

MILK THISTLE AND BREAST CANCER: SETTING THE RECORD STRAIGHT

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Recently, a publication has been widely circulated that makes the surprising claim that the herb milk thistle should be taken out of women's hormone balancing formulae and avoided by women who have breast cancer or are at risk of having breast cancer. It claims that milk thistle may cause breast pain and raises the alarm that it may even cause breast cancer.

Though we have, unfortunately, become very familiar with the need to defend herbs from attacks coming from conventional medical sources and mainstream media, this attack is surprising because it comes from within the natural health industry, being launched from an online natural health newsletter. Ironically, outside the natural health community, the mainstream medical and cancer organizations and publications have no accusations to make regarding the safety of milk thistle, are even positive about this herb, and sometimes even recommend it.

The National Cancer Institute (NCI) says that "Human studies of silymarin [the collective name for milk thistle's flavonolignans--which include silibinin, silydianin, silychristin—the main active ingredients in milk thistle] have shown minimal adverse effects in multiple large, blinded, placebo-controlled, randomized studies." It adds that, at recommended doses, "[s]ilymarin is well tolerated, with only rare reports of a mild laxative effect". The NCI goes on to admit that milk thistle may actually make the chemotherapy drugs doxorubicin and cisplatin work better against breast cancer (and ovarian cancer) and that it may even have direct anticancer activity against breast (as well as prostate and cervical) cancer. The German Commission E says there are no contraindications for milk thistle. It says that the only adverse effect is an occasional mild laxative effect. It goes on to endorse the herb as safe for pregnancy and breast feeding: a recommendation consistent with a positive hormone safety rating.

This attack on milk thistle's safety is also surprising because the herb has been very safely used for over two thousand years. It is one of the most extensively studied herbs and has an exceptional safety record. So what's the problem?

The criticism of milk thistle's safety is based on two studies. The first found that milk thistle given to rats for fourteen days increased circulatory levels of the hormone prolactin (1). It then goes on to make two claims. The first is that this result is enough to explain why some women develop painful swollen breasts when they take milk thistle, and the second is that this result sounds the alarm because elevated prolactin may cause breast cancer.

But the report that women experience painful swollen breasts when taking milk thistle appears nowhere else in the literature. A survey of important women's herbals produces no mention of this side effect. Nor does a survey of important books on herbal safety and contraindications. In our own experience, in Linda's many years of clinical experience as a herbalist, she has never seen any of the many women she has put on milk thistle develop painful, tender or swollen breasts. And Linda's experience is verified by the experience of other herbalists. Rosemary Gladstar, one of the best and most experienced herbalists and women's health experts, responded to our question whether she had ever seen a woman develop

swollen, tender or painful breast while taking milk thistle with the single word “never”. She says that in her experience, milk thistle is “a safe benign herb with no side effects” (2).

Milk thistle does not cause breast pain. And that means there’s something wrong with the critical conclusions drawn from the study. Either milk thistle does not increase prolactin in humans, or, if it does, you cannot infer that milk thistle’s increasing prolactin increases the risks associated with increasing prolactin, like breast pain and breast cancer, because it doesn’t increase breast pain.

But the problems with sounding the alarm over milk thistle’s safety based on this study are more serious than that. Though the criticism makes negative conclusions, it is crucial to realize that the study did not. The study made no negative conclusions about safety or anything else: it was a positive study that offered its results as an explanation of the success of milk thistle as a galactagogue, a herb that increases breast milk. The conclusion that the study’s authors make is that milk thistle is “a good candidate for the treatment of lactation insufficiency”. Drawing conclusions from a study that differ from the conclusions the study was designed to test is a risky endeavor.

Perhaps even more damaging is the design of the study itself. The researchers administered a standardized extract of milk thistle to rats at a dose of 25-200mg/kg. The recommended dose of milk thistle for humans is 140mg of silymarin two to three times a day. That means that if a milk thistle extract is standardized for the usual 70% silymarin, the proper dose is 400-600mg of milk thistle per day. But the study used 1,700-13,600mg of milk thistle extract a day. That is massively in excess of any dose a person could possibly take, raising serious questions about any results that can be drawn from this study about human use.

Drawing conclusions from this study regarding human use is also seriously impaired by the fact that the herculean dose was administered, not to humans, but to rats. As cancer expert John Boik, Ph.D. pointed out to us, “any rodent study is already suspect [since the] results might not transfer to humans” (3). Leaving aside the obvious ethical questions about experimenting on animals, that massive doses of milk thistle raise prolactin levels in rats does not prove that small amounts of milk thistle raise prolactin levels in humans.

But there is a more fatal flaw in this study. Though the researchers began giving the rats milk thistle extract at a dose of 25mg/kg, that did not raise their prolactin. Their prolactin levels did not begin to climb until 50mg/kg of milk thistle was given. That means that milk thistle does not raise prolactin levels until a human equivalent of 3,400mg of milk thistle is given a day. But that is 560%-850% greater than any dose a person would take. In contradiction to the warning inferred from this study that milk thistle dangerously elevates prolactin, the study demonstrates that milk thistle does not increase prolactin even in doses far in excess of the recommended dose for humans.

Though milk thistle does not increase prolactin, it does increase breast milk. When researchers actually tried giving silymarin to breast feeding women instead of to rats in a placebo-controlled study, the appropriate dose of 420mg increased milk production by 85.94% versus only a 32.09% increase in the

placebo group. In the human study, there were no unwanted side effects, and the researchers concluded that silymarin is safe and effective (4).

Contrary to the untransferable prolactin findings of the rat study, Michael T. Murray, ND, author of *How to Prevent and Treat Cancer with Natural Medicine*, pointed us to a more likely explanation of milk thistle's breast milk promoting powers (5). A recent study has suggested that milk thistle increases breast milk by increasing beta-casein gene expression (6).

So the first study that the milk thistle warning relies on raises absolutely no concerns for the herb. On the contrary, in so far as it is relevant at all, it once again highlights the safety of milk thistle even at excessively high doses. The second study found that silymarin, when administered to rodents, increased silibinin and mammary tumours (7). This result too is less convincing than it sounds.

The first problem with this study, as with the first, is that it is a study on rats and not on humans. That is always problematic because, as Boik pointed out, "any rodent study is already suspect [since the] results might not transfer to humans" (3). This concern is especially germane in the case of milk thistle given the extensive human research, the long history (over 2,000 years), the widespread use (in 2010, milk thistle was the seventh top selling herb in the US (8), and the unsurpassed safety record. This concern is also especially important here because silymarin is a group of flavonolignans, and Murray pointed out to us that "[t]hese sorts of rodent studies and *in vitro* studies are notorious for false positives with flavonoids" (5).

But even setting aside the limitations of this sort of study, there are problems within the study itself. The most glaring is that even though there were a greater number of rats with tumours in the silymarin group, "there was no clear dose-dependency on the silymarin content of the diet" (7). Causality is difficult to demonstrate without dose-dependency. If silymarin causes breast tumours, more silymarin should cause more breast tumours. As Boik told us, "If there is not a dose-response relationship in rodents, or the response has not been replicated, then the situation is even more unclear" (3).

And that's the next problem with drawing conclusions from this study. For results to be reliable, they need to be replicable. But though the warning for milk thistle is based on this study, a more recent study that gave silibinin to mice found no promotion of tumour development (9). The researchers concluded that "promotion of carcinogenesis is not a feature of silibinin consistent across rodent models of mammary carcinogenesis" (9). Even the authors of the negative study expressed surprise and noted that their results "were quite unexpected. . . . [and that][t]They were in sharp contrast to the results of several preclinical studies in animal models of carcinogenesis in other organ sites" (9). As examples, they cite animal studies that found that silymarin reduces tumours in colon (10), tongue (11), bladder (12), prostate (13) and lung (14) cancers.

Murray has also suggested the possibility that since the placebo group lost considerable weight, while the silymarin group did not, and since weight loss is associated with less mammary tumours, the lack of weight loss in the silymarin group may have masked its chemopreventive effect (5). Murray also points out that, as in the prolactin study, in other experiments in this study the doses of silymarin administered

to the rats was so much higher than the recommended human dose that “it is difficult to determine the relevance” (5).

A final problem is that milk thistle, like all herbs, is complex, and the effects of isolated components may not be the effects of the whole herb. That’s why drugs that isolate active components of herbs and synthesize them often have undesirable side effects that the whole herb does not.

So the second study, like the first, is very weak. It is a rodent study that failed to show dose dependence. It often used doses far in excess of human doses and may have masked the beneficial effect of the silymarin. Furthermore, a more current study failed to find this negative result.

That the safety concerns drawn from these studies are invalid is supported by the incredible safety record of milk thistle. A systematic review of meta-analysis funded by the National Institute of Health concluded that milk thistle is safe and associated with few, generally minor, adverse events (15). Drug monitoring studies have found adverse effects in just 1% of people using milk thistle, and the few adverse effects there were were mainly mild gastrointestinal complaints (16). And a systematic review of eighteen studies that included over 7,000 people found only gastrointestinal and allergic adverse effects. Though gastrointestinal complaints were the most common side effect of milk thistle, they actually occurred only with similar frequency to placebo. According to this systematic review, other adverse events were also similar to placebo (17). That’s about as safe as an active substance can get.

A survey of the most authoritative herbal safety and contraindication books turns up no cautions for milk thistle. Not one offers a contraindication. And so absent are hormonal concerns that they all list it as safe to use during breast feeding and pregnancy. As for the people with the clinical experience, every woman’s herbal we consulted not only listed milk thistle as safe for pregnancy and breast feeding, but recommended it for breast feeding and for certain conditions of pregnancy.

The warning about milk thistle’s safety also mentioned estrogenic effects of the herb. However, according to Murray—and others--, though the milk thistle fruit may have estrogenic effects, the milk thistle seeds do not. And it is the milk thistle seed that is used in herbal products. Murray calls such warnings un concerning, irrelevant and merely confusing to the consumer (18). It is also important to remember that phytoestrogens are weaker than human estrogen and compete with them for receptor sites. So phytoestrogens are able to gently raise estrogen when it is low, as in menopause, but lower it when it is high, as in breast cancer.

When a combination of herbs, including milk thistle, turmeric, artichoke, rosemary, schizandra, dandelion and milk thistle, were given in a placebo-controlled study of its effect on sex hormones, there were no substantial effects on estrogen measures (19). And when milk thistle was combined with black cohosh, dong quai and red clover in a double-blind, placebo-controlled study of menopause, hot flashes and night sweats were reduced without changes to estradiol or follicle-stimulating hormone (20). Estradiol is the kind of estrogen that causes breast cancer.

Also testifying to the hormonal safety of milk thistle is the unanimous approval of this herb during pregnancy and breast feeding. Even the National Cancer Institute notes this feature when it adds to its

assessment that “Silymarin has been well tolerated in high doses” the reference that “[s]ilymarin has been used in pregnant women with intrahepatic cholestasis at doses of 560 mg/day for 16 days, with no toxicity to the patient or the fetus” (21).

Far from being a concern for cancer, the anticancer research on milk thistle is extremely promising. It is of great value to cancer patients undergoing chemotherapy. One group of researchers concluded that milk thistle “can result in a strong protective effect” from the toxicity of chemotherapy, allowing patients to continue treatment, and that it may even work synergistically with the common chemotherapy drugs doxorubicin, cisplatin and carplatin (22). In fact, several studies have found milk thistle to work synergistically with doxorubicin while preventing its heart toxicity, an important ability since doxorubicin is a commonly used chemotherapy drug that can lead to irreversible damage to the heart muscles and even to congestive heart failure. Studies have also found silymarin to work synergistically with doxorubicin and cisplatin, another very commonly used chemotherapy drug, in the treatment of the estrogen sensitive ovarian cancer (23), suggesting again its value as a cancer treatment and its safety in estrogen sensitive cancers. Cisplatin can also cause kidney and liver toxicity, and silymarin has also been shown to protect against that (24), and it does so without interfering with cisplatin’s anticancer effects (25).

The most important study to date on milk thistle’s ability to prevent the side effects of chemotherapy was conducted on children with acute lymphoblastic leukemia, the most common type of childhood leukemia. Children with leukemia are often forced to stop chemotherapy because of the liver toxicity caused by the chemo drugs. That means they go untreated. But this double-blind, placebo-controlled study found that milk thistle was able to protect the liver from the chemo. The herb significantly reduced liver inflammation, significantly lowered AST and trended toward lowering ALT and bilirubin. While 73% of the kids on placebo had to reduce their dose of chemo due to toxicity, only 61% of the kids on milk thistle did. Once again, the milk thistle not only did not interfere with the chemotherapy’s effectiveness, but made it work better (26).

There is also very promising evidence of milk thistle’s own direct anticancer effects, as already seen from its ability to synergistically enhance chemotherapy. Several test tube (*in vitro*) studies have shown silibinin’s ability to protect breast cells against cancer (27) via apoptosis, angiogenesis, inhibiting proliferation, inhibition of growth, protein synthesis regulation and prevention of the expression of genes and enzymes involved in the development of breast cancer.

When prostate cancer cells were treated with either a chemo drug or silibinin or both, the silibinin boosted the chemo’s ability to inhibit the growth of the cancer cells and powerfully increased apoptosis (28).

Summarizing the anticancer effect of milk thistle, researchers have pointed out that silymarin prevents cancer in many different ways at all the stages of cancer. They identify its actions as including anti-inflammatory activity, induction of apoptosis, anti-angiogenesis, anti-metastatic and antioxidant activity. They say that, either *in vitro* or *in vivo*, silymarin has shown anticancer ability in breast, prostate,

ovarian, lung, skin, bladder and colon cancer (29). Silymarin has also demonstrated anticancer effects against cervical and tongue cancer.

In addition to cancer, milk thistle is a valuable herb for several other important reasons. It is probably the most important and best supported liver protecting herb, making it an important part of the treatment of hepatitis, cirrhosis, fatty liver and liver disease caused by alcohol, chemicals or toxins. Milk thistle is also valuable for protecting against the damaging side effects of drugs other than chemotherapy. It protects the liver from the damage caused by acetaminophen (Tylenol), antidepressants, antipsychotics, cholesterol lowering drugs, anticonvulsives and anesthesia.

Milk thistle is not only capable of protecting the liver from damage, it is actually able to regenerate it. Milk thistle increases the production of new, healthy liver cells to replace the old damaged ones.

Because milk thistle helps the liver to function at its peak, it is also a valuable herb for the many conditions that are helped by improving liver function, like digestion, constipation, mood disorders, psoriasis and acne. Because the liver is crucial for breaking down estrogen, milk thistle is also important in the treatment of any female hormonal condition.

And it's not just the liver that milk thistle helps. Research has now found that milk thistle can repair and regenerate kidney cells, increasing kidney cell replication by 25%-30%.

Milk thistle may also help with gallstones, ulcers and colitis, and research has found that it also helps with allergies (30). And when fifty-one people with type II diabetes were given either 200mg of milk thistle extract or a placebo three times a day for four months in a double-blind fashion, fasting blood glucose levels fell by 15% in the milk thistle group, while they went up by 13% in the placebo group. The milk thistle also dropped the levels of total cholesterol, LDL cholesterol and triglycerides (31).

Milk thistle is most often taken in pill form as a standardized extract. It should be standardized for 70%-80% silymarin and taken in doses of 140mg of silymarin two to three times a day. The dose of the milk thistle tincture is 1-2ml three times a day.

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