

Clinical application

Medicago sativa extracts

Alfalfa

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INTRODUCTION

Long appreciated for its value as a food for livestock, *Medicago sativa* (alfalfa) has also come to be widely considered as a "health food" and may be found in a variety of forms, including: seeds, sprouts, tablets and a variety of extractions. In addition to its well recognized nutritional value, *Medicago sativa* has several medical uses which can be of value in a naturopathic practice.

MEDICAGO PHYTOESTROGENS

One of the most promising new uses for *Medicago* appears to be in the treatment of endocrine imbalance. Its hormonal activity was first noted in veterinary medicine, where it was observed that animals grazing on alfalfa at times developed traits analogous to those animals treated with synthetic estrogens. Investigators were able to identify several hormonally active compounds in *Medicago*, the most important group of these being the phytoestrogens. These compounds are not true estrogens, yet they possess molecular structures similar enough to estrogen to bind to estradiol receptors. *Medicago* contains three major phytoestrogens: coumestrol, genistein and formonetin; and two less important ones, diadzein and biochanin A. Most phytoestrogens are isoflavones, while coumestrol is a coumarin derivative. Although all lack a true steroid structure, they do have at least one phenol ring and free hydroxyl groups in positions 7 and 12.

Coumestrol is the most hormonally active of the group, with a relative estrogenic activity 5% that of estradiol. This is followed by genistein

with 1% and formonetin with .01% activity. The amount of estrogenic activity of a particular batch of *Medicago* can vary greatly; the activity is highest in the full blooming and seeding stages, and lowest in the spring.

The practical importance of the phytoestrogens lies with their ability to alter the biological response to endogenous estrogen. Estradiol receptors will bind to a diverse group of chemical compounds, including other steroids, isoflavones and phytoestrogens. When phytoestrogens bind to estrogen receptors on cells, they translocate to the nucleus and stimulate cell growth in a manner similar to estradiol. Despite the apparently weak relative binding capacity of the phytoestrogens, they can have significant hormonal effects. This is due to their lower affinity for the serum estrogen binding proteins, this resulting in a net effect of enhancing the concentration of available phytoestrogen at the target tissue sites.

The relative weakness of their estrogenic action means that these compounds will have an "alterative" or "balancing" effect. Thus, phytoestrogens may be used therapeutically in both hypoestrogenism and hyperestrogenism states. It is precisely this quality that makes them so useful therapeutically, especially in a naturopathic setting.

In conditions of hypoestrogenism the plant estrogens will bind directly to estrogen receptors and provide a mild estrogenic effect. This is enhanced by the tendency of the phytoestrogens to concentrate in reproductive tissues, in preference to the serum proteins. This has been clearly demonstrated both in the field (feeding alfalfa to dairy cows can have effects similar to parenterally administered estrogens), and in the laboratory (uterine weight assays show effects equivalent to estradiol when sufficient phytoestrogen was used). This implies a useful role for the phytoestrogens as adjuncts in the treatment of hypoestrogenic conditions, including hot flashes, menopausal vaginal atrophy and treatment or prevention of osteoporosis.

These compounds are equally useful in conditions of hyperestrogenism. The relatively weak-acting phytoestrogens will compete for binding sites, thus reducing the number of receptors available to the stronger endogenous estrogens and reducing net estrogenic stimulation. This is most useful in estrogen excess

conditions such as premenstrual syndrome, fibrocystic breasts, uterine leiomyomas, and estrogen-responsive cancers of the breast and uterus.

Phytoestrogens are not the only hormonally active compounds found in *Medicago* extracts. At least one author has identified an anti-estrogenic compound distinct from the phytoestrogens. This compound is chloroform-soluble and reduces the estrogenic activity of phytoestrogens, diethylstilbestrol and estradiol. This compound appears to have a relative strength of approximately 12% that of the proestrogen activity of the phytoestrogens and would appear to have complementary effects desirable in the treatment of hyperestrogenism.

OTHER USES OF MEDICAGO

Medicago contains an additional compound with thyrotropin-releasing hormone (TRH) activity. Although widely distributed throughout the animal kingdom, TRH has not been isolated previously from the plant kingdom. This TRH analog is biologically active, probably via the hypothalamus rather than the pituitary, and has the additional effect of inhibiting prolactin release. These findings would suggest that *Medicago* extracts could be potentially therapeutic in the treatment of secondary hypothyroidism and conditions of prolactin excess such as polycystic ovaries.

Medicago extracts have been found to contain several other biologically active compounds. A flavone, triclin, has the ability to relax smooth muscle. It is poorly absorbed from the gastrointestinal tract and would thus be primarily useful in conditions of GI cramping or colic. Triclin also has weak estrogenic activity. Triclin is found in relatively small quantities and would not be a primary cause for prescribing *Medicago*. However, its smooth muscle relaxing activity might be a useful side effect when prescribing *Medicago* for other purposes.

Medicago sativa also contains a plant growth stimulating substance identified as Triacontanol. When applied to crops it increases the growth and yield of several species. Applying 117kg of Alfalfa to a hectare of tomatoes increases yields by 10 metric tons per hectare. This is relevant to medical practice only in the sense that it

indicates the wide diversity of biologically active compounds present in the plant. With further study we will no doubt identify even more. In addition to phytoestrogens, plant analogues of hormones have been identified in gluten, which exerts opioid-like activity, and *Avena sativa*, which contains a substance with leutinizing hormone releasing factor-like activity.

USE OF MEDICAGO IN HYPER-CHOLESTEROLEMIA

Cardiovascular disease is the number one killer in this country. Approximately half of all deaths are related to some form of this condition. One of the goals in treating cardiovascular patients should be to reduce their cholesterol values, while also addressing other issues as necessary, such as minerals, anti-oxidants, lifestyle, etc. *Medicago* extracts can be very useful for this purpose as there is a substantial amount of literature which supports their use in cholesterol reduction. All parts of the plant have been used in one or more studies, and in each study the component tested, whether it be the seeds, the roots or the meal, has demonstrated anti-cholesterolemic and anti-atherogenic activity.

Alfalfa meal appears to lower total cholesterol, triglycerides, low density lipoproteins (LDL) and very low density lipoproteins (VLDL) while not significantly lowering the desirable HDL substractions. This leads to a significant reduction of the total cholesterol/HDL ratios, one of the major predictors of cardiovascular risk. This action appears to be due to the reduced intestinal absorption of both endogenous and exogenous cholesterol and an increase in fecal biliary excretion.

The mechanism behind this reduction appears to be related to the phytosterols, and to a lesser extent the saponins, present in alfalfa. Phytosterols are plant sterols which have limited intestinal absorption but compete cholesterol for binding sites, thus decreasing total cholesterol absorption. The primary phytosterols in alfalfa are β -sitosterol and stigmasterol, with lesser amounts of campesterol and alpha spinesterol. Animal studies using rabbits, chicken rats and monkeys have shown a reduction of cholesterolemia and arteriosclerosis when plant sterols were fed in conjunction with a diet equivalent to the average

American intake of cholesterol.

The saponins in Alfalfa also have an anti-cholesterolemic effect. A diet of 1% alfalfa-top saponins added to the diet of rats significantly reduced cholesterol and triglycerides. This level of saponins had no deleterious effects on growth, survival, serum glucose, BUN, creatinine, sodium, potassium or chlorides, calcium, total protein, bilirubin, hematocrit or liver enzymes. At post mortem animals fed these levels of saponins for 6 months showed no differences in gross or microscopic pathology from controls on a similar diet without saponins.

CANAVANINE AND AUTO-IMMUNE DISEASE

Although the seeds of alfalfa have an anti-cholesterolemic activity they are a less desirable treatment for hypercholesterolemia because they also contain significant amounts of canavanine. This compound is a non-essential amino acid which competes with arginine and has been found to induce a reversible lupus-like condition in some individuals. This syndrome is characterized by anemia, antibodies to DNA, and deposition of immunoglobulins and complement in the skin. The suspected mechanism is a loss of T suppressor activity due to some action of the canavanine, perhaps combined with a polyclonal activation of B cells. Those individuals with HLA haplotypes and acetylator phenotypes appear to be more susceptible to this condition, as well as almost everything else known to go wrong with the human body. Canavanine is known to be present in the seeds of many leguminous plants, but alfalfa is one of the few which is consumed in large quantities in this country. In order to avoid the risk of developing this condition patients should be encouraged to use the mature tops of the alfalfa plant which contain both the saponins and phytosterols but no canavanine, rather than seeds or sprouts.

NUTRITIONAL EFFECTS OF MEDICAGO

Alfalfa is a good source of vitamins and minerals due to its deep roots which extract nutrients from the substrate even when surface soils are depleted due to poor agricultural methods. Alfalfa contains vitamins A, B1, B6, B12, C, E, niacin,

Condition	Desired affect
HYPOESTROGEN, MENOPAUSE, HOT FLASHES;	Will benefit from the phytoestrogens present in Medicago.
HYPERESTROGEN, FIBROCYSTIC BREASTS, PMS, BREAST CANCER:	The alterative effects of phytoestrogens competing for cell receptors will decrease estrogenic stimulation and benefit these conditions.
AUTOIMMUNE DISEASE:	Because many autoimmune conditions such as Systemic Lupus Erythematosus are aggravated by estrogens, patients may benefit from the hypoestrogenic effects of <i>Medicago</i> extracts. Clinicians should verify that the medication used is not formulated from alfalfa seeds which contain canavanine which would be contraindicated in these conditions.
HYPER-CHOLESTEROLEMIA:	The sterols and saponins in <i>Medicago</i> will reduce the uptake of cholesterol from the gut, lowering total cholesterol, triglycerides, LDL and VLDL without lowering HDL.
POLYCYSTIC OVARIES:	The TRH and antiprolactinemic properties of alfalfa, combined with the estrogen balancing capacity of the phytoestrogens, make <i>Medicago</i> an excellent addition to treatment protocol for this condition.
NUTRITIONAL SUPPORT:	By providing a source of many vitamins and minerals <i>Medicago</i> extracts are an important source of alternative nutritional supplementation for patients who object philosophically to taking synthetic vitamin pills but who are in need of concentrated nutritional support.

TABLE 1. Summary of conditions in which *Medicago* extracts may be indicated

pantothenic acid, folic acid, biotin, vitamin K1, amino acids, carotenes, chlorophyll, and most trace minerals. This high nutritional value of alfalfa explains its frequent use as a food source for livestock and as a favored "health food" since the turn of the century.

With the use of herbs such as alfalfa, it is truly possible to "let our foods be our medicines" and to learn to appreciate the power inherent in the wise use of our natural medicines. With the

*very non-holistic
& somewhat allopathic*

proper selection of dietary and botanical medicines we can treat many conditions without the need for more invasive therapies. When we use these plants medicinally as an alternative to synthetic drugs, it is essential to remember that we are utilizing the specific plant components in order to produce pharmacological actions. Thus, we would be well advised to utilize the most concentrated sources available. In the case of *Medicago* the preferred forms are solid extracts, fluid extracts and concentrated tinctures. Teas and tablets may not deliver enough active ingredient to be effective. Suggested doses are:

1/4 to 1/2 tsp of solid extract BID AC.

or

1 to 2 tsp of fluid extract or tincture concentrate BID AC

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