

Exploring the Relationship Between Toxicity and Hormonal Imbalance



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White paper summary

The modern world is full of toxins that we don't fully understand. Anyone who works in natural or holistic medicine can attest to the fact that chronic illnesses are on the rise. Examples of these illnesses include asthma, diabetes, heart disease and a variety of cancers. The rise of these diseases might be attributed, to some degree, to toxicity in the environment and how the body interacts with those toxins.

Science has shown a clear link between excess levels of toxins and hormonal imbalance. A 2004 study from the Environmental Working Group revealed that fetus cord blood contained 154 chemicals related to hormone disruption, and 186 chemicals associated with infertility. There can be little doubt that many of the issues patients face involving hormone imbalance are impacted by the level of toxicity we are exposed to every day.

There are two primary areas of support when dealing with hormone imbalance related to toxicity. First is improving liver function through the use of hepatoprotective herbs. Second is the use of botanicals to relieve ongoing symptoms of hormonal imbalance. Research and clinical usage show that specific botanical agents can play important roles in liver detoxification and restoration of hormone balance.

The most widely used and effective hepatoprotective herbs include:

- Milk Thistle (*Silybum marianum*)
- Dandelion (*Taraxacum officinale*)
- Turmeric (*Curcuma longa*)
- Schisandra (*Schisandra chinensis*)

Milk thistle has been used for more than 2,000 years and has been studied fairly extensively for use in various liver and gallbladder diseases. Its primary constituents, silymarin and silibinin appear to reduce serum transaminase levels and improve the cellular appearance of the liver. Dandelion can improve symptoms related to liver disease, while turmeric is useful for improving the digestion element of liver function. Schisandra also demonstrates hepatoprotective properties, and like turmeric, contains strong anti-oxidant properties.

Botanicals commonly used to treat problems stemming from hormonal imbalance include:

- Chaste tree berry (*Vitex agnus castus*)
- Red clover (*Trifolium pratense*)

Chaste tree berry can effectively address many issues stemming from hormone imbalance such as cyclic mastalgia, PMDD, PMS related symptoms and menstrual irregularities. Many research studies have shown chaste tree berry extract to have significant positive effects in conditions of hormone imbalance; in many cases, the improvement rate was higher than 90%. Red clover, known for its phytoestrogen properties, may also be used to improve menstrual irregularities and menopausal symptoms.

A summary of each botanical's recommended dosage, contraindications, and possible side effects follows:

Botanical	Dosage	Contraindications	Possible Side Effects
Milk thistle	160–800mg, in divided dose	Possible glucose lowering Cytochrome P450 medications Avoid in patients with: - Silybum allergy - Asteraceae family allergy	Rare—headache, GI upset
Dandelion	Leaf fluid extract, 4–8mL in 1:1 Root extract, 1-2 tsp in 1:5	GRAS status Avoid in patients with: - Asteraceae family allergy - Taraxacum family allergy	Rare—dermatitis, GI upset
Turmeric	1.0–7.5g daily, in divided doses	GRAS status CYP3A4 medications Avoid in patients with: - Curcuma family allergy - Gastric ulcers	Generally well tolerated
Schisandra	1.6–6g powder daily, in divided doses 2–4 mL liquid extract, tid	Platelet-activating factor antagonist Photosensitizer Possible glucose lowering Avoid in pregnancy and lactation Avoid in patients with: - Schisandraceae family allergy	Generally well tolerated
Chaste tree berry	20–160mg, tid 1 mL, 3–4 times daily	Use cautiously with oral contraceptives Avoid in patients with: - Vitex family allergy	Mild skin reactions
Red clover	40–160mg daily	Avoid in pregnancy and lactation Avoid in patients with: - Fabaceae family allergy	Generally well tolerated

Additional details on the clinical research behind these herbs, and a more comprehensive discussion of the dosing, safety, and contraindications of each botanical, can be found in the remainder of this white paper.

Toxicity is ever-present

It is estimated that about 30% of health is determined by genes. This is a number that no one has control over; it is predetermined from birth. The remaining 70% is determined by environmental factors, an area where some control and influence can be exerted.

The problem is toxicity is everywhere. The Environmental Working Group conducted a study in 2004 taking one blood sample from ten different people in the United States. Researchers focused specifically on cord blood from fetuses. The cord blood was tested for 413 different specific toxic chemicals and the study revealed that 287 of these toxic chemicals were found in the cord blood. About 200 chemicals were found per person in the study. These toxins fell into different categories: 28 were in waste product ingredients (such as dioxins, furans, car exhaust and VOCs) and 47 were consumer product ingredients (such as perfluorinated chemicals and flame-retardants). More than 212 industrial chemicals were found in the subjects of the study.

Chemicals from things such as pesticides on food pose a similar threat to health. While many of these pesticides were banned more than 30 years ago, traces of the chemicals can still be found in the soil in the United States. These chemicals appeared in the cord blood of some of the subjects. Obviously, foods imported from other areas of the world can have a wide range of chemicals.

According to the EPA, in 2004 more than 600 million pounds of 650 different pollutants were emitted into the air. There are an estimated 1,000 contaminants in air and water from utility and government tests.

There are more than 1,000 contaminants from food packaging that have been approved by the FDA. In the Environmental Working Group study there were 168 ingredients that are known to be toxic in 12 personal care products specifically used by women on a daily basis. There were 85 ingredients that are known to be toxic in 6 personal care products that are used by men on a daily basis. There were 134 chemicals found that related to the development of cancer. At least 151 chemicals found in the study were shown to have associations with birth defects.

Health effects from toxicity

Hormone disruption was found to be associated with about 154 chemicals in the Environmental Working Group study. Infertility, which is on the rise in the United States, was associated with 186 chemicals found in the study. Similarly, immune system disruption, which is also on the rise, was associated with 130 chemicals in the study. Neurotoxins were associated with 158 chemicals.

Some of the chemicals found in this study could also have multiple harmful effects on the body. What's more, some people are simply more vulnerable to the effects of toxic chemicals. The impact on multiple body systems means a strong, ongoing need for clinical, focused and specific support.

The relationship between toxicity and hormonal balance

Toxins can play a major role in hormonal disruption, imbalances and the acceleration of aging. They can even affect weight gain since toxins can potentially inhibit the body from processing fat. An increasing number of women report having cyclic mastalgia and menstrual irregularities. As noted earlier, infertility is also on the rise.

Botanical agents for liver detox and hormonal balance: Featured plants

There are two classes of herbs that are particularly effective at lessening the damaging effects of toxicity. Herbs that protect the liver, also known as hepatoprotective herbs can be particularly effective in decreasing the number of toxins that enter the body. Some of these hepatoprotective herbs include milk thistle, dandelion root and leaf, turmeric and schisandra. Similarly, herbs that provide hormone support can help minimize the hormone imbalance effects of toxicity. Some of these herbs include chaste tree berry and red clover.

Hepatoprotective herbs

Milk Thistle (Silybum marianum)

Milk thistle is among the most effective botanicals for protecting the liver. This herb provides broad-spectrum, robust support of hepatic and biliary function. It has been in use for more than 2,000 years. Its primary constituents are silymarin and silibinin. Silibinin, which is a flavonoid, has been shown to exhibit anti-cancer effects and to suppress cell growth.



Research

Research for milk thistle, specifically for the constituent silymarin fraction, suggests that this herb reduces serum transaminase levels. It has also been shown to improve cellular appearance of the liver, histology and survival times in patients who have cirrhosis or chronic hepatitis.

A systematic review and meta-analysis of milk thistle looked at the effects of the herb on liver disease. The review included 16 randomized, controlled trials, and 17 non-placebo trials. Across the 33 studies, most favored the use of milk thistle. Six trials looked specifically at chronic alcoholic liver disease, three looked at viral hepatitis, both acute and chronic, four looked at cirrhosis of the liver and three looked at hepatotoxins.¹

¹ Jacobs B, Dennehy C, Ramirez G, et al. Milk thistle for the treatment of liver disease: a systematic review and meta-analysis. *Am J Med* 2002; 113(6):506-515

Dosing

Dosing for milk thistle will range depending on treatment needs and goals. Here are some common dosages for a number of issues:

- Cirrhosis:
 - 180–600mg daily, oral ingestion
- Toxin-induced/drug hepatotoxicity:
 - 180–600 mg daily, oral ingestion
- Chronic hepatitis
 - 420 mg daily in 3 divided doses
- Hepatitis (acute, viral):
 - Doses ranging from 160–800mg daily, orally, have been used to treat hepatitis. Silymarin, 420 mg daily, in 3 divided doses.

Contraindications

Milk thistle is generally considered to be safe. There are no reports of toxicity with the use of milk thistle when used within the standard dosing range. Silymarin has been shown to decrease fasting plasma glucose levels in patients with insulin-dependent diabetes associated with cirrhosis.² Patients with known allergies or hypersensitivities to the Silybum family, Asteraceae family or any milk thistle constituents should avoid using milk thistle.

Dandelion (Taraxacum officinale)

Dandelion is a traditional springtime tonic and salad ingredient. The leaves are a source of vitamin A, up to 1,400 IU per 100g. This plant helps relieve symptoms of diseases in which impaired liver function plays a role, including hepatic detoxification functions.

² Velussi, M., Cernigoi, A. M., De Monte, A., Dapas, F., Caffau, C., and Zilli, M. Long-term (12 months) treatment with an anti-oxidant drug (silymarin) is effective on hyperinsulinemia, exogenous insulin need and malondialdehyde levels in cirrhotic diabetic patients. J Hepatol. 1997;26(4):871

Dosing

The dried root infusion or decoction of dandelion can be given in doses of 2–8g. The leaf fluid extract can be given in doses of 4–8mL of a 1:1 extract in a 25% alcohol base. The root tinctures can be given in doses of 1 or 2 tsp of a 1:5 tincture in about 45% alcohol base.



Contraindications

Dandelion is Generally Regarded as Safe (GRAS) by the FDA with rare side effects that may include contact dermatitis, diarrhea and gastrointestinal upset. There are no reported cases of toxicity with the use of dandelion when used within the standard dosing range. Patients with known allergy/hypersensitivity to the taraxacum (Asteraceae/Compositae) family (e.g. ragweed, daisies, marigolds and chrysanthemums) or any dandelion constituents, or to members of the Asteraceae family, should avoid using this botanical agent.

Turmeric (Curcuma Longa)

Turmeric, also known as curcuma longa, is a potent antioxidant and a free-radical scavenger. The average dietary intake in the Asian Indian population may range between 2 and 2.5g, as it a common herb used for both medicinal and flavoring purposes. Interestingly, it has been speculated as a source for this population's protection from arthritic symptoms.

Turmeric plays a role in liver and gallbladder disease, working specifically on the digestive side of liver function. When people experience dyspepsia, turmeric can be extremely helpful. It has traditionally been used to treat many GI disorders, particularly indigestion from fatty meals.

Research: Turmeric and liver/gallbladder disease

Turmeric is an effective herb at treating liver and gallbladder disease. A clinical study looked at the use of turmeric for dyspepsia. The dried root powder of this herb was given at 250mg doses four times a day. After one week, 71% of the turmeric patients had clinically improved, and 16% were considered to be cured. A second group was given a placebo. Only 42% of the placebo patients had clinically improved and 11% were considered to be cured.³

Another study evaluated the use of turmeric in treating biliary dyskinesia and chronic right upper-quadrant colic. A treatment group was given 45g of curcumin and 104mg of celandine. That group was compared to a placebo group. After three weeks of usage, a small but significant reduction in colic pain was noted in the treatment group versus the placebo group.⁴

A third study of turmeric looked at the herb's role in bile flow and gallbladder stasis. Preliminary human data from the abstract suggested that curcumin might play a role in the prevention of gallstones. This randomized, double-blind, crossover study examined the effects of 20mg of curcumin or placebo on gallbladder size in 12 healthy people. Participants were given 20mg of curcumin after a night of fasting and their gallbladder volume was measured with an ultrasound. There was a one week washout period where the subjects received alternative therapy. Gallbladder contraction was shown to occur in the curcumin group 30 minutes after administration. After two hours, there was a mean reduction in volume of 16%. In the placebo group, the initial contraction was similar to the curcumin group. After two hours the mean gallbladder volume increased to 31%.⁵

Dosing

Common dosing suggestions for turmeric are as follows:

- General use:
 - 1.5–7.5g of turmeric daily in 3–5 divided doses with food.
- As a tea:

³ Thamlikitkul V, et al. J Med Assoc Thai 1989;72(11):613-620

⁴ Niederau C, Gopfert E. Med Klin 1999;94(8):425-430

⁵ Rasyid A, Lelo A. Aliment Pharmacol Ther 1999;13(2): 245-249

- 1–1.5g of dried root steeped for 15 minutes in 150mL of water, twice daily.
- As an antioxidant:
 - Two 500mg oral doses daily can be used for 3 months.

Turmeric contraindications

Clearly, those with allergies or hypersensitivities to the Curcuma family (Zingiberaceae) or any turmeric constituents, including curcumin, other members of the ginger family, or certain yellow food colorings, should avoid using this botanical agent. It should not be taken in dosages higher than 8,000mg daily.⁶ Patients with bile duct obstructions or cholelithiasis should not take turmeric since this herb might be too stimulating and cause their situation to flare. Similarly, patients with gastric, duodenal ulcers or gastric hyperacidity disorders should not use this herb.

Schisandra (Schisandra chinensis)

Schisandra has many adaptogenic effects. It has been shown to improve stress resilience and resistance to adverse factors including those that are physical, chemical and biological. It also has numerous hepatoprotective properties.



⁶ Bayet-Robert, M., Kwiatkowski, F., Leheurteur, M., Gachon, F., Planchat, E., Abrial, C., Mouret-Reynier, M. A., Durando, X., Barthomeuf, C., and Chollet, P. Phase I dose escalation trial of docetaxel plus curcumin in patients with advanced and metastatic breast cancer. *Cancer Biol. Ther.* 2010;9(1):8-14.

There are several constituents of schisandra that possess strong antioxidant activity. Like turmeric, it has a component that offers healing from toxicity exposures. Schisandrin B, Schisandrin C and Schisanhenol were found to be more potent antioxidants than vitamin E (a well-known antioxidant) at similar concentrations. Schisandra enhances the hepatic glutathione antioxidant system, inducing the liver microsomal cytochrome P450 cycles and stimulating protein and liver glycogens.^{7, 8}

Dosing

Schisandra can be given in the following dosages:

- 1.5–15g of dried schisandra fruit daily for up to 100 days
- 2–4mL of schisandra tincture 3 times daily for up to a month
- 1.5–6g of schisandra powder daily, divided doses, three times per day
- 1–3 cups of tea daily, or 1–6 grams of dried berries in 1–3 cups of boiling water

Contraindications

Patients with known allergies to any of the constituents of schisandra or to the schisandra family should not use this herb. Schisandra should be avoided in pregnancy and lactation due to insufficient evidence about the effects of the herb on this population. Those with bleeding disorders due to proposed platelet-activating factor antagonist activity, or those with seizure disorders, high intracranial pressure or high blood pressure should avoid schisandra. Schisandra acts as a photosensitizer and should therefore be avoided in those with skin diseases. If a patient has GERD or peptic ulcer disease, schisandra may exacerbate these conditions by increasing gastric activity. Patients with neurologic disorders, or those engaging in activities that require alertness, may want to avoid schisandra due to secondary reports of CNS depression associated with the herb. Schisandra may lower blood sugar, therefore it should be avoided in patients with diabetes. Some schisandra preparations may even contain sugar which may increase blood glucose.

⁷ Lu, H. and Liu, G. T. Anti-oxidant activity of dibenzocyclooctene lignans isolated from Schisandraceae. *Planta Med* 1992;58(4):311-313.

⁸ Lu, H. and Liu, G. T. Effect of dibenzo[a,c]cyclooctene lignans isolated from *Fructus schizandrae* on lipid peroxidation and anti-oxidative enzyme activity. *Chem Biol Interact.* 1991;78(1):77-84.

Herbs that provide hormone support

Chaste tree berry (Vitex agnus castus)

Chaste tree berry can address numerous issues, particularly issues related to hormonal imbalance. This botanical can be used to treat cystic mastalgia, PMDD (premenstrual dysmorphic disorder) and PMS-related migraine headaches. Menstrual irregularities are on the rise, perhaps as a result of the increase in toxins in the environment. Chaste berry can help with these irregularities. It can also be used to treat luteal phase deficiencies. Finally, it can be used to treat hyperprolactinemia.



Research

There have been numerous studies conducted on the effects of chaste tree berry. A double-blind, placebo-controlled study showed significant improvement of cyclic mastalgia with the use of a chaste tree berry extract. The study looked at the response to stressful situations as well as aggravation by chronic stress. Serum prolactin levels and symptomology reports were shown to decrease.⁹

An open study of 1,634 patients demonstrated the efficacy of chaste tree berry extracts in relieving four common PMS symptom complexes. Key symptoms included cravings, anxiety,

⁹ Wuttke W, Jarry H, Christoffel V, Spengler B, Seidlová-Wuttke D. Chaste tree (Vitex agnus-castus)--pharmacology and clinical indications. *Phytomedicine* 2003 May;10(4):348-57.

depression and hyper-hydration (swelling, edema and bloating). Treatment time was for three menstrual cycles, or 90 days. In the study, 93% of patients reported a decrease of these symptoms or even complete cessation of PMS symptoms. What's more, 81% of patients related their status as "very much" or "much" better at the end of this study. For patients whose predominant symptom was mastalgia, after 3 months of treatment, all PMS symptoms were less severe.¹⁰

A three month, open label study for PMS and migraine headaches looked at 107 patients at the start of the study and 100 at the finish. The overall response for PMS reported symptoms showed that 66 women reported dramatic reduction of symptoms, 26 reported mild reduction and 8 reported no change. Ultimately, the overall effectiveness of chaste tree berry was 92%. The same study looked specifically at migraine symptoms. In this portion of the study, 42% of women had reduction of migraine frequency by more than half and 57% of women had reduction by more than half in the number of days each month with a migraine headache. No side effects were reported.¹¹

A research review of 12 RCTs with chaste tree berry extract contained 8 studies related to PMS, 2 on PMDD, and 2 regarding latent hyperprolactinemia and luteal phase deficiency. One of the PMDD studies found that chaste berry extract was equivalent to fluoxetine (Prozac), while the other study found fluoxetine to be better than the extract.

One of the studies on latent hyperprolactinemia and luteal phase deficiency showed that the chaste tree berry extract was superior to a placebo for normalizing a shortened luteal phase, reducing TRH-stimulated prolactin secretion and increasing mid-luteal progesterone and 17-beta estradiol levels. Yet another trial found the extract comparable to bromocriptine (Parlodel) for reducing serum prolactin levels and improving cyclic mastalgia symptoms. Adverse events with the extract were mild and generally infrequent.¹²

¹⁰ Loch EG, Selle H, Boblitz N. Treatment of premenstrual syndrome with a phytopharmaceutical formulation containing Vitex agnus castus. *J Womens Health Gend Based Med.* 2000 Apr;9(3):315-20.

¹¹ Ambrosini A, Di Lorenzo C, Coppola G, Pierelli F. Use of Vitex agnus-castus in migrainous women with premenstrual syndrome: an open-label clinical observation. *Acta Neurol Belg.* 2012 Jul 12. [Epub ahead of print]

¹² Van Die MD, Burger HG, Teede HJ, Bone KM. Vitex agnus-castus Extracts for Female Reproductive Disorders: A Systematic Review of Clinical Trials. *Planta Med.* 2012 Nov 7. [Epub ahead of print]

Dosing

Chaste tree berry can be given in the following dosages:

- For general PMS and related symptom relief
 - Dosage range used in the studies and for clinical practice is varied. In general, a patient may need to wait two to three months to see any tangible results from chaste berry for general PMS symptoms.
- Liquid, alcohol-based tinctures or encapsulated tinctures:
 - 4:1 extract at 1mL, 3–4 times daily with food
- Dried fruit:
 - 0.5–1.0g 3 times daily, or 3.5–4.5mg daily of dried extract

Dosing can range in the presence of different conditions. Common dosages are as follows:

- In hyperprolactinemia:
 - If a patient's blood has been tested and the prolactin levels have been shown to be elevated, dosage range varies in the research literature from 20mg daily to 160mg of chaste tree berry extract taken up to 3 times daily. This means that when prescribing chaste tree berry, severity and intensity should be important factors to the level of herb prescribed. It is also important to consider how much toxicity a patient has been exposed to over their lifetime.
- In cyclic mastalgia:
 - Dosing strategy can vary, from prescribing for daily use to prescribing just the week or two before the menstrual period is expected to begin (in women who have a regular, predictable menstrual cycle). Liquid alcohol-based tinctures or encapsulated tinctures of 4:1 extract can be given at around 1mL, 3–4 times daily.

Contraindications

There are no reports to date of toxicity of chaste tree berry when it is used within the standard dosing range. As is almost always the case, if a person has a known allergy or hypersensitivity to the Vitex family or any of its constituents, chaste tree berry should be avoided. Clinical trials have reported some mild skin reactions, including some itching and rash, eczema and urticarial, minor skin eruptions. Chaste tree berry should be used cautiously in patients taking oral contraceptives or hormone replacement therapy. It should also be avoided in patients who are pregnant, breastfeeding or those who are undergoing in vitro fertilization. Caution should

be used in patients taking dopamine agonists or antagonists and it should be avoided in patients with hormone-sensitive cancers or conditions.

When specifically talking about pregnancy and lactation, theoretically, chaste berry should be avoided during lactation because it competitively binds to dopamine receptors and has been shown to affect prolactin secretion, possibly resulting in decreased breast milk production. However, some clinicians actually use low doses to stimulate milk production with some reported benefits.

Red clover (Trifolium pratense)

Red clover is a nutritionally dense herb that contains numerous ingredients such as genistein, daidzein and biochannin-A. It is a member of the flavonoid family. A legume, this plant contains phytoestrogens, a plant-based compound that is structurally similar to estradiol and capable of binding to estrogen receptors as agonists or antagonists. It is generally used as a tonic for menstrual irregularities and menopausal symptoms.

Dosing

Clinical studies have used red clover isoflavones ranging from 40 to 160mg per day to assist with menopausal symptoms.



Contraindications

Red clover should be avoided in those with allergies or hypersensitivities to any of its constituents or to members of the Fabaceae family. Good tolerance has been demonstrated in studies of daily usage of up to a year. It can be a long-term supporter. It is not recommended during pregnancy and lactation due to its in vitro estrogenic activity. Extensive toxicology studies are not available at this time.

Conclusion

The toxicity of the modern world calls for proactive health protection plans. Hormonal balance is readily impacted by the prevalence of hormone disruptors and hormone mimickers in the environment. There is a compelling need to protect liver function as it is a key organ for detoxification and hormone processing. There are various botanicals that can aid in this process.

But these botanicals are not magic bullets and often require several months to show effects. Because of this, it is crucial to educate patients about the length of time needed to achieve results. It is also important to set expectations; for example, it is unrealistic for someone with a chronic problem like cyclic mastalgia with PMS problems, to be cured with botanicals in a few weeks. Informing patients that these botanicals can take up to four months to take effect will help to establish a realistic set of expectations around timeline.

Botanicals medicines play a key role in minimizing damage from toxicity and promoting recovery from toxic exposures. Chaste tree berry, milk thistle, dandelion, turmeric, red clover are all helpful, healing herbs for dealing with toxicity and hormonal imbalances.

Contributor

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Dr. Yates serves as a National Media Representative for the American Association of Naturopathic Physicians, appearing as an expert in natural medicine on TV shows in select metropolitan areas. She is a member of the Medical Advisory Board for Schwabe North America, and is on the Scientific Advisory Board for Gaia Herbs, Inc. and BSP Pharma, Inc. Recently, in response to Dr. Yates' contributions to community health, she provided testimony for the Tri-Caucus of the California legislature concerning the growing impact of obesity and diabetes in communities of color around the state and the country.

Dr. Yates is a nationally recognized author [book: Heart Health for Black Women: A Natural Approach to Healing and Preventing Heart Disease, Marlowe & Co., 2000] and contributing author [medical textbook: Maternal Newborn and Child Nursing: Family Centered Care, Prentice Hall, 2003].