): no effect on platelet aggregation, fibrinogen level, prothrombin time, whole blood coagulation time. ⁷¹⁻⁷³ Clinical studies (8–10 g/day of fresh garlic; healthy volunteers): inhibited platelet aggregation and increased clotting time. ⁷⁴⁻⁷⁵ Herb and Drug Aspirin: No published studies. Clopidogrel: Garlic tablet ("odorless", dose undefined) added to improve drug therapy, reduced platelet hyperactivity in two patients. ⁶⁴ Warfarin: Two cases of increased INR and clotting times, very few details (garlic pearls, garlic tablets; dosage undefined). ⁷⁶ Clinical trial: no effect in healthy volunteers (enteric-coated tablets equivalent to 4 g/day of fresh garlic). ⁴⁷	Monitor at doses equivalent to ≥ 3 g/day fresh garlic (low level of risk). Stop taking at least one week before surgery.
HIV protease inhibitors	Decreases drug level.	Ritonavir-boosterd atazanavir: Case report (6 stir-fried garlic cloves three times per week). ⁷⁷ Saquejavi: Two clinical studies (garlic extract, standardised for allicin content) with healthy volunteers ⁷⁸⁻⁷⁹ – in one study ⁷⁹ the effect was minor with large variability in results.	Monitor (medium level of risk).
Ginger <i>Zingiber officinale</i>			
Antacids	May decrease effectiveness of drug.	Theoretical concern since ginger increases gastric secretory activity <i>in vivo</i> (animals). ¹ Heartburn has been reported by some patients, although a review of clinical studies involving pregnant women using the herb found it to be a low risk. ⁸⁰	Monitor (low level of risk).
Antiplatelet and anticoagulant drugs	Phenprocoumon: May increase effectiveness of drug. Warfarin: Increased risk of spontaneous bleeding.	Case report (dosage undefined) - increased INR. ⁸¹ Concern based on antiplatelet activity and potential to inhibit thromboxane synthetase. Herb Alone Clinical studies: inhibition of platelet aggregation (5 g, divided single dose, dried ginger) in healthy volunteers, ⁸² and coronary artery disease patients (10 g, single dose, dried ginger), ⁸³ but no effect in healthy volunteers (2 g, single dose, dried ginger); ⁸⁴ or coronary artery disease patients (4 g/day, dried ginger); ⁸³ inhibition of platelet thromboxane production in healthy volunteers (5 g/day, fresh ginger). ⁸⁵ Herb and Drug Two case reports (dose unknown): bleeding ⁸⁶ , increase in INR but no bleeding. ⁸⁷ No pharmacokinetic or pharmacodynamic effects demonstrated in a clinical trial with healthy volunteers (3.6 g/day, dried ginger). ⁸⁸ Epidemiological study: ginger (as a complementary medicine) was significantly associated with an increased risk of self-reported bleeding in patients taking warfarin. ⁸⁹ These results should be viewed cautiously (see note L).	Monitor at doses equivalent to < 4 g/day dried ginger (low level of risk). Contraindicated unless under close supervision at doses equivalent to > 4 g/day dried ginger.

Drug	Potential Interaction	Basis of Concern	Recommended Action
Crizotinib	May increase side effects of drug due to increased drug level.	Case report (grated ginger, honey, lemon juice and hot water, up to more than 1 L/day). ⁹⁰	Monitor (medium level of risk).
Nifedipine	May produce a synergistic antiplatelet effect.	Clinical study (1 g/day, dried ginger) in healthy volunteers and hypertensive patients. ⁹¹	Contraindicated.
Ginkgo[®] <i>Ginkgo biloba</i>	Anticonvulsant medication eg carbamazepine, sodium valproate	Case reports: two with well-controlled epilepsy, ⁹² others anecdotal and uncertain. ^{93,95} One of these ⁹⁴ was subsequently analyzed as having probable causality (score 7). ⁹⁶	Monitor (medium level of risk). Increasing the intake of vitamin B6 may be advisable for patients taking anticonvulsants. ⁹⁴
Antiplatelet and anticoagulant drugs	Prolongation of bleeding and/or increased bleeding tendency	<p>Concern based on antiplatelet activity.</p> <p>Bleeding events associated with Ginkgo alone or in combination with these and other drugs have been reported but a causal relationship was not established conclusively. Although a retrospective population-based study found risk of hemorrhage was associated with elderly patients (65 years or older) who were taking Ginkgo alone.⁹⁷</p> <p>Herb Alone</p> <p>Rare case reports of bleeding.⁹⁸⁻¹⁰⁰</p> <p>Meta-analysis of randomized, placebo-controlled trials (healthy volunteers and patients): results indicate standardised Ginkgo extract does not increase the risk of bleeding.¹⁰¹ Randomized, 5-year trial (elderly participants; Ginkgo 50:1 extract, 240 mg/day): no significant difference in incidence of non-monic events.¹⁰²</p> <p>Herb and Drug</p> <p>Retrospective population-based study in Taiwan: the relative risk of hemorrhage associated with the use of Ginkgo extract combined with drugs (clopidogrel, clostazol, ticlopidine, warfarin) was not significant.⁹⁷</p> <p>See also note P.</p> <p>Aspirin: Case reports (2, bleeding,⁹⁸ one, extensive bruising after a fall – although possibly high Ginkgo dose (400 mg/day, undefined)).¹⁰³ Clinical studies: no additional effect on platelet function, platelet aggregation or bleeding time.¹⁰⁴⁻¹⁰⁶ no increase in vascular adverse events, including hemorrhages, in acute stroke patients despite the high dose (Ginkgo preparation, providing 200 mg/day of flavone glycosides and 45 mg/day of terpene lactones; taken for 6 months).¹⁰⁷</p> <p>Clostazol: Clinical studies with healthy volunteers (Ginkgo extract (undefined): single dose 120 mg) – bleeding time prolonged; no change in platelet aggregation or clotting time, and no significant correlation between prolongation of bleeding time and inhibition of platelet aggregation;¹⁰⁸ no effect on pharmacokinetics or bleeding time, the increase in platelet aggregation was not significant (Ginkgo extract (undefined): 160 mg/day).¹⁰⁹</p> <p>Clopidogrel: Case report (bruising and bleeding).¹¹⁰ Clinical study with healthy volunteers (Ginkgo extract (undefined): single dose 120 mg) – no effect on platelet aggregation, bleeding times.¹⁰⁸</p> <p>Ticlopidine: Case report (bleeding).⁹⁹ Clinical studies: no significant additional effect on bleeding time or platelet aggregation (Ginkgo 50:1 extract: single dose 80 mg; healthy volunteers).¹¹¹ and at the higher dose (120 mg/day) did not affect drug levels.¹¹² Increased inhibitory response of platelets to testing with two agonists (ie antiplatelet effect) for drug and herb compared with drug alone, although effect was small and statistical and clinical significance is unknown (Ginkgo extract (undefined): 160 mg/day; pilot study of patients who had an acute ischemic stroke or transient ischemic attack).¹¹³ Improved antiplatelet effects in clopidogrel-resistant patients undergoing carotid stenting without hematologic or adverse effects, such as decreased platelet count, punctate-site hematomata (Ginkgo extract (undefined): 160 mg/day; small patient numbers).¹¹⁴ Postmarketing study (80–160 mg/day of undefined Ginkgo extract): incidence of bleeding events in 4831 patients was 0.52%. i.e. 25 patients; the severity was mild in 19 patients, moderate in 3 and severe in 3.¹¹⁵</p> <p>Warfarin: Case report (bleeding).⁹⁸ Clinical studies (healthy volunteers and patients): no additional effect on INR, platelet aggregation, coagulation parameters or plasma drug level.^{108,116,117} A retrospective analysis of US veteran's medical records (2008–2014) found taking Ginkgo (dose and preparations unknown) concurrently with warfarin was significantly associated with higher risk of bleeding.¹¹⁸ See also note Q.</p>	Monitor (low level of risk), although additional caution may be warranted for the elderly and/or those taking warfarin.

Drug	Potential Interaction	Basis of Concern	Recommended Action
Antipsychotic medication eg haloperidol, olanzapine, clozapine	General: May potentiate the efficiency of drug in patients with schizophrenia, by reducing symptoms.	Randomized controlled trials [1]: Ginkgo 50:1 extract: 120-360 mg/day, for schizophrenic patients taking haloperidol, olanzapine, clozapine, chlorpromazine, sulphide, or a mixture (clozapine, chlorpromazine, sulphide, perphenazine and haloperidol). ^{19,20} Five of 8 trials reported on adverse effects, no difference between Ginkgo and placebo for total scores, the results for subscores varied in two trials (generally favoring Ginkgo), but without serious side effects; in one trial, 2 patients who received placebo and experienced treatment failure were then treated with Ginkgo alone at double the dose (480 mg/day) and had severe delusions after about 2 weeks. ¹⁹	Prescribe cautiously. Reduce drug if necessary in conjunction with prescribing physician.
Risperidone: May potentiate adverse effects of drug or cause idiosyncratic reaction.	Two case reports (mood dysregulation, 160 mg/day of undefined extract, ²¹ triptipramine, 160 mg/day of undefined extract). ²² Incidence of adverse effects not significantly different between groups in two controlled studies (schizophrenia, dose unknown, ²³ and autistic disorders in children 6 to 7 years, 80-120 mg/day of undefined extract). ²⁴	Clinical study with healthy volunteers (Ginkgo 50:1 extract: 240 mg/day) found an increase in plasma levels, due to large interindividual variability, not considered to be of clinical importance. (The drug's pharmacokinetics are known for considerable intra- and interindividual variability). ²⁵	Monitor (low level of risk).
Antiretroviral drugs	HIV integrase inhibitors eg raltegravir: May alter drug levels	Clinical study with healthy volunteers (Ginkgo 50:1 extract: 240 mg/day) found an increase in viral load after ongoing suppression (multiple supplements but the main one was an unspecified Ginkgo product (300 mg/day); ¹⁷ causality rated as probable (score 6) ⁹ , ⁹⁶	Monitor (medium level of risk).
Atorvastatin			
Benzodiazepines	May alter drug level.	Alprazolam: Clinical trial in healthy volunteers found no effect (Ginkgo 50:1 extract: 240 mg/day). ¹²⁸ Diazepam: Clinical trial in healthy volunteers found no effect (Ginkgo 50:1 extract: 240 mg/day). ¹²⁹ Midazolam: Clinical trials in healthy volunteers found conflicting results on drug levels: increased Ginkgo 50:1 extract: 360 mg/day; ¹³⁰ decreased (Ginkgo 50:1 extract: 240 mg/day); ¹³¹ and no effect (Ginkgo 50:1 extract: 240 mg/day). ¹³²	Monitor (low level of risk).
Hypoglycemic drugs	General (sulfonylureas): May decrease the hypoglycemic activity. See also <i>Glipizide</i> and <i>Tolbutamide</i>	Theoretical extrapolation from clinical studies (very small numbers of participants): improved pancreatic beta-cell insulin production in response to glucose load (healthy /normal glucose tolerant individuals), ¹³³ and in diabetics (only those with hyperinsulinemia treated with a range of oral hypoglycemic drugs and those with pancreatic exhaustion, and not diet-controlled diabetics i.e. those with medium to high insulin resistance), although no improvement in glucose metabolism (e.g. blood glucose) and no glycemia-related adverse effects - this suggests increased hepatic clearance of insulin and hypoglycemic agents. ¹³⁴ Later study confirmed no adverse effect on insulin resistance (small number of healthy volunteers, prediabetics and diabetics taking oral hypoglycemic drugs). ¹³⁵ Dose in each trial was Ginkgo 50:1 extract: 120 mg/day.	Monitor (low level of risk).
<i>Glipizide</i> : May cause hypoglycemia.		Observation from aborted trial: hypoglycemia occurred in volunteers with normal glucose tolerance within 60 minutes. ¹³⁶ Ginkgo 50:1 extract was administered as a single dose of 120 mg. ¹³⁷	Monitor (low level of risk).
<i>Metformin</i> : May enhance effectiveness of drug.		Clinical trial with very small number of diabetics taking a variety of metformin daily doses (0.5-2.55 g; Ginkgo 50:1 extract: 120 mg/day), effect on pharmacokinetics of drug were not substantially altered in those taking 0.5 g/day or less of the drug. No effect observed in healthy volunteers. ¹³⁶ Clinical trial (patients ineffectively managed): significantly improved glycemic parameters including HbA1c (Ginkgo 50:1 extract: 120 mg/day). ¹³⁸	Monitor (low level of risk in conjunction with prescribing physician).
<i>Pioglitazone</i> : May increase drug level.		Clinical trial with healthy volunteers (Ginkgo 50:1 extract: 120 mg/day). ¹³⁹	Monitor (low level of risk).
<i>Tolbutamide</i> : May decrease effectiveness of drug.		Clinical trials with healthy volunteers: nonsignificant reduction in glucose-lowering effect of drug (Ginkgo 50:1 extract: 360 mg/day); ¹³⁰ pharmacokinetics not altered (Ginkgo 50:1 extract: 240 and 360 mg/day). ^{130,132}	Monitor (low level of risk).
Nifedipine	May increase drug levels or side effects.	Clinical studies found mixed results for mean plasma drug level: increase (120 mg/day, undefined), ¹⁴⁰ although these results considered preliminary/inaccurate as AUC was not measured; ¹⁴¹ and no effect (240 mg/day, although results probably not robust as the herb was only administered for one day). ¹⁴² However, in the latter study, maximal plasma drug level and heart rate was increased with adverse drug reactions for participants with highest plasma drug levels (headache, dizziness, hot flashes). ¹⁴²	Monitor at doses >240 mg/day (medium level of risk). Contraindicated for higher doses.
Omeprazole	May decrease drug levels.	Clinical trials with healthy volunteers found conflicting results on drug levels: decreased (Ginkgo 50:1 extract: 280 mg/day; ¹⁴³ AUC decreased by 27-72% depending on genotype); ¹⁴³ and no effect (Ginkgo 50:1 extract: 240 mg/day). ¹³²	Monitor (low level of risk).

Drug	Potential Interaction	Basis of Concern	Recommended Action
Statin drugs	May decrease drug levels.	Meta-analysis of 8 randomized controlled trials conducted in China (and of low methodological quality) found that compared with statins alone, the combination of statins and Ginkgo achieved significantly greater improvements in lipids in patients with dyslipidemia. See also note R. In four trials atorvastatin was administered simvastatin in three and rosuvastatin in one trial. ¹⁴⁴ Atorvastatin: Clinical study with healthy volunteers (Ginkgo 50:1 extract: 360 mg/day). No adverse pharmacodynamic effect was observed. ¹⁴⁵ Simvastatin: Clinical study with healthy volunteers (Ginkgo 50:1 extract: 240 mg/day) – drug levels decreased, but active metabolite drug levels not affected. Pharmacodynamics (cholesterol lowering) of the drug not significantly affected, although there was a trend towards reduced ability to lower LDL-cholesterol. ¹⁴⁶	Monitor (low level of risk).
Tadalafil	May cause bleeding.	Case report (hematoma after surgery; patient also taking analgesic(s)). ¹⁴⁷	Monitor (low level of risk).
Talinolol	May increase drug levels.	Clinical trial with healthy volunteers. ¹⁴⁸	Monitor (low level of risk).
Golden Seal <i>Hydrastis canadensis</i>			
Drugs which displace the protein binding of bilirubin eg phenylbutazone	May potentiate effect of drug on displacing bilirubin.	Theoretical concern based on <i>in vitro</i> data (displaced bilirubin from albumin) and in animals with high dose of berberine by injection (reduced bilirubin serum protein binding). ¹⁴⁹	Monitor (low level of risk).
Nitazepam	May increase drug level.	Clinical trial. ¹⁵⁰	Monitor (low level of risk).
Green Tea <i>Camellia sinensis</i> (See also Polyphenol-containing and/or Tannin-containing herbs)			
Boronic acid-based protease inhibitors eg boroxenimib	May decrease efficacy of drug.	Theoretical concern based on initial <i>in vitro</i> data and in vivo animal study (green tea constituent: EGCG reduced tumor cell death induced by drug). ¹⁵¹ However, a further <i>in vivo</i> animal study found EGCG was not antagonistic to the activity of the drug. ¹⁵² See note S.	Contraindicated at high doses (around 600 mg/day EGCG or 1 g/day green tea catechins). ¹ More information required for doses below this level.
Digoxin	May decrease drug levels.	Clinical study with healthy volunteers (green tea extract providing 300 mg catechins). ¹⁵³	Monitor (medium level of risk at substantial doses of catechins).
Folate	May decrease absorption.	Clinical study with healthy volunteers. ¹⁵⁴ Clinical significance unclear, as was a one-day study (ie not ongoing administration), with 50 mg of green tea catechins administered before, during and up to 2 hours after folate (for a total of 250 mg of catechins).	If taken simultaneously, may need to increase dose of folate. The effect may be relatively small - more information is required.
Immunosuppressives eg tacrolimus	May increase drug levels.	Case report (patient was a CYP3A4 poor metabolizer). ¹⁵⁵	Monitor (medium level of risk).
Nadolol	May increase drug levels.	Clinical studies with healthy volunteers (two single doses, simultaneous ingestion, green tea extract containing 52 mg and 156 mg catechins); ¹⁵⁶ single dose, simultaneous and ingestion 1 hour prior, brewed green tea (4.5 g), ¹⁵⁷ although pulse rate and blood pressure were unchanged. ¹⁵⁶	Monitor (medium level of risk).
Sildenafil	May increase bioavailability of drug.	Clinical study with healthy volunteers (2 g, single dose, green tea powder containing 60 mg catechins). Blood pressure and electrocardiogram were unchanged. ¹⁵⁸	Monitor (low level of risk).
Statin drugs	May increase drug level and side effect of drug.	Fluvastatin: Clinical study with healthy volunteers. No significant effect on plasma concentrations for single doses of brewed green tea (300 mL) or extract providing 150 mg EGCG. ¹⁵⁹ Rosuvastatin: Clinical study with healthy volunteers found a slight, likely clinically irrelevant, decrease in drug levels for ongoing administration (300 mg/day of EGCG). ¹⁶⁰ Simvastatin: Case report of muscle pain, which is a known side effect (3 cups/day). ¹⁶¹ Subsequently analyzed as having probable causality (score 7). ¹⁶² Pharmacokinetic evaluation indicated green tea (1 cup, single dose) increased the bioavailability of simvastatin in this patient by a large amount (75%). ¹⁶¹ Ongoing administration of green tea beverage (healthy volunteers): ¹⁶² the increase was much smaller (7%); probably not clinically relevant), although in 25% of participants the increase was about 2-fold (dose: 335 mg/day of catechins); at a higher dose (638 mg/day of catechins), the increase in bioavailability was 28%, and the extent of the interindividual variability was similar.	Monitor (low level of risk).

Drug	Potential Interaction	Basis of Concern	Recommended Action
Sunitinib	May reduce bioavailability of drug.	Case report (effect appeared dose-dependent). Considering the pharmacokinetic data (interaction in mice), the authors recommended avoiding green tea intake or leaving an interval of 4 hours between beverage and drug intake. ¹⁶³	Contraindicated , unless taken at least 4 hours apart.
Warfarin	May decrease effectiveness of drug.	Case report (decreased INR; brewed green tea: 0.5–1 gallon/day). ¹⁶⁴	Monitor (very low level of risk).
Hawthorn <i>Crataegus monogyna</i> , <i>Crataegus laevigata</i> (<i>Crataegus oxyacantha</i>) (See also Polyphenol-containing and/or Tannin-containing herbs)	Clinical studies indicate a (beneficial) synergistic effect. ^{165,166} Pharmacokinetics not affected in a clinical study (healthy volunteers). ¹⁶⁷	Monitor (low level of risk).	
Digoxin	May increase effectiveness of drug.	Controlled trials where drugs known to be taken by all or many heart disease patients, blood pressure decreased significantly (2 trials). ^{168,169} decreased nonsignificantly (1 trial) ¹⁷⁰ and was unchanged (1 trial). ¹⁷¹ Significant decrease in blood pressure observed in diabetics taking hypotensive drugs (1 trial). ¹⁷²	Monitor (low level of risk).
Hypotensive drugs	May increase effectiveness of drug.	Controlled trials where drugs known to be taken by all or many heart disease patients, blood pressure decreased significantly (2 trials). ^{168,169} decreased nonsignificantly (1 trial) ¹⁷⁰ and was unchanged (1 trial). ¹⁷¹ Significant decrease in blood pressure observed in diabetics taking hypotensive drugs (1 trial). ¹⁷²	Monitor (low level of risk).
Horsetail <i>Equisetum arvense</i>	May cause virological breakthrough.	Two case reports (supplements containing horsetail). ¹⁷³	Monitor (medium level of risk).
Antiretroviral drugs			
Hypoglycemic herbs (See also Ginkgo, Korean Ginseng, Milk Thistle, St John's Wort)	May potentiate hypoglycemic activity of drug.	Theoretical based on potential additive effects, although there are many examples of clinical trials in which herbs have been administered to diabetics who were using hypoglycemic medications, and despite improvements in glycemic parameters no adverse hypoglycemic effects were observed. Examples: <ul style="list-style-type: none">▪ in uncontrolled trials, high dose, long-term administration of Gymnema extract (equivalent to 10–13 g/day dried leaf) reduced insulin and hypoglycemic drug requirements in diabetics.^{174,175}▪ Several trials have found no effect for garlic on blood glucose in type 2 diabetes, although in a double-blind, placebo-controlled trial (using enteric-coated tablets), a reduction in the dosage of oral hypoglycemic drugs was required (these patients had baseline fasting blood glucose above 8.0 mmol/L (144 mg/dL)).¹⁷⁶	Prescribe cautiously and monitor blood sugar regularly. Warn patient about possible hypoglycemic effects. Reduce drug if necessary in conjunction with prescribing physician.
Hypoglycemic drugs including insulin			
Kava <i>Piper methysticum</i>	Herb Alone and with Drug	Aspirin: Clinical study in Fiji with volunteers who were not kava drinkers (NKO), occasional (once/week; OK) or regular drinkers (RKO: every week, 20 or more bowls/day). Platelet aggregation was in the normal range for all groups (baseline), but after single dose of aspirin (100 mg) there was a significant difference between NKO and RKO, and OK and RKO, with the platelet aggregation <i>inhibited</i> (not decreased as much) in RKO. There was no significant difference between the groups when 300 mg was taken (aggregation decreased to a similar extent). The results suggest regular kava drinking (i.e. relatively high levels of kavalactones) may decrease aspirin sensitivity. ¹⁷⁷	Monitor (very low level of risk at typical doses).
Antiplatelet and anticoagulant drugs	May potentiate effect of drug.	Theoretical concern based on deliberations of German Commission E ¹⁶ and the anxiolytic activity of kava. Two apparent case reports (kava + benzodiazepines (alprazolam, flunitrazepam)). ^{178,179} Clinical trials with healthy volunteers: no additional side effects observed for kava (extract containing 240 mg/day of kava lactones) + benzodiazepine (bromazepam). ¹⁸⁰ and kava (extract containing 210 mg/day of kavalactones) + alcohol. ¹⁸¹ Clinical study with healthy volunteers: no effect on pharmacokinetic parameters of midazolam (extract provided 253 mg/day of kavalactones). ¹⁵⁰	Monitor (low level of risk).
CNS depressants eg alcohol, barbiturates, benzodiazepines	Potentiation of drug effects.	Case reports. ^{182,183} Although, kava is unlikely to be responsible for central dopaminergic antagonism (experimental model) ¹⁸⁴ and kava reduced parkinsonism induced by neuroleptic drugs (observational study, psychiatric patients). ¹⁸⁵	Contraindicated unless under close supervision.
<i>L-Dopa</i> and other Parkinson's disease treatments	Possible dopamine antagonist effects.	Haloperidol: Case report (patient consumed kava beverage i.e. probable high dose). ¹⁸⁶	Monitor (low level of risk at typical doses)
Other CNS drugs	May potentiate adverse effect possibly by decreased metabolism of drug.	Ropinirole: Case report (patient consumed kava beverage and kava tablets i.e. probable high dose). ¹⁸⁶	

Drug	Potential Interaction	Basis of Concern	Recommended Action
Korean Ginseng <i>Panax ginseng</i>			
Antihypertensive medications including nifedipine	General: May decrease effectiveness of drug.	Theoretical concern since hypertension is a feature of GAS. Clinical significance unclear. ¹ Assessment of 316 hospital patients found Korean ginseng to have a contrary effect only in a very small percentage: blood pressure increase in 5% of hypertensives, increase in 3% and decrease in 2% of normotensives; decrease in 6% of hypotensives. ³⁸ No information on concurrent medications. <i>Note for clinical trial data below:</i> Acute, single-dose trials excluded. High doses used in several trials.	Monitor (very low level of risk).
Herb Alone		Clinical trials: no significant effects found in healthy volunteers, ^{183,189} those with metabolic syndrome, ¹⁹⁰ type 2 diabetes ¹⁹¹ or glaucoma, ¹⁹² although baseline blood pressure may be a factor. ¹⁹⁰	
Herb and Drug		Clinical trials: <i>decreased</i> blood pressure in essential hypertension, ¹⁹³ and coronary artery disease ¹⁹⁴ but no effect in white coat hypertension ¹⁹³ and essential hypertension. ¹⁹⁵	
Nifedipine: May increase drug levels.	General: May potentiate effects of drug.	Clinical trial (results considered preliminary/inaccurate as AUC was not measured, and species not defined). ¹⁴⁰	Monitor (low level of risk).
Antiplatelet and anticoagulant drugs		Herb Alone Two epidemiological studies in Korea: long-term intake (3-5 years) prolonged plasma clotting times (APTT). ^{196,197} and decreased platelet aggregation. ¹⁹⁶ (Dosage in Korea is generally high) Clinical trial (healthy volunteers): inhibited platelet aggregation, but no effect on coagulation (PT, APTT). ¹⁹⁸ Case reports: perioperative bleeding and impaired coagulation, possibly due to high preoperative intake of undefined ginseng (1 case); ¹⁹⁹ postmenopausal women with spontaneous hematomas (3 cases). ²⁰⁰	Monitor (low level of risk).
Herb and Drug		Aspirin: Clinical study found inhibitory effect on arachidonic acid-induced platelet aggregation (1 of 24 healthy volunteers) after several day's consumption of concentrated extract (providing 30 mg/day of ginsenosides); no clinically relevant bleeding events occurred. Taking with aspirin did not further suppress platelet function and prothrombin time was not impaired. ⁴⁹	
Acenocoumarol: May decrease effectiveness of drug.		Case report (decreased INR, herb dose unknown, causality rated as possible (score 4) ^b). ¹	Monitor (low level of risk).
Warfarin: May decrease effectiveness of drug.		Herb and Drug Two cases reported (decreased INR without thrombotic episode, likely modest level of ginsenosides, ²⁰¹ thrombosis, ginseng product undefined). ²⁰² No effect demonstrated in three clinical trials (healthy volunteers and patients) for INR, prothrombin time and platelet aggregation. ^{203,205} Although the design of the trials has been criticized. See note U. ²⁰⁶	Monitor (low level of risk).
CNS stimulants	May potentiate effects of drug. ¹	Theoretical concern since CNS stimulation is a feature of GAS. Clinical significance unclear.	Monitor (low level of risk).
HIV integrase inhibitors eg raltegravir	May potentiate adverse effect possibly by altered metabolism.	Case report (elevated liver enzymes, dosage unknown, causality rated as probable (score 6) ^c). ²⁰⁷	Monitor (low level of risk)
Hypoglycemic drugs including insulin	May potentiate hypoglycemic activity of drug. ³⁵	Theoretical concern based on clinically observed hypoglycemic activity of ginseng in newly diagnosed type 2 diabetes. ²⁰⁸ Clinical significance unclear. No effect on insulin sensitivity or beta-cell function after very high doses in newly diagnosed type 2 diabetics or those with impaired glucose tolerance. ²⁰⁹ Korean red ginseng (2.7 g/day) reduced the requirement for insulin in about 40% of diabetics in a small uncontrolled trial. ²¹⁰ No adverse effects in three trials of type 2 diabetes well controlled with diet and/or oral hypoglycemic drugs. ^{193,211,212}	Monitor (low level of risk).
Imatinib	May potentiate adverse effect possibly by altered metabolism.	Case report (hepatotoxicity, ²¹³ causality rated as probable (score 5) ^b). ³⁶	Monitor (low level of risk).
Lamotrigine	May cause tide effect due to elevated drug level.	Case report (combined with deer antler velvet; DRESS syndrome; causality rated as probable (score 5) ^b). ²¹⁴	Monitor (medium level of risk).

Drug	Potential Interaction	Basis of Concern	Recommended Action
MAO inhibitors eg phenelzine	May cause side effects such as headache, sleeplessness, tremor.	Case reports. ²¹⁵⁻²¹⁷	Contraindicated.
Midazolam	May decrease drug level.	Clinical studies with healthy volunteers; effect on drug levels conflicting – decreased (extract providing about 45 mg/day of ginsenosides Rb1, Rb2, RC, Rd, Re, Rg1, Rg3), ¹⁴ and no relevant effect (extracts providing about 62 mg/day of ginsenosides Rb1, Rb2, RC, Re, Rg1, ²¹⁸ and 85 mg/day of ginsenosides Rb1, Rb2, RC, Rd, Re, Rg1, Rg3, Rh1). ²¹⁹	Monitor (low level of risk).
Sildenafil	May potentiate effects of drug.	Theoretical concern based on <i>in vitro</i> studies which show ginseng increases nitric oxide release from corpus cavernosum tissue. ^{20,221}	Monitor (very low level of risk).
Laxative (anthraquinone-containing) herbs eg cascara (<i>Frangula purshiana</i>), yellow dock (<i>Rumex crispus</i>)			Avoid excessive doses of laxatives. Maintain patients on a high potassium diet.
Antiarrhythmic agents	May affect activity if potassium deficiency resulting from long-term laxative abuse is present.	German Commission E and ESCOP recommendation. ^{15,222}	
Cardiac glycosides	May potentiate activity if potassium deficiency resulting from long-term laxative abuse is present.	German Commission E and ESCOP recommendation. ^{15,222}	Monitor (low level of risk at typical doses).
Potassium-depleting agents eg thiazide diuretics, corticosteroids, licorice root (<i>Glycyrrhiza glabra</i>)	May increase potassium depletion.	German Commission E and ESCOP recommendation. ^{15,222}	Avoid excessive doses of laxatives. Maintain patients on a high potassium diet.
Licorice^v <i>Glycyrrhiza glabra</i>	General: May decrease effectiveness of drug.	When consumed in sufficient doses, licorice can cause pseudogout and high blood pressure. Herb or Constituent Alone Hypertension demonstrated in case reports, usually from long-term intake and/or very high dose. ²²³ Hypokalemic paralysis reported (184 mg/day of glycyrrhizin for 2 months), although hypertension was mild, possibly due to coexisting sodium wasting related to uropathy from prostate cancer. ²²⁴ Dramatically elevated blood pressure with hypertensive retinopathy and nephropathy reported (225 mg/day of glycyrrhizin for 3 years). ²²⁵ Clinical studies (up to 200 g/day of licorice); dose-dependent relationship found between licorice and increase in blood pressure, more pronounced effect in hypertensive patients than in normotensive volunteers; adverse effect greater in women, and effect shown for dose as low as 50 g/day of licorice. (75 mg/day of glycyrrhetic acid = 130 mg/day of glycyrrhizin) ^v taken for 2 weeks. ²²⁶⁻²²⁸ Other studies show variation of effects on blood pressure (see note X) – renal function may be a factor. ²²⁹ The increase in blood pressure after taking glycyrrhetic acid (874 mg/day of glycyrrhizin) was more pronounced in salt-sensitive than salt-resistant volunteers. ²²⁹ The mechanism involves increased extracellular volume and enhanced pressure wave reflection from the peripheral circulation (licorice containing 290-370 mg/day of glycyrrhizin), taken for 2 weeks in normotensive volunteers, ²²⁹ although the results may be underestimated if measurements are taken only at rest. ²²⁹ Clinical study to establish a no-effect level for glycyrrhizin (healthy female volunteers); significant results (eg blood pressure, serum potassium and aldosterone) compared to controls found for daily dose of 4 mg/kg (220-332 mg/day) taken for 8 weeks, but no effect at lower doses of 1-2 mg/kg (55-166 mg/day) of glycyrrhizin. ²²³ Herb and Drug Case reports (licorice tea, 3 L/day, patient still hypertensive despite treatment with drugs; ²³⁴ decoction of Chinese herbs containing 5 g licorice; taken for 14 days). ²³⁵	Avoid long-term use at doses > 100 mg/day glycyrrhizin unless under close supervision. ^v Place patients on a high potassium diet.
ACE-inhibitor: May mask the development of pseudogout and hypertension.		Case report (patient consumed licorice herbal medicine (200-240 mg/day glycyrrhizin)). Drug dosage was reduced, leading to pseudogout and hypertension. ²³⁶ See note Z.	Avoid long-term use at doses > 100 mg/day glycyrrhizin unless under close supervision. ^v Place patients on a high potassium diet.
Cilostazol	May cause hypokalemia which can potentiate the toxicity of the drug.	Case report (patient taking 150 mg/day of glycyrrhizin). Serum potassium levels were stable prior to administration of drug. ²³⁷	Monitor (medium level of risk). Place patients on a high potassium diet.

Drug	Potential Interaction	Basis of Concern	Recommended Action
Corticosteroids	Cortisol: May potentiate the action (rather than increase level of drug).	Inhibition of the enzyme 11beta-HSD2 by glycyrrhizin leads to an increased level of cortisol in the kidney. This does not happen in the liver. The plasma half-life of cortisol may be prolonged when herb and drug are coadministered, but drug concentrations remain normal, possibly because of a concomitant fall in cortisol production. ²³⁸ Prolonged half-life of cortisol may suggest the potential for licorice to prolong clearance (and hence, activity) of the drug. <i>Studies involving patients with Addison's disease or on hemodialysis are not listed here.</i>	Monitor (very low level of risk at typical doses).
Herb or Constituent Alone		Clinical studies with healthy volunteers ^{227,229,239,245} and patients with essential hypertension ²²⁷ (ongoing oral administration); increase in urinary excretion of cortisol, but no significant change in plasma cortisol ^{227,229,239,245} (although plasma cortisone decreased ^{229,240,246}) and diurnal variation of plasma cortisol was unaffected. ²⁴² Dosage was high: 100–200 g/day of licorice candy (containing glycyrrhizin or glycyrrhetic acid equivalent to 262–2440 mg/day of glycyrrhizin ^y) ^{227,241,242,253} 3.5 g/day of licorice tablets containing 266 mg/day of glycyrrhizin, ²⁴³ 4.8 g/day of licorice extract (containing glycyrrhetic acid = 587 mg/day of glycyrrhizin), ²⁴⁴ 225 mg/day glycyrrhizin, ²³⁹ glycyrrhetic acid (= 227–874 mg/day glycyrrhizin). ^{227,240} Clinical study with healthy volunteers and hypertensive patients (single dose, placebo-controlled; oral administration of glycyrrhetic acid equivalent to 874 mg/day of glycyrrhiziny ^w): increased plasma cortisol/cortisone ratio (due mostly to a decrease in plasma cortisone), salivary cortisol increased. ²⁴⁷ Clinical study with healthy volunteers (topical application of a cream containing glycyrrhetic acid): no effect on plasma cortisol. ²⁴⁸	
Herb or Constituent and Drug		Clinical studies: increased plasma half-life of cortisol (oral administration of licorice candy (200 g/day, containing 580 mg/day glycyrrhizin) + intravenous cortisol to 7 healthy volunteers ²⁴¹ ; oral administration of glycyrrhetic acid = 227 mg/day of glycyrrhiziny ^w + oral cortisol) to 2 volunteers). ^{249,250} See also Note A4. <i>Ex vivo</i> study (skin samples from healthy volunteers and patients with psoriasis and eczema): glycyrrhetic acid and drug (topically applied): activity of hydrocortisone potentiated by glycyrrhetic acid. ²⁵¹	Monitor (low level of risk at typical doses)
Prednisolone: May potentiate the action or increase level of drug.		Herbal Constituent and Drug Two clinical studies with healthy volunteers (oral administration of glycyrrhizin or glycyrrhetic acid, ^w prednisolone administered intravenously) increased drug level ²⁵² and increased prednisolone/prednisone ratio ²⁵³ in urine and plasma. ²⁵³ Dosage was high: 200 mg/day glycyrrhizin, ²⁵² and 400 mg/day glycyrrhetic acid (= 700 mg/day glycyrrhizin). ²⁵³	Avoid long-term use at doses > 100 mg/day glycyrrhizin unless under close supervision. ^y Place patients on a high potassium diet.
Digoxin		Herb Alone Hypokalemia demonstrated in case reports and clinical studies, usually from long-term intake and/or very high dose, however effect has been demonstrated in sensitive individuals at low doses (licorice containing 100 mg/day of glycyrrhizin). Side effects would be common at 400 mg/day of glycyrrhizin. ^{227,254,255} Herb and Drug Case report (patient taking herbal laxative containing licorice (1.2 g/day) and rhubarb (<i>Rheum</i> spp., 4.8 g/day)). In addition to digoxin, patient was also taking a potassium-depleting diuretic. ²⁵⁶	
Spironolactone (potassium-sparing diuretic): Reduce side effects of drug.		Clinical study: in women with PCOS addition of licorice extract (containing about 463 mg/day glycyrrhizin) reduced side effects related to the diuretic activity of drug. ²⁵⁷	Monitor (low level of risk at typical doses).
Diuretics		Thiazide and loop (potassium-depleting) diuretics: the combined effect of licorice and the drug could result in excessive potassium loss. ^z	Contraindicated unless under close supervision at doses > 40 mg/day glycyrrhizin.
		Herb or Constituent Alone Hypokalemia demonstrated in case reports and clinical studies, usually from long-term intake and/or very high dose, ^{234,254,259,265} however effect has been demonstrated for ongoing treatment of glycyrrhizin as low as 80 mg/day ²⁵⁸ clinical trial (candy containing 40 mg/day of glycyrrhizin): decreased plasma potassium, with 20% of healthy volunteers hypokalemic in the first week. ²⁶⁶ Retrospective cohort study: of 389 elderly patients treated with two licorice-containing Japanese traditional medicines for 6–2788 days, 24.2% developed hypokalemia and of these patients, 35.3% were coadministered potassium-lowering drugs (loop or thiazide diuretics, glucocorticoids or other glycyrrhizin-containing preparations (less frequently)). ²⁶⁷ Full dose of these products provides about 70 mg/day of glycyrrhizin. ²⁶⁸	

Drug	Potential Interaction	Basis of Concern	Recommended Action
Immunosuppressives eg sirolimus	May decrease drug clearance.	Population pharmacokinetic study with 112 Chinese adult renal transplant recipients: clearance of sirolimus decreased in those patients with abnormal ALT values who were taking herbal formulations containing glycyrrhizin (route and dosage unknown). ²⁶⁹	Monitor (medium level of risk) in hepatically impaired patients.
Midazolam	May decrease drug level.	Clinical study with healthy volunteers (potassium salt of glycyrrhizin, equivalent to 287 mg/day of glycyrrhizin). ²⁷⁰	Monitor (low level of risk at typical doses).
Omeprazole	May decrease drug level.	Clinical study with healthy volunteers (potassium salt of glycyrrhizin, equivalent to 287 mg/day of glycyrrhizin). ²⁷¹	Monitor (low level of risk at typical doses).
Potassium-depleting drugs other than thiazide and loop diuretics eg corticosteroids, stimulant laxatives	May result in excessive potassium loss.	Concern based on known adverse effect of herb. Hypokalemia demonstrated in case reports and clinical studies usually from candy intake (high dose), however effect has been demonstrated in sensitive individuals at low doses (licorice containing 100 mg/day of glycyrrhizin). Side effects would be common at 400 mg/day of glycyrrhizin. ^{23,25,26}	Avoid long-term use at doses > 100 mg/day glycyrrhizin unless under close supervision. Place patients on a high potassium diet.
Terbutaline	May cause hypokalemia and apparent mineralocorticoid excess.	Case report ("nonspecific intake of licorice" with high intake of water (4-5 L/day) and excessive use of drug (3-4 times normal dose)). ²⁷²	Monitor (very low level of risk under normal circumstances).
Marshmallow Root <i>Althea officinalis</i>			
Prescribed medication	May slow or reduce absorption of drugs.	Theoretical concern based on absorbent properties of marshmallow root.	Take at least 2 hours away from medication.
Meadowsweet <i>Filipendula ulmaria</i> (See also Polyphenol-containing and/or Tannin-containing herbs)			
Warfarin	May potentiate effects of drug.	Theoretical concern based on <i>in vivo</i> animal study demonstrating anticoagulant activity (dosage unavailable). ²⁷³	Monitor (very low level of risk).
Milk Thistle™ <i>Silybum marianum</i>			
Domperidone	Increases drug levels, and therefore potential toxic side effects.	Clinical study with healthy volunteers (silymarin: 1000 mg/day). ²⁷⁴	Contraindicated at this dose, effect at typical doses not known.
Hypoglycemic drugs including insulin	May improve insulin sensitivity	Controlled trials: improved glycemic control and reduced insulin requirements in patients with type 2 diabetes and cirrhosis (silymarin: 600 mg/day), ²⁷⁵ although insulin requirements unchanged in another trial (silymarin: 200 mg/day). ²⁷⁶ Improved glycemic control in diabetes treated with hypoglycemic drugs (silymarin: 200 and 600 mg/day). ^{278,279} Improved blood glucose, blood insulin and insulin resistance in PCOS patients treated with metformin (silymarin: 750 mg/day), ²⁸⁰ but no effect on glucose metabolism in NAFLD patients including those with insulin resistance (silymarin: 280 and 600 mg/day). ^{24,27,282}	Prescribe cautiously and monitor blood sugar regularly. Warn patient about possible hypoglycemic effects. Reduce drug if necessary in conjunction with prescribing physician.
Immunosuppressives eg sirolimus	May decrease drug clearance.	Population pharmacokinetic study with 112 Chinese adult renal transplant recipients: clearance of sirolimus decreased in those patients with abnormal ALT values who were taking silymarin formulations (route and dosage unknown). ²⁶⁹	Monitor (medium level of risk) in hepatically impaired patients.
Losartan	May reduce efficacy of drug by inhibiting metabolism.	Clinical study (healthy volunteers; clinical significance unclear): inhibited metabolism of drug; the inhibition was greater in those of a particular CYP2C9 genotype (silymarin: 420 mg/day). ²⁸³ See note CC.	Monitor (low level of risk).
Metronidazole	May decrease absorption of drug, by increasing clearance.	Clinical Study with healthy volunteers (silymarin: 140 mg/day). ²⁸⁴	Monitor (medium level of risk).
Nifedipine	May delay the absorption rate of drug.	Clinical study with healthy volunteers (2x silymarin: 280 mg, single dose), but bioavailability unchanged and pharmacodynamic effects were minor. ²⁸⁵	Monitor (low level of risk).
Ornidazole	May increase drug levels.	Clinical study with healthy volunteers (silymarin: 140 mg/day). ²⁸⁶	Monitor (medium level of risk).
Talinolol	May increase drug levels.	Clinical study with healthy volunteers (silymarin: 420 mg/day). ²⁸⁷	Monitor (low level of risk).
Oregon Grape <i>Berberis aquifolium</i>			
Drugs that displace the protein binding of bilirubin eg phenylbutazone	May potentiate effect of drug on displacing bilirubin.	Theoretical concern based on <i>in vitro</i> data (displaced bilirubin from albumin) and in animals with high dose of berberine by injection (reduced bilirubin serum protein binding). ¹⁴⁹	Monitor (low level of risk).

Drug	Potential Interaction	Basis of Concern	Recommended Action
Phellodendron[®] <i>Phellodendron amurense</i>			
Drugs that displace the protein binding of bilirubin eg phenylbutazone	May potentiate effect of drug on displacing bilirubin.	Theoretical concern based on <i>in vitro</i> data (displaced bilirubin from albumin) and in animals with high dose of berberine by injection (reduced bilirubin serum protein binding). ¹⁴⁹	Monitor (low level of risk)
Immunosuppressives	Cyclosporin: Increase drug levels.	Observations in some transplant patients. ²⁸⁸ Clinical studies (600 mg/day of berberine): increased drug level but no renal toxicity or chronic rejection occurred in renal transplant patients, ²⁸⁸ mixed results in healthy volunteers: no effect and increased drug level, possibly due to timing – when intake was separated by 12 hours, the pharmacokinetics were not substantially altered. ²⁸⁸ Regarded as a beneficial interaction in China, as berberine allows the dose of drug to be decreased. ²⁸⁸	At substantial doses of berberine, contraindicated unless under close supervision and/or in contact with prescribing physician.
Tacrolimus: Increase drug levels and hence, adverse effects.		Case report (600 mg/day of berberine in a 16-year-old), ²⁹⁰ causality rated as possible (score 4) ⁸¹ .%	Monitor (medium level of risk at substantial doses of berberine).
Midazolam	May increase drug levels.	Clinical trial with healthy volunteers (900 mg/day of berberine). ²⁹¹	Monitor (low level of risk).
Polyphenol-containing and/or Tannin-containing herbs²⁰			
Immunosuppressives eg cyclosporin	Decreases drug levels, due to impaired absorption or increased metabolism.	Three case reports in transplant patients (2 L/day of a tea containing 9 herbs including peppermint, chamomile, lemon balm), 1-1.5 L/day of chamomile tea; 'large quantities' of fruit tea containing hibiscus extract, and a drink containing black tea). Confirmed by rechallenge in one case, but no signs of refection. ²⁹² Interactions subsequently analyzed as having probable causality (score 7) for chamomile tea, and possible causalities (score 4) for the other teas. ⁸¹ %	Monitor (medium level of risk). Also advisable not to take simultaneously.
Iron	Inhibition of non-heme iron ^f absorption.	Clinical and epidemiological studies, many of which have investigated black tea, have produced mixed results, but overall, a substantial dose of polyphenols/tannins may inhibit iron absorption. ²⁹³⁻²⁹⁷ Results for green tea have been conflicting (adverse effect, no effect, beneficial effect) in the healthy and those with anemia and dosage may be a factor. ^{298,299} Factors that affect the consistency of results include: timing of consumption ^f , presence of inhibitors (such as phytate ³⁰⁰) and type of study results from single test meals may exaggerate the effect of iron inhibitors and enhancers. ³⁰¹ Inhibition more likely to occur in those with poor iron status and iron-deficiency anemia. Examples:	In anemia and where iron supplementation is required, do not take simultaneously with meals or iron supplements.
		<ul style="list-style-type: none"> ▪ Clinical study (using test meal): decreased absorption in healthy volunteers (included herb teas (German chamomile, vervain, lime flower, peppermint; all 3 g/300 mL), beverages (e.g. black tea, coffee, cocoa)): effect dependent on polyphenol content (per serving: 20-400 mg catechin equivalents).³¹³ See also note <i>H/H</i>. ▪ Mixed results in other studies (healthy volunteers; test meals): rosemary (32.7 mg of phenolic substances: rosmarinic acid, carnosol, carnosic acid)³¹⁴ and cayenne (high dose: 4.2 g, dried weight¹¹; containing 25 mg polyphenols)³¹⁵ reduced absorption chamomile³¹⁶ and turmeric (0.5 g, dried weight, containing 50 mg polyphenols)³¹⁵ did not. See also note <i>KK</i>. ▪ Crossover, multiple-dose study (test meals; 4-week periods of 30-250 and 1500 mg/day of condensed tannins/procyanidins from grape seed extract): no effect on iron bioavailability and status in nonanemic women.³²⁴ ▪ Clinical study: 1-hour time interval between consumption of a meal containing iron and drinking black tea reduced the inhibitory effects on iron absorption.³¹⁷ 	
			<p>Case report with rechallenge: anemia caused by high intake of green tea (> 1.5 L/day, 5 days/week for 20 years).³²¹ Epidemiological studies: decreased serum ferritin and slight reduction in hemoglobin especially at high levels of green tea consumption but no increase in anemia (Japan);³²² higher serum hemoglobin and less anemia (China, presumably green tea).³²⁸ Clinical study (150-300 mg/day EGCG): decreased absorption in healthy women with low iron stores when administered together with an iron solution. Results significant only at higher dosage.³²⁸ Case report of iron-deficiency anemia (likely high dose of turmeric).³²⁹</p> <p>See also note <i>LL</i> (<i>potential effect of Milk Thistle</i>).</p>

Drug	Potential Interaction	Basis of Concern	Recommended Action
Red Clover <i>Trifolium pratense</i>			
Antiplatelet and anticoagulant drugs	May potentiate effect of drug and/or cause bleeding.	Herb Alone Case report of bleeding from the nose and lips, bruising, hematuria with INR > 7 and "detection of warfarin in the patient's blood" despite no history of warfarin use (red clover and alfalfa tea 5-6 cups/day for 2 weeks). Authors incorrectly assume red clover contains coumarins. ³³⁰ Case report of subdural hematoma with normal INR and impaired platelet function ("red clover extract containing 40 mg isoflavones" for 8-10 years). ³³¹	Monitor (very low level of risk).
Methotrexate	May improve insulin sensitivity	Case report (severe vomiting and epigastric pain, liver function test normal; preparation strength and standardization unknown); ³³² causality rated as possible (score 4) ³³³ .	Monitor (low level of risk).
Rhodiola <i>Rhodiola rosea</i>			
SSRIs	Potentiation effects possible in regard to serotonin levels.	Escitalopram: Case report (supraventricular tachycardia, possibly due to serotonin syndrome). ³³³ Paroxetine: Case report (some symptoms of serotonin syndrome). ³³⁴ Sertaline: Clinical trial (mild to moderate depression): significantly fewer adverse events in those taking herb and drug compared to drug alone. ³³⁵	Monitor (very low level of risk).
Saw Palmetto <i>Serenoa repens</i>			
Antiplatelet and anticoagulant drugs	May potentiate effect of drug.	Herb Alone Case report (hemorrhage during surgery). ³³⁶ Clinical trials (BPH patients): reduced intraoperative bleeding from TURP procedure with preoperative use of liposterolic extract (2 trials); blood loss not different when compared with drug treatment (5-alpha reductase inhibitor, 1 trial). ³³⁷ Herb and Drug Case reports (2): increased INR (warfarin + simvastatin, ³³⁸ aspirin + clopidogrel ³³⁹ – in the first case, the interaction may have been due to the vitamin E also present in the preparation; ³³⁸ in the second case, six times the usual dose of extract was taken).	Monitor (very low level of risk).
Schisandra <i>Schisandra chinensis</i>			
Immunosuppressives	May increase drug levels.	Siroimus: Observations in some liver transplant recipients. Clinical study: markedly increased drug levels in healthy volunteers ³⁴⁰ , given <i>S. sphenanthera</i> extract, providing 67.5 mg/day of deoxyschisandrin ^{WW} . Tacrolimus: Observations in some renal and liver transplant recipients. Clinical studies (<i>S. sphenanthera</i> extract): markedly increased drug levels in healthy volunteers ³⁴¹ and transplant recipients. Clinical studies (<i>S. sphenanthera</i> extract): providing 67.5 mg/day of deoxyschisandrin ^{WW} , in patients with idiopathic membranous nephropathy (extract, providing 33.75 mg./day of deoxyschisandrin); ³⁴² reduced the dose of the drug required to treat patients with idiopathic membranous nephropathy (dose unknown); ³⁴³ and transplant recipients (extract, providing 22.5 mg./day of deoxyschisandrin). ³⁴⁴ Although the drug levels were increased, there were no adverse effects on allograft function, and graft survival appeared to be facilitated, in renal transplant recipients (dose not clearly defined, possibly extract, providing 22.5 mg./day of deoxyschisandrin). ³⁴⁷	Monitor (medium level of risk at typical doses).
Midazolam	May increase drug levels.	Increased drug level, increase in sleeping time and increase in mild to moderate adverse effects found in healthy volunteers, given <i>S. sphenanthera</i> extract, providing 67.5 mg/day of deoxyschisandrin ^{WW} . ³⁴⁸	Monitor (low level of risk at typical doses)
Prescribed medication	May accelerate clearance from the body	Theoretical concern based on <i>in vivo</i> animal studies demonstrating enhanced phase I/II hepatic metabolism. ³⁴⁹⁻³⁵⁰	Monitor (low level of risk).
Talinolol	May increase drug levels.	Increased drug level and decreased clearance found in healthy volunteers, given <i>S. chinensis</i> extract, providing 33.75 mg./day of deoxyschisandrin ^{WW} . ³⁴⁸	Monitor (low level of risk at normal doses).
Slippery Elm Bark <i>Ulmus rubra</i>			
Prescribed medication	May slow or reduce absorption of drugs.	Theoretical concern based on absorbent properties of slippery elm	Take at least 2 hours away from medication.

Drug	Potential Interaction	Basis of Concern	Recommended Action
St John's Wort^{NN} <i>Hypericum perforatum</i> (See also Polyphenol-containing and/or Tannin-containing herbs)			
Ambisertan	May decrease effectiveness of drug.	Clinical study with healthy volunteers ³⁵¹ : effect on pharmacokinetics probably not clinically relevant (e.g. AUC decreased by 17-25% depending on genotype).	Monitor (low level of risk).
Amitriptyline	Decreases drug levels. ³⁵²	Clinical study (patients with depression using hyperforin-rich extract).	Monitor (medium level of risk).
Anticonvulsants eg carbamazepine, nephenytoin, phenobarbitone, phenyltoin	May decrease drug levels via CYP induction. ³⁵³⁻³⁵⁵	Theoretical concern. An open clinical trial demonstrated no effect on carbamazepine pharmacokinetics in healthy volunteers. ³⁵⁶ Case report: increase in seizures in patient taking several anti-epileptic drugs, two of which are not metabolized by cytochrome P450. ³⁵⁷ Clinical study (healthy volunteers; clinical significance unclear): increased excretion of a mephénytoin metabolite in extensive metabolizers, but not in poor metabolizers. ³⁵⁸ See note PP.	Monitor (low level of risk).
Antiplatelet, anticoagulant and antithrombotic drugs	Clopidogrel: May potentiate effects of drug.	Clinical studies: increased responsiveness (decreased platelet aggregation or improved residual platelet reactivity) in hyporesponsive volunteers and patients, ³⁵⁹⁻³⁶² possibly via the formation of the active metabolite (CYP2A11 activity was increased), thus providing a beneficial effect in these patients. This is a complex situation, with the meaning of clopidogrel resistance/hyporesponsiveness debated. ^{359,363}	In patients with known clopidogrel resistance: Monitor (medium level of risk). In other patients: Monitor (risk is unknown).
Rivaroxaban	May decrease plasma drug levels.	Clinical study. ³⁶⁵	Contraindicated.
Phenprocoumon: Decreases plasma drug levels.		Clinical Study with healthy volunteers. ³⁶⁴	Monitor (medium level of risk).
Warfarin: May alter INR (most frequently increase).		Case reports: decreased INR (nine cases), increased INR (three cases). ³⁶⁶⁻³⁶⁸ One of these cases ³⁶⁸ was subsequently analyzed as having probable causality (score 6) ^{3,9} . Clinical study with healthy volunteers (decreased drug level and INR). ²⁰³	Contraindicated.
Bosentan	May alter drug levels.	Clinical study (healthy volunteers): minor decrease overall, but large interindividual variability occurred in clearance (from 51% decrease to up to 88% increase). ³⁶⁹	Monitor (low level of risk).
Benzodiazepines	Decrease drug levels.	Alpazolam: Mixed results for drug levels in two clinical studies (similarly low amount of hyperforin, ~4 mg/day) – no effect (dried herb equivalent: 1.1 g/day) ³⁷⁰ and decrease. ³⁷¹ Case report of successful use in alpazolam withdrawal (dried herb dose unknown). ³⁷²	Monitor (medium level of risk).
beta-Blockers (topical)	May decrease effect of drug.	Midazolam: Clinical studies with healthy volunteers. ^{373-375,379} Decrease in drug exposure correlated with increasing hyperforin dose. ³⁷³ Effect not regarded as clinically relevant for low (< 1 mg/day) hyperforin extracts. ^{373,375} Another study that administered a low-hyperforin product also found no clinically relevant interaction, however, the direction of the effect was opposite: there was an increase in drug level. ³⁷⁶	Hyperforin-rich extracts: Monitor (medium level of risk). Low-hyperforin extracts: Monitor (low level of risk).
Calcium channel antagonists	Decreases drug levels.	Quazepam: Decreased drug levels, but no effect on pharmacodynamics (sedation). ³⁷⁷	Monitor (low level of risk).
Cancer chemotherapeutic drugs eg imatinib, nilotinib	Decreases drug levels.	Case report. ³⁷⁸	Monitor (low level of risk).
Clozapine	Decreases drug levels.	Nifedipine: Clinical study. ³⁷⁹	Contraindicated.
Dextromethorphan	May increase drug levels.	Verapamil: Clinical study. ³⁸⁰	Contraindicated.
Digoxin	Decreases drug levels.	Clinical Studies. ³⁸¹⁻³⁸⁴	Contraindicated.
Docetaxel (intravenous)	May decrease effectiveness of drug.	Case report. ³⁸⁵ (causality rated as probable (score 6) ^{3,9}).	Contraindicated.
		Clinical study (healthy volunteers). ³⁷⁶	Monitor (low level of risk).
		Clinical studies: several studies showed decrease, one study showed no effect ^{370,386-388} but effect is dependent upon dose of herb and the hyperforin content. ³⁸⁸	Contraindicated at doses equivalent to > 1 g/day dried herb, especially for high-hyperforin extracts.
		Clinical study with cancer patients: ³⁸⁹ effect on pharmacokinetics probably not clinically relevant (eg plasma levels decreased by only 60%); drug-induced side effects were also reduced. Two of the 10 patients had an increase in AUC. See also note QQ.	Contraindicated.

Drug	Potential Interaction	Basis of Concern	Recommended Action
Fexofenadine	May decrease drug levels.	Clinical Studies (healthy volunteers). ^{390,391} Another study that administered a low-hyperforin product found no clinically relevant interaction, however, the direction of the effect was opposite: there was an increase in drug level. ³⁹⁶	Monitor (low level of risk).
Finasteride	May decrease drug levels.	Clinical study with healthy volunteers. ³⁹² Case report: PSA level elevated (due to decreased efficacy of drug?) in patient with BPH. ³⁹³	Contraindicated.
HIV non-nucleoside transcriptase inhibitors eg nevirapine	Decreases drug levels.	Case report. ³⁹⁴	Contraindicated.
HIV protease inhibitors eg indinavir	Decreases drug levels.	Clinical Study (healthy volunteers). ³⁹⁵	Contraindicated.
Hypoglycemic drugs	Gliclazide: May reduce efficacy of drug by increased clearance.	Clinical study with healthy volunteers, but glucose and insulin response to glucose loading were unchanged. ³⁹⁶	Contraindicated.
	Metformin: May affect glucose tolerance.	Herb Alone Mixed results in clinical studies with healthy volunteers – glucose tolerance reduced, due to reduced insulin secretion, ³⁹⁷ and improved glucose tolerance. ³⁹⁸	Monitor (low level of risk).
		Herb and Drug Clinical study with healthy volunteers: no significant effect on pharmacokinetics, but glucose tolerance improved, due to enhanced insulin secretion. ³⁹⁹	
		Repdamidine: May alter metabolism of drug.	Clinical study with healthy volunteers: no effect, and glucose and insulin response to glucose loading were unchanged. ⁴⁰⁰
		Tolbutamide: May affect blood glucose.	Two clinical studies (healthy volunteers) no effect on pharmacokinetics ^{390,391} but there was an increased incidence of hypoglycemia in the trial using hyperforin-rich extract (33 mg/day of hyperforin). ³⁷⁴
Immunosuppressives	Decreases drug levels.	Cyclosporin: Case reports, ⁴⁰¹⁻⁴⁰⁹ case series, ^{410,411} Clinical studies (healthy volunteers, ³⁹¹ patients ^{412,413}) Interaction is dependent upon the hyperforin content. ^{404,412}	Contraindicated especially for high-hyperforin extracts.
Nabradine	May decrease drug levels.	Tacrolimus: Case report and clinical studies. ⁴¹⁴⁻⁴¹⁶	Monitor (medium level of risk).
S-ketamine (oral)	May decrease drug levels.	Clinical trial with healthy volunteers. No pharmacodynamic effect was observed. ⁴¹⁷	Monitor (medium level of risk).
		Clinical study with healthy volunteers. No pharmacodynamic effect was observed (eg analgesic effect not altered). ⁴¹⁸	
Methadone	Decreases drug levels, possibly inducing withdrawal symptoms.	Case reports. ⁴¹⁹	Contraindicated.
Methylphenidate	May decrease efficacy.	Case report, ⁴²⁰ but clinical significance unclear.	Monitor (low level of risk).
Morphine (oral)	May potentiate effects of drug.	Clinical study (healthy volunteers). ⁴²¹ pain scores were decreased when morphine coadministered with standardised extract at a dose of herb below those used to obtain an antidepressant or analgesic effect. The effect was dependent hyperforin content, but not hyperforin. The authors suggest the herb may be able to decrease the dose of morphine while obtaining the same analgesic effect.	Monitor (medium level of risk).
Omeprazole	May decrease drug levels.	Clinical trial (healthy volunteers; AUC decreased by 38-44% depending on genotype). ⁴²² Another study that administered a low-hyperforin product found no effect. ³⁹⁶	Monitor (low level of risk), lower risk for low-hyperforin extracts.
Oral contraceptives	May increase metabolism and reduce effectiveness of drug.	Breakthrough bleeding reported which was attributed to increased metabolism of drug. ^{366,401} Contradictory results for effect on bioavailability, hormone levels and ovulation demonstrated in three clinical studies, although some breakthrough bleeding occurred. ⁴²³⁻⁴²⁸ In one clinical trial an extract low in hyperforin did not affect plasma contraceptive drug levels or cause breakthrough bleeding. ⁴²⁹ Clinical trial: clearance of levonorgestrel at emergency contraceptive doses increased (not statistically significant). ⁴³⁰ Clinical study: antidiarrhetic effect of contraceptive not affected. ⁴³¹	Hyperforin-rich extracts: Monitor (medium level of risk), Low-hyperforin extracts: Monitor (very low level of risk),
Oxycodone	Decreases drug levels.	Clinical trial with healthy volunteers. ⁴³²	Monitor (medium level of risk).

Drug	Potential Interaction	Basis of Concern	Recommended Action
SSRIs eg paroxetine, trazodone, sertraline and other serotonergic agents eg nefazodone, venlafaxine	Potentiation effects possible in regard to serotonin levels.	Case reports: clinical significance unclear. ⁴³³⁻⁴³⁸	Monitor (very low level of risk).
Statin drugs	May decrease effect and/or drug levels.	Atorvastatin: Clinical study, serum LDL-cholesterol increased by 0.32 mmol/L (12.3 mg/dL) which corresponds to a decrease in effect of drug in patients by about 30%. Serum total cholesterol was also increased. ⁴³⁹ Pravastatin: Clinical study, no effect on plasma level in healthy volunteers. ⁴⁴⁰ Rosuvastatin: Case report ⁴⁴¹ (causality rated as possible (score 3) ^b). ⁹⁶ Simvastatin: Two clinical studies, decrease in drug levels in healthy volunteers, ⁴⁴⁰ and small increases in serum total cholesterol and LDL-cholesterol in patients. ⁴⁴²	Monitor blood cholesterol regularly (medium level of risk).
Talinolol	May decrease drug levels.	Clinical study (healthy volunteers). ⁴⁴³	Monitor (medium level of risk).
Theophylline	May decrease drug levels.	Case report. ⁴⁴⁴ No effect observed in clinical study with healthy volunteers. ⁴⁴⁵	Monitor (low level of risk).
Voriconazole	Decreases drug levels.	Clinical study. ⁴⁴⁶	Contraindicated.
Zolpidem	May decrease drug levels (but with wide interindividual variability). ⁹⁸	Clinical study (healthy volunteers). ⁴⁴⁷	Contraindicated.
Tannin-containing herbs Refer to Polyphenol-containing and/or Tannin-containing herbs (above)			
Turmeric⁵⁵ <i>Curcuma longa</i>			
Antiplatelet and anticoagulant drugs	May potentiate effect of drug.	Herb Alone and with Drug Aspirin: Clinical study found inhibitory effect on arachidonic acid-induced platelet aggregation in 5 of 24 healthy volunteers after several days' consumption of highly concentrated Turmeric extract (providing 475 mg/day of curcuminoids), no bleeding events were reported and no effect on platelet aggregation by other agonists. Taking with aspirin did not further suppress platelet function and prothrombin time was not impaired. ⁴⁹	Monitor (low level of risk).
Etoricoxib	May potentiate adverse hepatic effect of drug.	Case report of acute liver injury (long-term use of herb). ⁴⁴⁸	Monitor (low level of risk).
Tacrolimus	May increase drug levels.	Case reports: nephrotoxicity in liver transplant patient; high dose with food, estimated at "15+ spoonfuls daily" starting roughly 10 days prior to rehospitalization ⁴⁴⁹ (causality rated as probable (score 7) ^b). ⁹⁶ elevated drug level in transplant patient (meal containing a lot of turmeric). ⁴⁵⁰	Monitor at high doses (medium level of risk).
Talinolol	May decrease drug levels.	Clinical study with healthy volunteers (300 mg/day of curcuminoids).No effect on pharmacodynamics (blood pressure or heart rate). ⁴⁵¹	Monitor at high doses (\geq 300 mg/day curcumin, low level of risk).
Valerian <i>Valeriana officinalis</i>			
CNS depressants or alcohol	May potentiate effects of drug.	Theoretical concern expressed by US Pharmacopeial Convention. ⁴⁵² However a clinical study found no potentiation with alcohol. ⁴⁵³ Case report of adverse effect with benzodiazepine drug (lorazepam) ⁴⁵⁴ – herb dosage undefined but likely high (tablet contained extracts of valerian and passion flower (<i>Passiflora incarnata</i>)); causality rated as possible (score 3) ^b . ⁹⁶ Alprazolam: Clinical study in healthy volunteers found no effect on drug levels (extract provided 11 mg/day total valerenic acids). ⁴⁵⁵	Monitor (very low level of risk).

Drug	Potential Interaction	Basis of Concern	Recommended Action
Willow Bark <i>Salix alba</i> , <i>Salix daphnoides</i> , <i>Salix purpurea</i> , <i>Salix fragilis</i> (See also Polyphenol-containing and/or Tannin-containing herbs)			
Warfarin	May potentiate effects of drug.	Clinical study observed very mild but statistically significant antiplatelet activity (extract containing 240 mg/day of Salicin). ¹⁵⁶	Monitor (low level of risk).
Wormwood <i>Artemisia absinthium</i>	May potentiate effects of drug.	Case report (gastrointestinal bleeding due to increased INR; Ingestion of herb (although plant part undefined), the dose of which was increased after several days). ⁴⁵⁷ Subsequently analyzed as having possible causality (score 4½). ⁴⁵⁸	Monitor (medium level of risk).

CODE FOR RECOMMENDED ACTION

Contraindicated: Do not prescribe the indicated herb.

Monitor: Can prescribe the indicated herb at typical therapeutic doses, but maintain close contact and review the patient's status on a regular basis. Note that where the risk is assessed as medium, self-prescription of the herb in conjunction with the drug is not advisable.

Herb-Drug Interaction Chart: General Prescribing Guidelines

- Exercise great caution when prescribing herbs for patients taking drugs with a narrow therapeutic window. These drugs may become dangerously toxic or ineffective with only relatively small changes in their blood concentrations. Examples include digoxin, warfarin, antirejection (immunosuppressive) drugs, many anti-HIV drugs, theophylline, phenytoin and phenobarbital. These patients need to be monitored on a frequent, regular basis.
- Exercise great caution when prescribing herbs for patients taking drugs (these patients need to be monitored on a frequent, regular basis):
 - if heart, liver, or kidney function is impaired,
 - in elderly patients,
 - in pregnant women,
 - in those who have received an organ transplant,
 - in those with a genetic disorder that disturbs normal biochemical functions.
- Care should be exercised with patients who exhibit long-term use of laxative herbs or potassium-depleting diuretics.
- Critical drugs should be taken at different times of the day from herbs (and food) to reduce chemical or pharmacokinetic interactions. They should be separated by at least 1 hour, preferably more.
- Stop all herbs approximately 1 week before surgery. Milk thistle may help reduce the toxic after-effects of anesthetic drugs, so it can be taken up to the day before, and then again, after surgery.
- Carefully monitor the effects of drugs such as antihypertensives and antidiabetic drugs when combining with herbal remedies.
 - The herbs may make them more or less effective. In the ideal situation the dose of the drug could be adjusted.
 - Interactions may be dose related for the herb and the drug, for example, St John's Wort and digoxin.
 - The use of antioxidants (including herbs) in conjunction with chemotherapy and radiotherapy for cancer is controversial. Health care professionals should be aware of the issues and make informed recommendation to their patients.
 - Reference and further reading: Mills S, Bone K (eds). *The Essential Guide to Herbal Safety*. Churchill Livingstone, USA, 2005.

NOTES

- * This chart contains information the authors believe to be reliable or which has received considerable attention as potential issues. However, many theoretical concerns expressed by other authors have not been included. Due to the focus on safety, positive interactions between herbs and drugs, and the effect of drugs on the bioavailability of herbs are generally not included.
- A. Pharmacokinetic parameters were unchanged.
- B. Assessed using the Drug Interaction Probably Scale (DIPS). Total DIPS score of greater than 8 is highly probable causation, 5-8 is probable, 2-4 possible and a score of less than 2 denotes a doubtful causation. Note: this assessment does not consider the dose of the herb compared to normal therapeutic doses.
- C. Chaste tree has been evaluated for treatment of premenstrual syndrome (5 trials)⁴⁵⁸⁻⁴⁶² and cyclical mastalgia (1 trial).⁴⁶³ OCP use was permitted providing the dose was maintained throughout.^{458-460,462,463} or documented.⁴⁶¹ Three trials noted that 12.8%, 30.2% and 22.7% of those receiving the herb used concomitant OCPs. In these trials, the administered dose was equivalent to 72-270 mg/day of dried fruit.^{458,461,462} Four of the trials were placebo-controlled.^{458,459,462,463} one was uncontrolled⁴⁶¹ and one used magnesium as a comparator.⁴⁶⁰ There were either no adverse events found or they were mild, and occurred with similar incidence rate to the placebo and comparator groups. For example, 4 events occurred in the 86 women who received chaste tree (180 mg/day of dried fruit; one case of intermenstrual bleeding), and 3 events occurred in the 84 who received placebo.⁴⁵⁸ There was one case of mild interim spotting among 36 women treated with chaste tree (72 mg/day of dried fruit).⁴⁶² In the uncontrolled study, there were 5 cases of spotting among the 43 that completed the study (180 mg/day of dried fruit), and one woman withdrew from the study due to pregnancy which was described as not related to the herbal treatment.⁴⁶¹
- D. Analysis of Chinese skullcap root samples from Japan found the baicalin content varied from 3.5 to 12%. For a dose of 150 mg/day of baicalin, 1.2-4.3 g/day of dried root would be required.⁴⁶⁴
- E. Single-strength (freshly squeezed, 100%) cranberry juice is highly acidic and astringent, making it unpalatable. For this reason, cranberry juice is usually diluted and sweetened (often known as cranberry juice drink). Cranberry juice cocktail usually contains 25% cranberry juice, although can be up to 35%. Cranberry juice drinks contain about 10% cranberry juice. Cranberry sauce is about half the strength of cranberry juice
- F. The cranberry 'juice' administered was similar in concentration to a reference cranberry juice containing about 25% cranberry juice,⁴⁶⁵ but with a higher concentration of anthocyanins, and lower in catechins and organic acids. See also note E.
- G. No effect overall when midazolam was administered orally: oral clearance and AUC were unchanged.
- H. Eleutherosedes from Eleuthero and ginsenosides from Korean ginseng have some structural similarity with digoxin. Because of this similarity interference with serum digoxin measurements is possible, as confirmed when mice fed these herbs demonstrated digoxin activity in their serum. More specific assays are able to negate the interference.⁴⁶⁶
- I. These four trials used tablets containing a concentrated, standardised extract. A dosage of 900 mg/day of dry extract was equivalent to about 2.7 g/day of fresh garlic.⁴⁶⁷ and was said to provide 12 mg/day of allicin.^{65,74} although there is some doubt as to the amount of allicin released from this brand of tablet from around 1995 to 2000.⁴⁶⁸
- J. Although the contents of the garlic tablets were not defined in the published results, information obtained from the manufacturer of the product indicated the disclosed amount (1.25, 25, 3.75 g) corresponded to fresh weight of garlic.⁴⁶⁹ All volunteers received aspirin and after a washout period, one of three doses of garlic.
- K. There may have been variation in patients' interpretations (of bleeding) and the significant association between ginger use and bleeding was based on 7 self-reported events in 25 users.⁴⁷⁰
- L. Information is provided for specialized and/or concentrated extract, rather than galenical form of herb.
- M. Ginkgotoxin (4'-O-methylpyridoxine) is present in substantial amounts in Ginkgo seed, and convulsions arising from ingestion of Ginkgo seed have been documented in Japan (infants are particularly vulnerable). Ginkgotoxin is known to inhibit vitamin B6 phosphorylation, which may lead to increased neuronal excitability.⁴⁷¹ Poisoning by ginkgotoxin can be counteracted by vitamin B6.⁴⁷¹ In cases of poisoning it is administered by intravenous injection.^{472,473} Ginkgotoxin is present in very small amounts in standardised Ginkgo leaf extracts,⁴⁷⁴ but is below the detection limits in human plasma after oral doses (240 mg of 50:1 extract).⁴⁷⁵ According to the manufacturer, despite the extensive use of this special extract (more than 150 million daily doses per year for more than two decades) no cases of epileptic seizure have been attributed to this extract.⁴⁷⁵ (Ginkgo preparations associated with the above case reports were undefined.) Strictly speaking this is a potential adverse effect (rather than a herb-drug interaction) as there is no pharmacokinetic data indicating an interaction for coadministration of Ginkgo and anticonvulsants in humans. An interaction is suggested though, because Ginkgo has been found to induce CYP2C19 activity (see entry for omeprazole), an enzyme involved in the metabolism of some anticonvulsants.
- P. Analysis of over 320 000 patients in a German adverse drug reaction reporting system (1999-2002) found no increase in prevalence of bleeding during Ginkgo intake compared to periods without Ginkgo in those taking anticoagulant or antiplatelet medication.⁴⁷⁶ In a trial involving 3069 healthy volunteers treated for an average of 6.1 years, there were no statistically significant differences between placebo and Ginkgo in the rate of major bleeding or the incidence of bleeding in individuals taking aspirin. Compliance during the trial was however low: at the end of the trial, about 60% were taking Ginkgo/placebo.⁴⁷⁷ Another randomized dementia prevention trial that enrolled 2854 patients found no significant difference in the incidence of hemorrhagic events between those receiving Ginkgo 50:1 extract (240 mg/day) or placebo. The treatment period was 5 years and compliance was 95%.⁴⁷⁸ In Korea, Ginkgo extract is administered with ticlopidine for the prevention of ischemic stroke or acute coronary syndrome.⁴⁷⁹
- Q. Final analysis included 722 142 records. The data was adjusted for age (75 years or older) and comorbidities. The hazard ratio was 1.38 (95% CI: 1.20-1.58, p < 0.001).
- R. For example, the pooled results show a mean difference for serum levels of total cholesterol of -0.61 mmol/L (-23.6 mg/dL). The dose of *Ginkgo biloba* administered was reported as 120-576 mg/day, and it is likely (from information in the English abstracts of two of the trials) that this refers to standardised extract.
- S. The *in vitro* reduction by EGCG was overcome when the concentration of the drug was increased (to a level expected clinically i.e. in plasma from the standard drug dose).⁴⁸⁰ A further *in vivo* study found no reduction in the activity of the drug (when EGCG administered by injection to achieve plasma levels of 11-16 micromol).¹⁵²
- T. The *in vitro* reduction by EGCG was overcome when the concentration of the drug was increased (to a level expected clinically i.e. in plasma from the standard drug dose).⁴⁸⁰ A further *in vivo* study found no reduction in the activity of the drug (when EGCG administered by injection to achieve plasma levels of 11-16 micromol).¹⁵²
- U. The *in vitro* reduction found a pronounced reduction in the cytotoxic effect of the drug for a concentration of 2.5-5 micromol of EGCG, and when applied as green tea polyphenols a very substantial effect occurred at a EGCG concentration of 1 micromol (the other polyphenols may contribute to the activity).¹⁵¹ A pharmacokinetic study with healthy volunteers found a EGCG plasma

CC.	Several variants of CYP2C9 have been identified in humans; the most important mutations are CYP2C9*2 and CYP2C9*3. The CYP2C9*3 variant shows decreased metabolic activity for many drugs metabolized by CYP2C9. CYP2C9 is the main enzyme responsible for transforming losartan to its active metabolite.	(<i>Rubus idaeus</i>), St John's wort (<i>Hypericum perforatum</i>), willow bark (<i>Salix spp.</i>) or those providing substantial amounts of a key constituent e.g. resveratrol from <i>Polygonum cuspidatum</i> that might inhibit iron absorption. Some herbs may contain constituents that improve iron absorption (e.g. ascorbic and organic acids in cranberry), and hence overall may be less of a concern.
DD.	Polyphenols are considered to be a dietary factor responsible for influencing iron absorption. This is due to studies in the 1970s and 1980s that found inhibition of iron absorption by beverages such as tea and coffee, and by gallic acid, tannic acid, and to a lesser extent, chlorogenic acid. The potential effect of a food was estimated from its polyphenol content (measuring for example, galloyl groups, catechin equivalents, tannic acid equivalents etc.), in addition to considering other factors including phytate and ascorbic acid. ^{484,485} The problem arises however, in the estimation of polyphenols, due to inaccuracies based on different methods of analysis, ⁴⁸⁵ and possibly, differences in classification. The term 'tannin' has long-established and extensive usage although it is considered in more recent years to lack precision. Polyphenol is the preferred term when considering the properties at a molecular level. Historically, plant polyphenols have been broadly divided into proanthocyanidins (condensed tannins) and polymers of esters based on gallic and/or hexahydroxydiphenic acid and their derivatives (hydrolyzable tannins). ⁴⁸⁶ (This classification ignores flavonoids, which are also regarded as polyphenols). The terms 'tannin' and 'polyphenol' have been used interchangeably. For example, the results of a clinical study are described: "polyphenols present in tea and coffee inhibited iron absorption in a dose-dependent manner". The 'polyphenol' content was measured using a spectrophotometric method for the determination of "tannins and other polyphenolics". ³¹¹ Depending on the analytical method used, it is possible that the polyphenol content may actually be the content of tannins or tannins + polyphenols. ⁴⁸⁷ It is not known if herbs containing substantial amounts of flavonoids will have similar interactions, and this may depend on the chemical structure. In one of the studies listed, the researchers assessed a variety of "polyphenolic-containing" beverages: coffee (containing chlorogenic acid), herbs such as chamomile, lemon balm, verbena and peppermint containing monomeric flavonoids and black tea and cocoa which contained polymerized polyphenols. The polyphenol contents of the teas and cocoa were expressed as catechin equivalents and as chlorogenic acid for coffee. ³¹³ It is difficult then, to assess how the iron-absorption research relates to herbs. Whilst some herbs have polyphenols, tannins, oligomeric procyandins and phenolic acids (such as chlorogenic acid) as characteristic or prominent constituents, such as cayenne (<i>Capسium annuum</i>), chamomile (<i>Matricaria recutita</i>), hawthorn (<i>Crataegus spp.</i>), rosemary (<i>Rosmarinus officinalis</i>), sage (<i>Salvia officinalis</i>), it is probably only those herbs with a high content (e.g. 10% or higher) such as cinnamon (<i>Cinnamomum verum</i>), grape seed extract (<i>Vitis vinifera</i>), green tea (<i>Camellia sinensis</i>), meadowsweet (<i>Filipendula ulmaria</i>), raspberry leaf	(<i>Rubus idaeus</i>), St John's wort (<i>Hypericum perforatum</i>), willow bark (<i>Salix spp.</i>) or those providing substantial amounts of a key constituent e.g. resveratrol from <i>Polygonum cuspidatum</i> that might inhibit iron absorption. Some herbs may contain constituents that improve iron absorption (e.g. ascorbic and organic acids in cranberry), and hence overall may be less of a concern.
EE.	Heme iron is derived from hemoglobin and myoglobin mainly in meat products. Non-heme iron is derived mainly from cereals, vegetables and fruits.	Another clinical study also found a dose-dependent effect, and the reduced absorption was most marked when coffee was taken with the meal or one hour later. No decrease in iron absorption occurred when coffee was consumed one hour before the meal. ³¹⁰
FF.		GG. Sorghum also contains phytate. Both phytate and polyphenols inhibit nutrients such as iron. ^{488,489} Clinical studies (healthy volunteers): reduced iron absorption (sorghum containing 0.15% tannins) ⁴⁹⁰ and dose-dependent inhibiting effect for condensed tannins (dephytinized sorghum). ⁴⁹¹
HH.		At an identical concentration of total polyphenols, black tea was more inhibitory than all the herb teas excluding peppermint: black tea was of equal inhibition to peppermint tea. ³¹³ The type of polyphenols present, as well as the concentration, may affect iron absorption.
JJ.		JJ. Administered in freeze-dried form (from 14.2 g, fresh weight), which would be expected to have a lower inhibitory effect than with the use of fresh chili; as freeze drying probably decreased the ascorbic acid content (ascorbic acid enhances iron absorption). ³¹⁵
KK.		KK. The different results for cayenne and turmeric under the same experimental conditions, suggest it is not only the quantity of polyphenol present that determines the inhibition, but also for example, the structure of the polyphenol (and hence mechanism of iron binding). ³¹⁵
LL.		LL. There may be implications for conditions of iron overload. Clinical study (black tea consumed with meals over one year): decrease of iron absorption (from a single test meal) and consequently reduced storage iron reaccumulation (but to a smaller, nonsignificant extent than expected from studies using single doses) in those with hemochromatosis. ⁴⁹² Reduced serum ferritin levels in patients with beta-thalassemia major (clinical study: green tea consumed as a tea: 2.5 g in 150 mL of hot water, 3 times a day for 8 weeks), ⁴⁹³ and in a patient with beta-thalassemia intermedia (green tea consumed for 11 months). ⁴⁹⁴ Although concentrated extract of milk thistle (known as silymarin) is a complex of flavonolignans, which have different chemical structures to most of the polyphenols studied, a
U.	A better design would have volunteers take warfarin alone for a period long enough to allow the drug to reach its maximum effect (about 3–5 days) before adding the herb.	
V.	Information is provided for dried root and extracts containing glycyrrhizin. See elsewhere for information on extracts containing only a minimum amount of glycyrrhizin (deglycyrrhizinated licorice).	
W.	Glycyrrhetic acid, is the aglycone of glycyrrhizin. Glycyrrhizin, is the glycoside and contains the aglycone (glycyrrhetic acid) and a sugar unit.	
X.	No effect on blood pressure in healthy volunteers in three studies (130 mg/day of glycyrrhetic acid = 227 mg/day of glycyrrhizin) for 14 days; ²²⁹ licorice tablets (266 mg/day of glycyrrhizin) for 56 days; ²⁴³ 300 mg/day of potassium salt of glycyrrhizin = 287 mg/day of glycyrrhizin, for 14 days); ²⁷⁰ including where plasma renin levels were high (3.1 ng/mL/h), ²⁴³ but in another study, blood pressure increased in healthy volunteers taking 546 mg/day of glycyrrhizin for 4 weeks, only for those with plasma renin activity greater than 1.5 ng/mL/h. ⁴⁸² Hypertension, or hyperkalemia, did not occur in acute ischemic stroke patients treated with licorice extract made from roasted root that provided 106 and 212 mg/day of glycyrrhizin, taken for up to 7 days. ⁴⁸³	
Y.	This is a guide, based on a recommendation from the German Commission E for long-term consumption of licorice as a flavoring. Glycyrrhizin is also known as glycyrrhizic acid and glycyrrhetic acid.	
Z.	ACE-inhibitors cause mild natriuresis (an increase in sodium excretion in the urine) and occasionally hyperkalemia. The mechanism of the interaction is not known, although it may involve opposing effects on 11beta-hydroxysteroid dehydrogenase type 2 (glycyrrhizin inhibiting, ACE-inhibitor promoting), thus affecting mineralocorticoid receptor activity. Reduction of drug dosage revealed the existing hypokalemia caused by this dosage of glycyrrhizin.	
AA.	Maximum plasma cortisol (exogenous) was not increased in one volunteer, ²⁵⁰ in the other, plasma (exogenous) cortisone/cortisol ratio decreased, ²⁴⁹ suggesting increased (exogenous) cortisol while (endogenous) cortisol decreased (although statistical and clinical significance is unknown, and may have been within the normal range). In these studies isotope-labelled cortisol was administered, which allowed exogenous and endogenous cortisol to be measured.	
BB.	A higher prednisolone/prednisone ratio indicates decreased conversion of prednisolone (active) to prednisone (inactive).	

possible iron-chelating effect has been suggested in preliminary research involving 10 hemochromatosis patients (single dose: 140 mg; test meal),⁴⁹⁵ and it has significantly reduced serum ferritin levels in patients with beta-thalassemia major in three of five controlled trials (small patient numbers; adults and children, 420 mg/day).⁴⁹⁶

MM. Fructus Schisandra has historically been defined as the fruit of *Schisandra chinensis* or *Schisandra sphenanthera* in traditional Chinese medicine. In more recent years, the Chinese Pharmacopoeia lists the two species under separate monographs, with separate and different minimum marker levels but with similar properties and indications.⁴⁹⁷ The major constituents are dibenzocyclooctene lignans. Several factors including harvest season, origin of herb and extraction solvent affect the levels of the individual lignans. Aqueous or ethanolic extracts of *S. chinensis* are not likely to contain more than 2.5 mg/g of deoxyschisandin.^{498,499} Using these analyses as a guide, a maximum dose of *S. chinensis* extract equivalent to 4 g/day, would provide 10 mg/day of deoxyschisandin.

NN. As noted for several drugs, the hyperforin content of the St John's Wort preparation, as well as the dosage of herb, affects the extent of the interaction. All types of preparations can contain hyperforin, including dry extracts used in tablets and capsules. Hyperforin is however, unstable – particularly when in solution.⁵⁰⁰ Tinctures and liquid extracts made using a standard ethanol content (45%) contain negligible amounts of hyperforin. Liquid extracts using a higher ethanol content (such as 60%) will contain a higher initial amount of hyperforin than standard liquid extracts. Over time the hyperforin content is substantially reduced and after a few months tinctures and liquid extracts contain no hyperforin.⁵⁰¹

PP. Genetic polymorphisms are important in determining differences in the response to drugs, and may influence interactions. There are many genetic variants of the CYP genes, including the CYP2C19 gene. Phenotypes of CYP2C19 have been classified functionally as extensive metabolizers and poor metabolizers, the latter having a deficiency of CYP2C19 activity.^{27,1502}

QQ. Two of the 10 patients with the highest hyperforin levels prior to drug administration showed the greatest decrease in the AUC_{0-∞} of docetaxel, for the other patients, no apparent correlation was observed.

RR. Of the 14 volunteers, in three, a small increase in AUC was observed after administration of St John's Wort.

SS. Information is provided for herb containing standard levels of active constituents. See elsewhere for information on more bioavailable forms.

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