

Contaminants in Natural Products: How Serious Are They?

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Imagine yourself standing in your dispensary and surveying all of the products on your shelves. As you look around, can you pick out the bottles that have a contaminant in them? Maybe it shocks you that I'd ask such a question. Perhaps you never considered that some of the very products you prescribe do, in fact, contain one or more contaminants. Unfortunately this *is* the case, and it's up to you to determine how much contaminant and what differing kinds. Does the level of contamination vary from batch to batch? Does one company have more or less contamination than another? Will it harm my patients, family members, or friends? What acute or chronic ill effects will I likely see from certain levels of specific contamination? The questions I often ponder as a clinician are, "Would I ever even know if a product is contaminated?" and "Am I causing harm?" To me, that's the scary part. Our hearts, minds, and spirits are focused on helping our patients. It is difficult to fathom that the very products we recommend may contribute to thwarting our healing efforts or even cause harm.

I apologize for putting forth such a notion, but I am tainted by experience. For the past several years, I have tested many batches of raw materials that go into the manufacturing of natural products. I have rejected a significant number of them because they were contaminated with bacteria or mold, lead, mercury, illegal fungicides, unacceptable pesticides, chemical solvents, environmental pollutants, and rancidity markers. It is not a question of "if" some raw materials contain one or more contaminants; the questions really are "How much?" and "What is an acceptable level?" I did say "acceptable level." My preference as a clinician would be to have zero tolerance for contamination. It makes perfect sense. However, I've seen the reality that contamination exists in the industry and probably isn't going away. Companies that sell the raw materials and companies that manufacture the finished products have a duty to look high and low for contamination—the responsibility is on their shoulders to establish and diligently follow acceptance criteria that reject materials with high levels of contaminants and to agree to use only materials that contain a very low level of contamination. Sadly, not all companies do this.

Who determines the "acceptable level," and how is it decided?

The US Food and Drug Administration (FDA), federal and state governments, World Health Organization (WHO), and other scientific and regulatory bodies establish acceptable levels of various contaminants. It is up to the manufacturers to obtain this information and incorporate it into their acceptance or rejection criteria.

Acceptable levels are usually based on the raw material's contaminant starting level and a calculation of what this level will be in a typical daily dose. Let's say we had a raw material with a lead level of 1 part per million (ppm; 1 μg of lead per gram of raw material). Assume that some regulatory body set the acceptable daily intake limit of lead at 0.5 $\mu\text{g}/\text{day}$. This raw material was used to manufacture 2 products, Product A and B. Product A has a recommended daily dose of 100 mg per day—translating into a daily lead intake of 0.1 μg per day, which is acceptable given that the daily limit is 0.5 μg . Product B has a recommended dose of 1,000 mg per day. This translates into a daily lead intake of 1 μg per day—clearly surpassing the acceptable limit of 0.5 μg . This is the routine evaluation process that all natural product manufacturing companies must apply as a part of the acceptance or rejection criteria for each raw material with any level of contaminant. Of course, that assumes natural product suppliers are broadly looking for contamination in the first place and, unfortunately, most are not.

Are the natural products from one company cleaner than another?

I just made the assertion that most natural product suppliers/manufacturers are not looking broadly for contamination. Why? Logically, it seems to be the right thing to do. However, I have had many raw material suppliers and manufacturers directly tell me the reason they don't do quality assurance testing or don't do enough (as in broad contamination testing) is because it costs too much.

Although it's possible that products from one company are cleaner than another, I recommend you dispel this notion unless you have proof of due diligence regarding contamination testing. As I stated in my column last issue, our decision to buy from a particular supplier should be based on a thorough examination of objective quality-assurance evidence and not on subjective criteria (eg, you like the company or their marketing material is impressive). It is simple to determine which companies are doing the right thing and looking broadly for contamination. Just ask for proof to establish due diligence. Without it, you are operating in the dark.

In this regard, I have found that the most common contaminants to check for are bacteria, yeast, and mold; chemical solvent residues left over from the manufacturing process; herbicides, pesticides, and fungicides; rancidity markers in oil products; heavy metals (cadmium, mercury, lead, arsenic); aflatoxins; and environmental pollutants such as dioxins and polychlorinated biphenyls (PCBs). In most cases, companies should test each and every batch of raw material for contaminants and not engage in skip-lot testing (ie, testing only some batches throughout the year).

Bacteria, Yeast, and Mold

This is probably the easiest and simplest test to do. A microbiology profile should be taken on every batch of raw material and also every batch of finished product in case contamination occurred during the manufacturing process. The standard micro profile would include total aerobic bacterial count, *Enterobacteriaceae*, yeast and mold counts, *Salmonella* species, *E coli*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*.

Solvent Residues

Most people are unaware that many raw materials (vitamins, minerals, herbal extracts, and others) are created using solvents or other chemicals. Some residue may remain in the finished raw material. The more diligent suppliers have instituted processes that either completely remove the chemical residue or reduce it to minute quantities. This is the area that challenges me the most. When I test raw material and find a high level of residue, I reject the material and do testing over and over until I find one that has an acceptable residue level or no residue.

Currently, there are no enforceable or even published chemical residue guidelines that the natural products industry must meet or comply with. It sounds rather astonishing that such an important part of the natural products industry is completely undefined and not enforced, but that's the case. I use the pharmaceutical solvent residue guidelines that are published by the FDA and the US Department of Health and Human Services (HHS). They establish maximum allowable levels in drug products and provide a method for determining the level of permitted daily exposure.

Another very challenging aspect of the chemical/solvent residue issue is that many raw material suppliers do not indicate on their certificate of analysis (COA) that any solvent(s) was used in making the product. When I ask for that information, I am not always given the correct answer. On numerous occasions I have been told that there was no solvent used, but testing revealed the presence of solvents, or one solvent was indicated on the COA but testing uncovered two, three, or four. Because of this occasional deception, running a panel of commonly used solvents is now the routine.

Following is a list of raw materials whose manufacture requires the use of solvents. The final product may or may not have a residual level. That's why solvent testing is a necessity. This is only a partial list.

<u>Raw Material</u>	<u>Chemical Solvent(s)</u>
Alpha Lipoic Acid	Cyclohexane, Toluene, Ethyl Acetate, (1, 2- Dichloroethane)
Acetyl L Carnitine	Methanol, Acetone
Boswellia Extract	Isopropyl Alcohol, Ethyl Acetate
Bromelain Powder 2,400 gdu	Methanol
Calcium Ascorbate	Methanol
Calcium Citrate-Malate	Isopropyl Alcohol
Calcium Pantothenate	Methanol (carbinol)
Carnitine	Methanol
<i>Curcuma longa</i> Extract	Isopropyl Alcohol, Acetone
Hydroxocobalamin	Acetone
Iron Aspartate	Isopropyl Alcohol
Magnesium Glycinate	Isopropyl Alcohol
Milk Thistle Extract	Acetone

Heavy Metals

Botanical material and some minerals such as calcium and magnesium should be tested for the presence of lead, mercury, cadmium, and arsenic. In 1997, the California department of Health tested 260 Chinese patent medicines for lead, mercury, arsenic, drugs, and chemicals. They published the results and called the report the "Compendium of Asian Patent Medicines." Many products were found to contain drugs and chemicals, but most alarming was the number of products that were contaminated with toxic metals. Forty-two products (16%) contained arsenic, 214 (82%) contained lead, and 42 contained mercury—the total is more than 100% because some products had more than one contaminant. According to the US Pharmacopoeia, oral products that contain more than 10 ppm of lead or 3 ppm of arsenic or mercury are considered unsafe. Although not all the products that contained heavy metals exceeded this standard, it would seem that any level when used repeatedly or long-term is unsafe. Lead varied from 0 ppm to 184 ppm, mercury from 0 ppm to 5,070 ppm, and arsenic from 0 ppm to 114,000 ppm. It would seem prudent that *all* herbal products (every batch) should be tested for toxic metals to ensure the product is free of this contamination or that the level is acceptable based on a calculated daily dose.

Pesticide, Herbicide, and Fungicide Residue in Plant Products

The need to test for these is obvious, especially given the fact that many botanical products are manufactured in Asia, India, Eastern Europe, South America, and Mexico. The environmental regulations and standards in these areas may be far less stringent than in the United States, Canada, or Europe. Not long ago, I found dichlorodiphenyltrichloroethane (DDT) in a sample of *Gymnema sylvestre*. Every batch of botanical product (other than certified organic) should be tested for a wide array of pesticide, herbicide, and fungicide residues. If a residue is found, you need to determine whether it is acceptable and whether the total daily dose is a permitted daily exposure. Remember, it is impossible to determine a raw material's acceptability if no testing is performed.

Aflatoxin Residue In Plant Products

Aflatoxins are poisonous metabolites produced by certain fungi that are in or on foods and plant materials. Four different aflatoxins, B1, B2, G1, and G2, have been identified, with B1 being the most

toxic, carcinogenic, and prevalent. Aflatoxins are probably the best known and most intensively researched fungal toxins in the world. They have been associated with various diseases, such as aflatoxicosis in livestock, domestic animals, and humans throughout the world. Aflatoxins have received greater attention than any other fungal toxins because of their demonstrated potent carcinogenic effect in susceptible laboratory animals and their acute toxicological effects in humans. Many countries have attempted to limit exposure to aflatoxins by imposing regulatory limits on human food and animal feed. The FDA has set a limit of less than 20 parts per billion (ppb) for total aflatoxins in food and feed. Every botanical product (including organic certified) should be tested for residual amounts of aflatoxins and must meet this FDA specification.

Dioxins, PCBs, and Rancidity Markers in Oils

Dioxins: The term *dioxin* is generic, used to describe a family of 210 compounds. The most dangerous are 17 members characterized by the presence of chlorine atoms in the 2, 3, 7, and 8 positions. Each of those 2, 3, 7, 8-substituted congeners has been assigned a toxic equivalent factor (TEF), which is used to compute the toxic equivalency quotient (TEQ). This scale is used in risk-assessment studies to calculate the probability of a dioxin causing cancer and other life-threatening diseases in humans.

In 2001, The Council of the European Union adopted a directive that set legally binding maximum limits on the presence of dioxin and related contaminants in food and animal feed. Many dioxins are known human carcinogens. They are extremely resistant to chemical and biological degradation and therefore persist in the environment and accumulate in the food chain. More than 90% of human dioxin exposure derives from food, with animal feeds normally contributing about 80%. The EU maximum legal limit for dioxin and related contaminants in fish oil is 6 parts per trillion (ppt), and the recommended and preferred limit is 1.5 ppt. No US company is required to meet this stringent EU standard and, staggeringly, most do not even test their products for this.

PCBs: Consisting of a mixture of individual chemicals, PCBs are no longer produced in the United States, but, as with dioxins, they are extremely resistant to chemical and biological degradation so are persistent in the environment and accumulate in the food chain. They are particularly prevalent among farmed fish, especially salmon. Health effects associated with PCBs exposure include acne-like skin conditions in adults and neurobehavioral and immunological changes in children. PCBs are known to cause cancer in animals, leading the HHS to conclude that they are likely carcinogenic in humans.

Oil Rancidity: The testing required to assess rancidity in fish and plant oils (eg, evening primrose oil) looks for primary oxidation by-products (peroxide levels) and secondary oxidation by-products (anisidine levels). A high level of either indicates rancidity of long-chain fatty acids. It is critical to test for both, as peroxides are transitory and can drop to a low level while they transform into secondary oxidation by-products. Rancid oil can cause cellular and tissue damage. The degree of potential harm that may be caused by long-term ingestion of slight or significantly elevated amounts of rancid substances is considerable. The need to test every batch of fish and plant oil product to assess contamination is sensible and apparent.

Take-Home Message

Nutritional supplements are obviously beneficial to promote health, restore balance, and treat disease. Our patients often take them for long periods of time, if not years. A sensible strategy for limiting contaminants in nutritional supplements is to require suppliers to prove that they routinely do a thorough check for a broad array of contaminants, similar to what I have outlined here. All clinicians

need to consistently ask for legitimate proof of quality assurance. Your patients, family members, and friends will thank you.