NTP Botanical Dietary Supplements Program

What are botanical dietary supplements?
Botanical dietary supplements, sometimes called herbals or herbal dietary supplements, are products made from plants. The Food and Drug Administration (FDA) defines dietary supplements, in part, as products taken by mouth that contain a “dietary ingredient,” which could be vitamins, minerals, amino acids, herbs, botanicals, or other substances intended to supplement a diet. Dietary supplements may be found in many forms, such as tablets, capsules, gummies, liquids, or powders.

The market for these products is large. According to the American Botanical Council, U.S. consumers spent $12.4 billion on herbal dietary supplements in 2021.¹

Not all products from plant sources, which are sold in stores and online, are safe. The safety of a botanical depends on many factors, such as its chemical structure, how it works in the body, how it is prepared, and the dose taken. These supplements may contain active ingredients with strong biological effects that may interact with over-the-counter and prescription drugs.

If you become ill or have other adverse health events related to a dietary supplement, contact the FDA Safety Reporting Portal at www.safetyreporting.hhs.gov.

Why is the National Toxicology Program (NTP) studying botanical dietary supplements?
The scientific evidence available on the safety of different botanical supplement ingredients varies, partly because product safety testing is not required by the FDA. Federal law also does not require dietary supplements to be tested for effectiveness before they are marketed. The FDA regulates dietary supplements under a different set of regulations than those covering foods and conventional drugs.²

Studying the potential effects of botanical dietary supplements has several challenges. One challenge is that botanical dietary supplements typically contain a complex mixture of ingredients. Also, the complexity of the ingredients, including the number of components within them, make it difficult to identify and link a specific component to a specific health effect.

Growing, harvesting, and processing conditions can affect the chemical makeup of a botanical supplement, leading to challenges in manufacturing identical product batches after batch. Possible product contaminants (e.g., heavy metals, microbes, undeclared ingredients, or pesticides), either accidental or intentional, should be determined as part of routine quality control as these factors can affect product safety.

How does NTP evaluate botanical dietary supplements?
NTP characterizes the chemical and physical composition of botanical dietary supplements through its testing program. NTP conducts cell-based studies to better understand potential effects of supplements. It also conducts toxicology studies in animal models to understand what happens after a supplement enters the body.

In toxicity testing, NTP conducts studies of short-term exposure to high doses, long-term exposure to lower doses, or other combinations of conditions. NTP also examines toxicities to certain body functions, including reproductive, neurological, cardiovascular, and immune systems. Some studies focus on determining the potential for harmful health effects, such as cancer.
What do NTP findings mean for me?
Public concern about botanical dietary supplements includes questions about labeling, product quality, health benefits, and risk of harmful effects. NTP studies offer scientific data that can inform decisions by health care providers, government regulators, and consumers. The following examples highlight how NTP’s work can improve public use of botanical dietary supplements.

<table>
<thead>
<tr>
<th>Botanical Dietary Supplements Currently Studied by NTP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echinacea Purpurea</td>
</tr>
<tr>
<td>Garcinia Cambogia</td>
</tr>
<tr>
<td>Valerian</td>
</tr>
</tbody>
</table>

### Ongoing NTP studies

**Botanical Dietary Supplements Currently Studied by NTP**

| Botanical Dietary Supplement | Rodent Study Results and Links to Select NTP Publications | Findings and Levels of Evidence of Carcinogenic Activity*
|-------------------------------|----------------------------------------------------------|------------------------------------------------------|
# Completed long-term NTP studies

<table>
<thead>
<tr>
<th>Botanical Dietary Supplement</th>
<th>Rodent Study Results and Links to Select NTP Publications</th>
<th>Findings and Levels of Evidence of Carcinogenic Activity*</th>
</tr>
</thead>
</table>
| **Aloe Vera**               | NTP Technical Report on the Toxicology and Carcinogenesis Studies of a Noncolorized Whole Leaf Extract of Aloe Barbadensis Miller (Aloe Vera) in F344/N Rats and B6C3F1 Mice (Drinking Water Studies) [link](https://ntp.niehs.nih.gov/go/tr577) | Male Rats: Clear Evidence  
Female Rats: Clear Evidence  
Male Mice: No Evidence  
Female Mice: No Evidence  
Cancer of the large intestine in male and female rats, but not mice  
Weak cancer effect in mice with simulated sunlight on skin |
Female Rats: Clear Evidence  
Male Mice: No Evidence  
Female Mice: No Evidence  |
| **Black Cohosh**            | NTP Technical Report on the Toxicology and Carcinogenesis Studies of Black Cohosh Root Extract (CASRN 84776-26-1) Administered by Gavage to Sprague Dawley (Hsd:Sprague Dawley® SD™) Rats and Female B6C3F1/N Mice [link](https://ntp.niehs.nih.gov/go/tr603) | Male Rats: Not Tested  
Female Rats: Equivocal Evidence  
Male Mice: Not Tested  
Female Mice: No Evidence  
No evidence of causing cancer in male rats when mothers were exposed; decreased litter size in rats |
Female Rats: Clear Evidence  
Male Mice: Clear Evidence  
Female Mice: No Evidence  
Cancer of the thyroid glands in male and female rats and male mice; cancer of liver in male and female mice |
Female Rats: Clear Evidence  
Male Mice: Clear Evidence  
Female Mice: No Evidence  
No evidence of causing cancer in rats or mice |
Female Rats: Clear Evidence  
Male Mice: Clear Evidence  
Female Mice: No Evidence  
Cancer of the liver in male and female rats and male mice, but not female mice |
| **Green Tea Extract**       | NTP Technical Report on the Toxicology Studies of Green Tea Extract in F344/NTac Rats and B6C3F1/N Mice and Toxicology and Carcinogenesis Studies of Green Tea Extract in Wistar Han[Crl:WI(Han)] Rats and B6C3F1/N Mice [link](https://ntp.niehs.nih.gov/go/tr585) | Male Rats: Clear Evidence  
Female Rats: Clear Evidence  
Male Mice: Clear Evidence  
Female Mice: No Evidence  
No evidence of causing cancer in rats or mice, but saw damage to the liver |
| **Kava or Kava Kava**       | NTP Technical Report on the Toxicology and Carcinogenesis Studies of Kava Kava Extract in F344/N Rats and B6C3F1 Mice [link](https://ntp.niehs.nih.gov/go/tr571) | Male Rats: Clear Evidence  
Female Rats: Clear Evidence  
Male Mice: Clear Evidence  
Female Mice: No Evidence  
Cancer of the liver in male and female mice, and some increases in tissue damage |
Female Rats: Clear Evidence  
Male Mice: Clear Evidence  
Female Mice: No Evidence  
No evidence of causing cancer in rats or mice |
| **Senna**                   | NTP Report on the Toxicology Study of Senna in C57BL/6NTac Mice and Toxicology and Carcinogenesis Study of Senna in Genetically Modified C3B6.129F1/Tac-Trp53tm1Brd N12 Haploinsufficient Mice [link](https://ntp.niehs.nih.gov/go/gmm15) | Male Rats: Clear Evidence  
Female Rats: Clear Evidence  
Male Mice: Clear Evidence  
Female Mice: No Evidence  
No evidence of causing cancer in genetically modified mice; damage to large intestine |
What are next steps for NTP’s botanical dietary supplements program?

A public-private partnership, called the Botanical Safety Consortium, was formed by the FDA, the National Institute of Environmental Health Sciences (NIEHS), and the nonprofit Health and Environmental Sciences Institute (HESI) in November 2019. It provides an international forum in which scientists from government, academia, consumer health groups, industry, and nonprofit organizations can collaborate.

This consortium has already hosted a number of events as it works to create a sound scientific basis for integrating existing data and the latest toxicology tools to evaluate the safety of botanical dietary supplements. Learn more at www.botanicalsafetyconsortium.org.

Botanical Dietary Supplements
Where can I find more information?

NIH National Center for Complementary and Integrative Health: Herbs at a Glance
www.nccih.nih.gov/health/herbsataglance.htm

NIH Office of Dietary Supplements: Botanical Supplement Fact Sheets
www.ods.od.nih.gov/factsheets/list-botanicals

U.S. Food and Drug Administration: Dietary Supplements
www.fda.gov/food/dietarysupplements

Founded in 1978, NTP is an interagency program that includes NIEHS of the National Institutes of Health (NIH), the National Center for Toxicological Research of the FDA, and the National Institute for Occupational Safety and Health of the Centers for Disease Control and Prevention.

These agencies are all part of the U.S. Department of Health and Human Services (HHS).

For more information on the National Toxicology Program, go to https://ntp.niehs.nih.gov.


4 NTP (National Toxicology Program). 2013. Toxicology and Carcinogenesis Studies of a Nondecolorized Whole Leaf Extract of Aloe Barbadensis Miller in F344/N Rats and B6C3F1 Mice (Drinking Water Study) Available: https://ntp.niehs.nih.gov/publications/reports/tr/500s/tr577