Graeco-Roman physician Galen (AD 131-201)

Their properties increase, rather than decrease with ageing. The traditional medicine of South-East Asia also uses alcohol as a base for herbal medicines. For example, in Thailand ya dong (a mixture of medicinal herbs in alcohol) is used by women to warm up and cleanse the body after childbirth. Herbs are considered to be more effective and faster acting when prepared in alcohol rather than water. Written records for the years 1650–1800 examining the traditional medicine of the Khoi-Khoi and San, some of the earliest inhabitants of South Africa, record the use of several medicinal plants administered in the form of tinctures. Although decoction of fresh herbs is the most common method used to prepare herbal mixtures in eastern Cuban traditional medicine, they are also macerated in water or alcohol, fried in oil or the juice is extracted. Use of a form of medicated wine/beer known as a galone is also documented.

Vitex agnus-castus

Liquid Extracts in Western Herbal Medicine

History

The Graeco-Roman physician Galen (AD 131–201) was the first to write about liquid preparations of plants, which are called galenicals in honour of his contribution. Examples include decoctions, infusions, liquid extracts, tinctures, vinegars and oxymels (honey + acetic acid). Dioscorides, writing earlier (AD 40–80) describes the action of chaste tree (*Vitex agnus-castus*): "A weight of 1 drachma in wine makes the menses come on earlier, detaches the embryo, attracts the milk, goes to your head and brings sleep". The first official *British Pharmacopoeia*, the *London Pharmacopoeia*, was issued in 1618. It contained a section outlining ethanolic fluid extracts and drew heavily on the classics. Nicholas Culpeper, the 17th-century English herbalist and one of the best-known advocates of western herbal medicine, described the distillation of one or more herbs in wine, and the maceration of spices in alcohol. Single herbs, such as dried wormwood (*Artemisia absinthium*), rosemary (*Rosmarinus officinalis*), eyebright (*Euphrasia officinalis*) were steeped in wine and set in the sun for 30–40 days to make a physical wine. Medicinal plants have been used to prepare tonic wines in France.

Ethanol Strength Determines Quality

Ethanolic liquid extracts and tinctures are the most popular dispensing form amongst modern herbalists. In addition to the longer shelf life, these herbal liquids are more concentrated than infusions and decoctions, allowing a smaller quantity to be dispensed in a dosage. Liquid (or fluid) extracts and tinctures are prepared by macerating or percolating the herb, most often with ethanol/water solutions. Herbs are complex substances, containing a variety of plant constituents contained within cell walls. When preparing to extract, a liquid (the solvent) is chosen that will have the best chance of dissolving the plant constituents. Insoluble constituents are left behind (in the solid waste material, called the marc). Examples of traditionally-used solvents include water, alcohol (ethanol), a mixture of water and ethanol, glycerol (glycerine), vinegar (acetic acid) and vegetable oils. Ethanol is chosen when water-insoluble constituents need to be dissolved (extracted) and when the extract is to be kept for any length of time. The importance of this first function cannot be overstated. Mixtures of water and ethanol are highly efficient for the extraction of a wide variety of plant constituents. However, it is important to choose the correct ethanol percentage in order to maximise the quality of liquid preparations. For example:

- 55% ethanol was found to be the optimum percentage for the extraction of the essential oil from the flowers of chamomile (*Matricaria chamomilla*).
- Around 60% ethanol is a good solvent to extract saponins.
- Higher ethanol percentages do not necessarily mean higher activity.

- Alkylamides, the important active, tingling constituents in good quality Echinacea root, are better extracted at higher ethanol percentages.
- Extracts of St Mary's thistle (*Silybum marianum*) fruit prepared in 25% ethanol or less will not contain the active constituent silymarin, because it is insoluble at this concentration.

Professor Kerry Bone recommends these basic guidelines for the choice of the ethanol percentage to optimise the activity of the final liquid:

- 25%: water-soluble constituents such as mucilage, tannins, and some glycosides (including some flavonoids and a few saponins).
- 45–60%: essential oils, alkaloids, most saponins and some glycosides.
- 90%: resins and oleoresins

It would be very difficult to administer some herbs without using ethanol as a solvent. For example, highly resinous herbs such as myrrh (*Commiphora myrrha*) require extraction using a high percentage of ethanol or the resin remains solid. Ginger (*Zingiber officinale*) also requires 90% ethanol as a solvent, or a poor quality liquid extract, containing low quantities of the pungent (hot) principles (which are part of the oleoresin) would be obtained. Even if extraction using water did dissolve the resinous constituents, they will most likely precipitate out of solution, resulting in a poor quality extract for the patient.

There are however examples where ethanol would not be a suitable solvent. Examples include herbs that require high water solubility. As a consequence slippery elm (*Ulmus rubra*) and psyllium (*Plantago ovata, P. psyllium, P. indica*) are best administered in powder form and mixed in water. Marshmallow (*Althaea officinalis*) root is often prescribed as a glycetract (where glycerol mixed with water is used as the solvent). Glycerol however is a poor solvent for most plant constituents. Ethanol is the best solvent to sterilise the dried plant material when extraction begins and to preserve the resulting extract. For this purpose a concentration of at least 20–25% ethanol is required. In contrast glycerol is a poor preservative. In addition, the stability of the active constituents of glycetracts in the long term has not been documented. It is possible to prepare a liquid extract using ethanol as a solvent, then remove the ethanol and finish making up the liquid extract using glycerol and water. This type of manufacture can be used to prepare St Mary's thistle (*Silybum marianum*) fruit glycetract. Analysis of the glycetract using high performance liquid chromatography (HPLC) can ensure the important flavanolignans (calculated as silymarin) are extracted from the fruit and retained in the final glycetract. If this type of manufacture is not done very carefully however, the resulting liquid extract may be very poor in quality with low levels of active constituents. For example, when extracting essential-oil containing herbs, removal of the ethanol may also remove the essential oil


Silybum marianum

from the final extract. A further reason that this process may not automatically guarantee a quality extract is that some active constituents extracted from the starting herb and made soluble by ethanol may not remain soluble once the ethanol is removed – they may form a precipitate in the final glycerol-water solution. The complexity of herbal extraction cannot be underestimated. The original selection of ethanol percentages was perhaps in large part via trial and error, with information documented and passed down in traditional texts such as the *British Herbal Pharmacopoeia* 1983. In recent times, analytical techniques including HPLC can be utilised to assess the quality of extraction at various ethanol percentages. The HPLC profile of a finished extract ensures the quality of the starting herbal material is retained in the product throughout the manufacture. Use of HPLC can also ensure that the full spectrum of soluble plant constituents is obtained in the extract, not just one or two key active constituents.

Safety of Liquid Extracts

The difference between a therapeutic and a toxic effect is usually only a question of dose. Ethanol is no exception to this rule. A 5 mL dose of herbal extract contains as much ethanol as about one-sixth of a glass of beer or wine. This small intake of ethanol is rapidly metabolised by the liver. It is only a much higher intake of ethanol that overloads the metabolising capacity of the liver and leads to adverse effects.

There are some cases where use of an ethanolic extract is not suitable, e.g. children, Muslims, ex-alcoholics and those with significant liver disorders. (Patients with mild liver conditions are not likely to be adversely affected by a small ethanol intake, such as that from a liquid extract.) In these cases other forms of remedy can be used, such as well-manufactured tablets, or the ethanol content of the liquid extract can be reduced by carefully evaporating off the alcohol (not advised for essential oil-containing extracts).

Like ethanol, the small amounts of glycerol encountered in glycetracts are unlikely to cause an adverse health effect.

However, glycerol is metabolised in a similar way to glucose, so consideration should be given when administering substantial quantities of glycerol to diabetics. A very small minority of patients are genuinely sensitive to alcohol. In others, a presumed sensitivity may be an exaggerated reflex response to the medicine which can usually be alleviated by lower doses at greater frequency, taken with food or water. Because a liquid extract made using a high ethanol percentage may be more concentrated in active constituents, less liquid can be prescribed to achieve a desired therapeutic outcome. As a consequence the patient's ethanol intake could be lower than when prescribing a higher quantity of a low ethanol extract.

* *Written in June 2009 by Michelle Morgan. References available upon request*

The Importance of Quality Herbal Manufacturing

All herbal products in Australia are manufactured under pharmaceutical Good Manufacturing Practice (GMP). This code is a fail-safe system of quality assurance and quality control that defines a number of procedures. In practice, herbal manufacturing under pharmaceutical GMP is more complex than conventional drugs because a herb is biologically defined and:

- May be incorrectly identified
- May vary in chemical content and hence efficacy
- Carries with it a history (eg may be contaminated)
- Processing of herbs may enhance or impair their safety and efficacy
- Stability may be hard to define or measure

It is important that herbal products be manufactured under pharmaceutical GMP, however a specialised knowledge of phytochemistry is also required to effectively deal with these issues. Under the guidance of Professor Kerry Bone, MediHerb has developed an understanding of phytochemistry that is second to none. The work we have done over the past 25 years has influenced the quality of herbal medicines internationally. Herb quality starts with the sourcing of the herb and vigilance is required in every step of the process, right through to how you store your herbs in your clinic.

Sourcing of Herbs

MediHerb is the largest purchaser and processing plant of herbs in Australia and since the beginning we have actively supported Australian and New Zealand herb growers. Our priority is to source herbs from local growers as much as possible and assist with technical support on how best to grow herbs. This support includes information on:

- Varietal selection
- Climatic and soil requirements
- Time of harvest
- Harvesting techniques
- Drying parameters
- Storage requirements post-drying
- Providing feedback to growers on herb quality

By working with herb growers in this way, we have been able to increase the level of knowledge and awareness of issues affecting herb quality.

Wherever possible we aim to source organically grown and wildcrafted herbs, and also work with growers to help cultivate endangered species, for example Golden Seal. We are very fortunate in Australia and New Zealand to have healthy soils and a wonderful climate for herb growing, as a result MediHerb source products from local growers where ever possible.

We also source herbs from overseas where the climatic conditions and specific handling requirements are the optimum, for example Devil's Claw from the Kalahari Desert and Cat's Claw from Peru. It is particularly important for these indigenous communities who depend on the income of the herb crops for their wellbeing that they understand the quality issues and how best to grow or sustainably harvest the herb. Together we can ensure that they will sell their crops and provide income for their community.

Storage and Handling of Herbs

After approval by the Quality Assurance process, all herbs are transferred to our refrigerated warehouse, which is maintained at a constant 15°C and 40% humidity.

Refrigerated storage, although expensive to maintain, avoids the need for any pesticides to be used for insect control. This ensures our organic herbs remain organic and that all our herbs remain free of insect contamination prior to processing.

Herbs are handled and processed at every stage with the utmost care. For example, herbs are milled in preparation for extraction under very low temperature cryogenic conditions to protect against excessive heating, which can damage the fragile active components.

Quality of Extraction: The Birth of MediHerb

MediHerb was co-founded by Kerry Bone, a first class honours graduate of Melbourne University who won the Masson Memorial Prize as Australia's top Chemistry student. Whilst working as a research scientist, Kerry studied naturopathy at the Southern School of Natural Therapies for two years before deciding to relocate to the UK to study phytotherapy in-depth.

Upon completing the four-year Diploma in Phytotherapy from the world renowned School of Phytotherapy in England, he returned to Australia to practice. However he became

increasingly frustrated with the poor quality of herbal extracts available at that time and the resulting effects for his patients. By applying his scientific training he set about developing an extraction method that would be strong enough to enable therapeutic doses (like a 1:1), but preserve the full phytochemical spectrum of the starting herb (like a 1:5 tincture). This led to the development of a unique method of extraction, 1:2 Cold Percolation. Word of these high quality herbal products spread and requests were soon received from health care professionals for supply around Australia and so MediHerb was born.

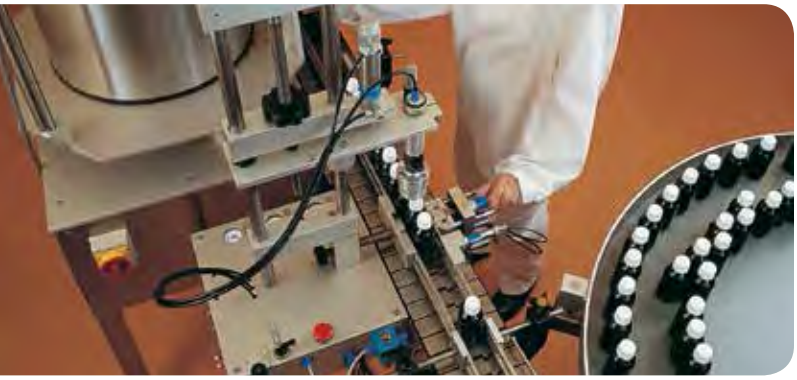
Berberis vulgaris

Why 1:2?

When Kerry Bone set about to develop his own liquid extracts he was faced with a problem. 1:1 liquid extracts theoretically provided a 'stronger' extract, however they also left behind a lot of the phytochemistry of the herb. A true, well-made 1:1 liquid extract cannot be made without using a concentration step (meaning that at least 2L of percolate needs to be produced for every 1kg of herb, which is then concentrated back to 1L). This problem occurs because of the bulky nature of most herbs means that the volume of 1kg generally far exceeds the volume of 1L of liquid. Hence 1:1 liquids can mean that phytochemicals are lost or changed during the concentration step or the herb is poorly extracted by limiting the amount of solvent, leaving most of the phytochemicals still in the raw herb.

Tinctures such as 1:3 and 1:5 solve this problem by providing a true full galenical extract that accurately reflected the chemistry of the original plant, however large volumes would need to be consumed in order to achieve a therapeutic dose.

This led Kerry to develop 1:2 extracts made by cold percolation as they represented the best of both worlds. Similar to tinctures, they didn't need heating or concentrating which could damage the delicate balance of the phytochemical spectrum of the original herb, however they were sufficiently potent to allow the convenient use of therapeutic doses.



Unique Extraction: 1:2 Cold Percolation Process

The MediHerb 1:2 Cold Percolation method is unlike other herbal extraction processes; no heat or concentration is used, both of which may cause damage to the delicate plant material. The greatest care is taken to prevent any contamination from outside sources throughout the extraction process:

- All extraction equipment is designed and built from stainless steel.
- Air used in the manufacturing complex is thoroughly cleaned using pharmaceutical standard filtering units.

In addition to the herb itself, we use only two other raw materials in manufacturing our herbal extracts, ethanol and purified water. Both are chosen very carefully to ensure the most efficacious product and meet pharmaceutical standard specifications.

All process water used in extraction is purified by reverse osmosis. First, it is filtered through numerous filter beds to remove particulate matter and organic compounds, then passed through reverse osmosis cartridges to remove the ionic materials before finally passing through an ultra-fine filter. The water produced is very low in all contaminants – organic, ionic and particulate – and is tested to comply with the *British Pharmacopoeia* specification for purified water BP2014.

MediHerb only uses ethanol that complies with the *British Pharmacopoeia* specification for ethanol, BP2014. Ethanol is essential to extract the full phytochemical profile of the plant, this cannot be achieved using water or glycerol alone. Ethanol has been used for hundreds of years in herbal extraction and old herbal texts discuss steeping herbs in wine over long periods. The human liver is naturally conditioned to metabolise small amounts of ethanol from ripe fruit and naturally fermented food. Any toxic effects from ethanol are dose-related and there is minimal risk of potential ethanol toxicity with herbal extracts due to the low daily dosage required. The usual recommended dose of most 1:2 herbal extracts is only 5 mL three times per day and in 5 mL there is approximately the same amount of ethanol as 1/6 of a standard glass of beer or wine.

Quality Guaranteed – The MediHerb 'Quantified Activity' Program

The MediHerb Quantified Activity (QA) program aims to establish meaningful quality guidelines for the manufacture of herbal extracts. It is a system for ensuring the production of consistent quality extracts with guaranteed minimum levels of active constituents.

To date, MediHerb has quantified the activity of over 70 herbs through this program. To our knowledge such a program has never been undertaken in Australia, nor has it been matched anywhere in the world.

The constituents chosen as 'quality indicators' are carefully selected under the guidance of Kerry Bone and represent the most up-to-date scientific knowledge available.

The process of developing Quantified Activity extracts is complex and involves many steps.

However, once the constituents are selected and the quantified activity levels are set, the main focus is to ensure the supply of consistent quality raw material and the retention of the constituents throughout the manufacturing process.

It is important to point out that Quantified Activity extracts are not purified single constituent extracts. They are whole galenical extracts of carefully selected whole herbs, manufactured using the MediHerb 1:2 Cold Percolation process, and still contain the complex range of active constituents from the raw herb.

Quantified Activity and Standardisation

At times, we receive a herb that has higher levels than our minimum specification, so you as the practitioner receive that higher level of activity. We never dilute to meet a minimum specification. Herein lies the difference between Quantified Activity and standardisation. With standardisation, extracts with an active level that exceeds the specified standard would then be diluted to fall within that standard. (For more information on standardisation view the MediHerb Professional Library at www.mediherb.com.au)

With the MediHerb Quantified Activity program, we have linked together all of the possible parameters that can affect product and extract quality and can guarantee that a high quality, efficacious extract will be produced every time.