Progesterogenic Herbs?

BY KERRY BONE

A number of writers refer to a class of herbs which deliver progesterogenic activity in the body. Herbs placed in this category often include *Dioscorea villosa* (Wild Yam). This association of Wild Yam with progesterogenic effects has arisen for a number of reasons, in particular the fact that progesterone can be synthesized from the steroidal saponin dioscin (aglycone:diosgenin) which occurs in Wild Yam. The purpose of this article is to examine the evidence for progesterogenic effects from plants and thereby arrive at a realistic appraisal of the value, if any, of this concept for modern phytotherapeutic practice.

In order for a plant to have progesterogenic effects, it must do one or more of the following:

- Contain progesterone
- Contain one or more phytochemicals which mimic the effect of progesterone at the progesterone receptor
- Contain one or more phytochemicals which provide chemical precursors for progesterone which stimulate additional progesterone biosynthesis
- Indirectly stimulate the body's normal production of progesterone.

1 Plants as Sources of Progesterone

Plants do synthesize minute quantities of some mammalian steroid hormones, including progesterone.[1] However, the levels of these hormones are too low to cause significant hormonal effects after normal oral doses of these plants. In addition, no studies exist which demonstrate that the levels of these hormones are significantly higher in plants attributed with oestrogenic or progesterogenic activity. Hence, any progesterogenic activity of plants due to their content of progesterone can be discounted as insignificant.

2 Plants and the Progesterone Receptor

It is now widely acknowledged that many phytochemicals are capable of mimicking oestrogen and interacting with the oestrogen receptor.[1] So common is this observation that the special term "phytoestrogen" has been coined to describe these compounds (see *Modern Phytotherapist,* Vol 1 No 2).

However, there are no studies which demonstrate significant binding of phytochemicals to the progesterone receptor. It can be concluded that the progesterone receptor is highly selective, and while significant progesterogenic compounds may exist in plants, they are yet to be discovered. It should also be kept in mind that many plants contain polysaccharides and tannins which can interact non-specifically with many receptors. Such findings do not have clinical significance since, after oral dosage, these compounds are not sufficiently bioavailable or mobile in the body to reach the progesterone receptors. Good technique in receptor assay screening involves the prior removal of such non-specific compounds.

3 Phytochemicals as Precursors for Progesterone

It has been claimed in some circles that the body can manufacture steroid hormones from precursors in some plants. In particular, diosgenin from Wild Yam is said to act as a precursor for both DHEA and progesterone, thereby stimulating their production in the human body. Figure 1 shows the normal biosynthetic pathway for the manufacture of progesterone. It is clear from this diagram that the body manufactures progesterone and other steroid hormones from cholesterol. In other words, the normal precursor of progesterone is cholesterol. However, no-one is suggesting that an increased intake of cholesterol will increase the body's biosynthesis of progesterone. Regulatory factors other than the supply of the precursor determine how much progesterone is made, if any. By the same logic, an increased intake of diosgenin will not lead to increased levels of progesterone.

But there is an even greater problem for the above argument. In Figure 2 the chemical structure of progesterone is compared to that of diosgenin. It is clear from this figure that there are many significant differences between the two molecules. In fact, in living organisms it would be much more difficult to manufacture progesterone from diosgenin than from

cholesterol, and no mammalian enzymes exist which can effect this conversion (it can be done in a laboratory or factory using harsh chemical reagents). There is no study published in a peer review journal to support the contention that the body can make, or is stimulated to make, progesterone after diosgenin intake.

4 Plants which Stimulate Endogenous Progesterone

Plants which stimulate endogenous progesterone can only do so in the premenopausal woman. This is because the ovaries cease to function after menopause and natural progesterone production is halted. A number of herbs are said to stimulate the body's production of progesterone. However, at a clinical level, this has only been proven for two plants.

The commonly accepted understanding of the mode of action of *Vitex agnus castus* is that it stimulates progesterone production by the corpus luteum through stimulating luteinizing hormone (LH) from the pituitary gland. However, recent pharmacological and clinical studies are forcing a reappraisal of this theory. While it has been clinically established that Vitex increases LH and progesterone, it may only do this significantly in women who have deficient luteal phases due to latent or frank hyperprolactinaemia[2] or other causes. Hence, the observed activity of Vitex might be more as a consequence of its dopaminergic activity.[3] Further studies are required to clarify this issue, however the evidence is there that Vitex increases endogenous progesterone production under some circumstances.

In a double blind, randomized, placebo-controlled trial, it was shown that daily intake of 10 g of Linseed (*Linum usitatissimum*) caused a mild non-significant increase in progesterone production in healthy premenopausal women.[4] What was larger and statistically significant was the relative shift in the luteal phase oestrogen/progesterone ratio towards progesterone. This is a favourable finding since many female disorders, including breast cancer, may arise from oestrogen over-exposure in the premenopausal decades. The length of the luteal phase was also significantly increased by an average of 1.2 days. Linseed contains phytoestrogens, and it is likely that other plants containing phytoestrogens will act in a similar way.

The Wild Yam Debate

The theories of Dr John Lee advocate the use of natural progesterone supplementation in postmenopausal women.[5] In this context, natural only means that the progesterone in the administered preparation, which is usually a cream, has the same chemical form as progesterone in the body. While this approach may have clinical merit, the semantics are highly misleading. There is nothing natural about giving progesterone to a postmenopausal woman. This is a time when normal progesterone production has ceased. Therefore progesterone supplementation is basically a form of hormone replacement therapy.

For reasons lost in obscurity, the use of Wild Yam, particularly in creams, has somehow become confused with natural progesterone creams. While a Wild Yam cream may be clinically effective in the control of menopausal symptoms (most herbalists prefer to give oral doses of Wild Yam for this condition), the reasons are probably other than a putative progesterogenic activity. In fact, the opposite is probably true. Wild Yam benefits menopausal symptoms because of its subtle oestrogenic effects.

Rather than discuss in detail the probable mode of action of Wild Yam or diosgenin during menopause, the proof for any progesterogenic activity will be examined. There is little here to go on. Animal studies of diosgenin have shown that while it has oestrogenic activity, it lacks progesterogenic activity.[6] When women were administered Wild Yam cream or tablets, saliva analysis found that their progesterone levels were no different from untreated women.[7] Also, Wild Yam products were found to be inactive in a progesterone receptor assay.[7] Convincing evidence published in a peer review journal for the progesterogenic effect of Wild Yam in postmenopausal women is therefore yet to be provided.

Conclusions

Plants exhibit significant progesterogenic activity only by stimulating luteal phase progesterone in the premenopausal woman. Despite the rhetoric and the controversy, there is no solid evidence for any other kind of progesterogenic activity from plants.

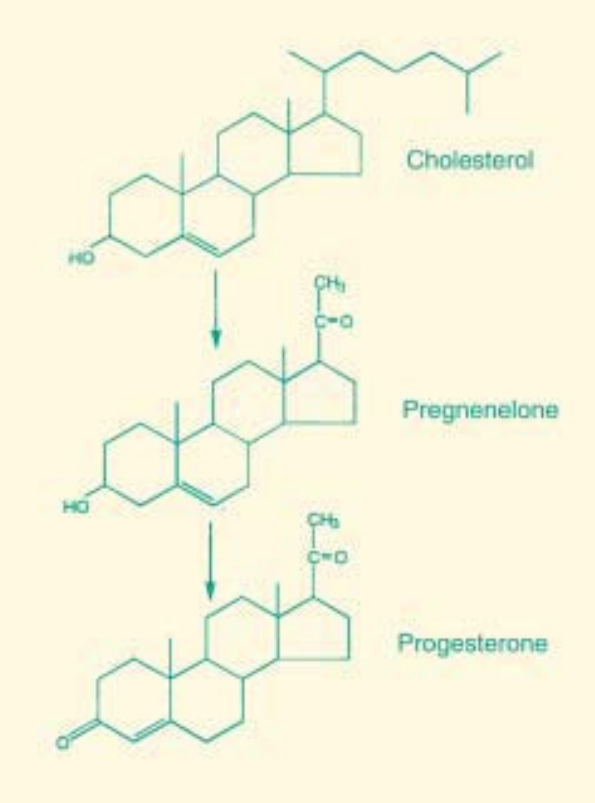

Figure 1: Pathway of progesterone synthesis.

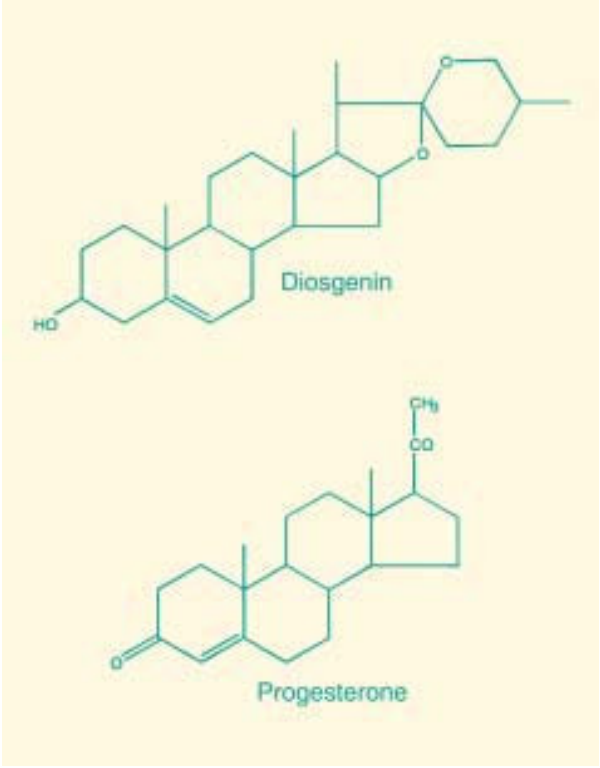

Figure 2: Chemical structures of diosgenin and progesterone.

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