

Top-Selling Herbs: What you need to know!

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Disclosures: None

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Objectives

Review Top 10 Selling Herbs

Review available evidence for use and identify interactions with traditional prescribed medications or disease process

Make an informed recommendation to your patients

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Herb Sales

US sales of herbal supplements continues to grow.

In 2018, US sales increased by 9.4%. This is the largest percent growth in U.S. Supplement sales since 1998.

According to the HerbalGram report, published by American Botanical Council annually, US consumers spent an estimated **\$8.84 BILLION** on herbal supplements in 2018. This is an increase of \$747 Million from the previous year.

This report documents consistent growth of consumer demands for natural remedies and is indicative of long-term trend toward natural medicine and consumer's interest in taking responsibility for their own health.

<http://www.nutritionaloutlook.com/herbs-botanicals/us-herbal-supplement-sales-77-2016>


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Herbal Supplement Sales in US Increase by 9.4% in 2018
Record growth driven by sales of CBD, mushrooms, and immune-health products

By Tyler Smith,^a Michelle Gillespie,^b Veronica Eckl,^b Jake Knepper,^b and Claire Morton Reynolds^c

^a American Botanical Council; Austin, Texas
^b SPINS; Chicago, Illinois
^c Nutrition Business Journal; Boulder, Colorado

Herbal supplement sales in the United States experienced record growth in 2018, increasing by an estimated 9.4% from 2017, according to the *Nutrition Business Journal* (NBJ). Consumers spent a total of \$8.842 billion on herbal supplements across all market channels in 2018 — an increase of roughly \$757 million in sales from the previous year. This marks the strongest US sales growth of herbal supplements since 1998.¹



AMERICAN BOTANICAL COUNCIL
Your source for reliable herbal medicine information

Table 1. Total US Retail Sales of Herbal Supplements*

Year	Total Sales	% Change
2018	\$8.842 billion	9.4%
2017	\$8.085 billion	8.5%
2016	\$7.452 billion	7.7%
2015	\$6.922 billion	7.5%
2014	\$6.441 billion	6.8%
2013	\$6.033 billion	7.9%
2012	\$5.593 billion	5.5%
2011	\$5.302 billion	4.5%
2010	\$5.049 billion	3.3%
2009	\$5.037 billion	5.0%
2008	\$4.800 billion	1.0%
2007	\$4.756 billion	4.4%
2006	\$4.558 billion	4.1%
2005	\$4.378 billion	2.1%
2004	\$4.288 billion	3.4%
2003	\$4.146 billion	-2.3%
2002	\$4.275 billion	-2.8%
2001	\$4.361 billion	3.2%
2000	\$4.225 billion	2.9%

Source: Nutrition Business Journal

* Includes sales in all channels. NBJ primary research includes NBJ surveys of supplement manufacturers, distributors, multilevel marketing firms, mail order, internet, and raw material and ingredient supply companies, as well as interviews with major retailers (Walmart, Costco, etc), manufacturers, suppliers, and industry experts. Secondary sources include IRI, SPINSScan Natural, Nielsen, Natural Foods Merchandiser, Insight, The Hartman Group, company data, and other published material.

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Movement in Healthcare

Merging complementary and alternative medicine with conventional medicine has been an active influence on present health-care practices and is increasingly used by clinicians and researchers under the term of “integrative medicine”.

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Herbal Medicines

Any products originating from plants and used to preserve or recover health.

Historical data show that herbal medicines have been used for over 5000 years.

In the 1890's, 59% of the products in the US Pharmacopoeia were based on herbs or herbal combinations.

Rashrash, M. Schommer, J. Brown, L. Prevalence and Predictors of Herbal Medicine Use Among Adults in the United States. Journal of Patient Experience 2017, Vol 4(3) 108-113

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Herbal Medicine Use

Currently, thousands of herbal products are available over the counter.

In below cited study, 33% of respondents reported current use of herbal medicine.

Respondents born before 1946 reported higher use of herbal medicine.

Education level was also statistically significant. 37% of people with post-high school education reported current use of herbal medicine.

Rashrash, M. Schommer, J. Brown, L. Prevalence and Predictors of Herbal Medicine Use Among Adults in the United States. Journal of Patient Experience 2017, Vol 4(3) 108-113

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Suggested Practice Changes

Providers should become familiar with what our patients are taking into their bodies.

Identify a reliable resource for you to access to quickly look up information.

Make sure to add botanicals and supplements to electronic medical record.

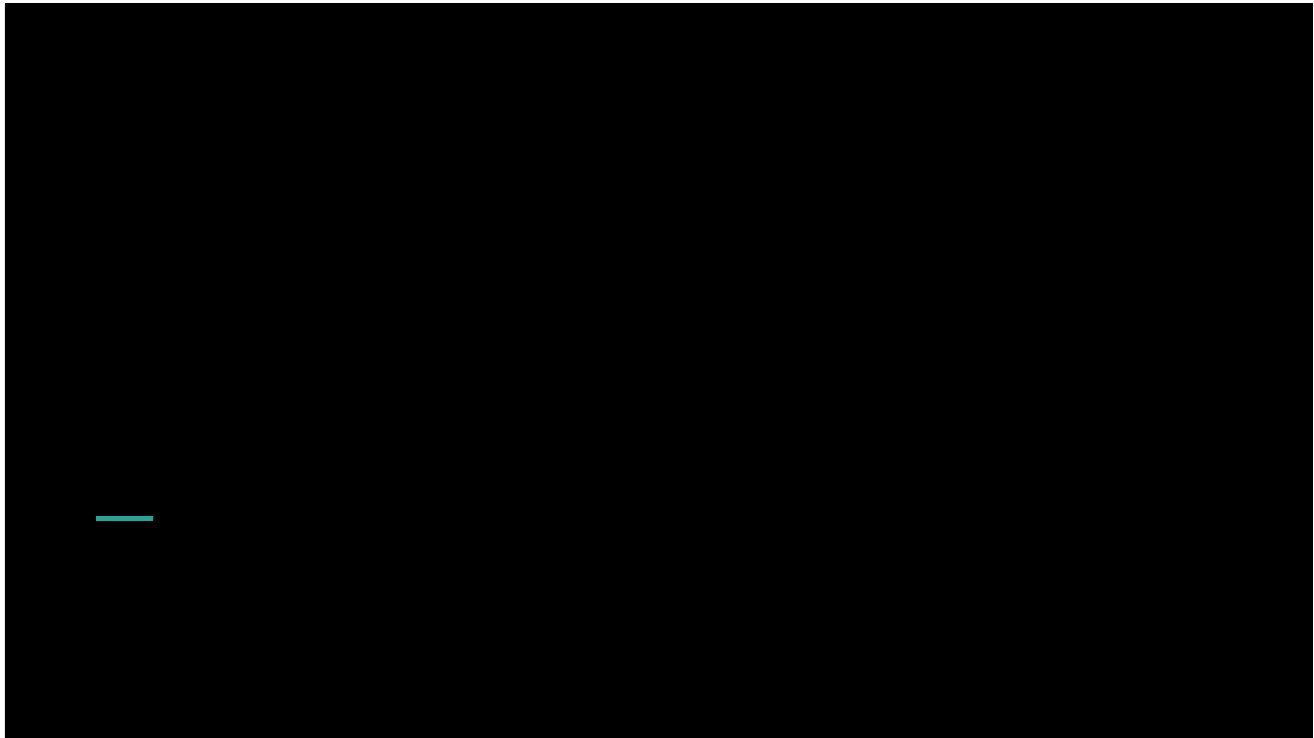
Nutrition is medicine.

Exercise is medicine.

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TOP SELLING HERBS ON US NATURAL CHANNEL 2018

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Table 5. Top-Selling Herbal Supplements in 2018 — US Natural Channel

Rank	Primary Ingredient	Latin Binomial	Total Sales	% Change from 2017
1	Cannabidiol (CBD)	<i>Cannabis</i> spp.	\$52,708,488	332.8%
2	Turmeric ^a	<i>Curcuma longa</i>	\$51,213,502	0.4%
3	Elderberry	<i>Sambucus nigra</i>	\$25,374,666	93.9%
4	Wheatgrass / Barley grass	<i>Triticum aestivum</i> / <i>Hordeum vulgare</i>	\$19,484,470	-3.3%
5	Flax seed / Flax oil	<i>Linum usitatissimum</i>	\$13,903,851	-7.5%
6	Aloe vera	<i>Aloe vera</i>	\$13,788,574	-1.0%
7	Ashwagandha	<i>Withania somnifera</i>	\$12,426,468	16.9%
8	Milk thistle	<i>Silybum marianum</i>	\$10,419,926	3.5%
9	Echinacea ^b	<i>Echinacea</i> spp.	\$9,979,769	11.0%
10	Oregano ^c	<i>Origanum vulgare</i>	\$9,925,727	9.9%
11	Psyllium	<i>Plantago</i> spp.	\$8,348,322	6.2%
12	Maca	<i>Lepidium meyenii</i>	\$8,246,315	-9.8%
13	Mushrooms (other)	—	\$7,800,366	40.9%
14	Saw palmetto	<i>Serenoa repens</i>	\$7,702,838	-2.1%
15	Cranberry	<i>Vaccinium macrocarpon</i>	\$7,454,158	6.2%
16	Garlic	<i>Allium sativum</i>	\$6,894,668	2.7%
17	Valerian	<i>Valeriana officinalis</i>	\$6,706,263	4.8%
18	Echinacea-Goldenseal combo	<i>Echinacea</i> spp. / <i>Hydrastis canadensis</i>	\$6,271,607	8.7%
19	Nigella	<i>Nigella sativa</i>	\$5,839,472	21.1%
20	Horsetail	<i>Equisetum</i> spp.	\$5,406,810	2.0%
21	Ginkgo	<i>Ginkgo biloba</i>	\$4,632,234	-0.3%
22	Hemp products	<i>Cannabis</i> spp.	\$4,172,735	-9.9%
23	Cherry fruit	<i>Prunus</i> spp.	\$3,638,295	0.2%
24	Kava	<i>Piper methysticum</i>	\$3,626,397	2.9%
25	Fenugreek	<i>Trigonella foenum-graecum</i>	\$3,546,222	-6.9%
26	Ginger	<i>Zingiber officinale</i>	\$3,453,791	15.9%
27	Holy basil	<i>Ocimum tenuiflorum</i>	\$3,421,090	-3.0%
28	Ginseng	<i>Panax</i> spp.	\$3,339,628	2.8%
29	Olive leaf	<i>Olea europaea</i>	\$3,269,066	0.5%
30	Papaya	<i>Carica papaya</i>	\$3,214,680	5.5%

<http://cms.herbalgram.org/herbalgram/issue119/hg119-herbmktrpt.html>

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CBD (Cannabidiol): Background

- First isolated from wild hemp and Egyptian cannabis and studied in 1940
- One of over 80 cannabinoids in the Cannabis sativa plant
- Second most abundant making up 40% of cannabis extracts
- Does not have psychotropic effects, unlike delta-9-tetrahydrocannabinol (THC)
- CBD oil is commonly sourced from marijuana or hemp, two different forms of Cannabis sativa

<https://www.health.harvard.edu/blog/cannabidiol-cbd-what-we-know-and-what-we-dont-2018082414476>

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CBD (Cannabidiol): Background

- Marijuana contains about 15% THC while Hemp is standardized not to exceed exceed 0.3% THC
- CBD oil is commonly sourced from hemp rather than marijuana
- Hemp is an industrial product, used for rope, textile, clothing. High fiber content so also used as a food product.
- CBD does not activate Cannabinoid type 1 and 2 receptors CB1/CB2
- May limit THC's psychotropic effects
- May modulate 5HT1A and endocannabinoid systems
- Some evidence of anticancer, antipsychotic, sedative activity

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Epidiolex - FDA approved CBD extract

- Approved for use in June 2018 for seizures caused by Lennox-Gestaut and Dravet Syndromes
- 100mg/mL pure cannabidiol extract from marijuana plant
- Schedule V controlled substance
- Approved for use in children age 2 and over and in adults
- Most common side effects somnolence and diarrhea. Can cause increased LFTs at high doses.

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Legal standing

Farm Bill of 2018 exempted hemp extracts including cannabidiol from Controlled Substances Act.

Any therapeutic claims regarding hemp extracts must be approved by FDA

Because Epidiolex an FDA approved Controlled Substance as of 2019, the legality of CBD is complicated. Technically no CBD extract other than Epidiolex is approved.

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CBD - Reported Uses


Oral, topical and inhaled uses reported

Bipolar Disorder	Anxiety	Diabetes	Epilepsy	Multiple Sclerosis
Schizophrenia	Smoking Cessation	Crohn's Disease	Dystonia	Epilepsy
GVHD	Pain	Rash	Appetite Stimulation	Fragile X syndrome

+

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Googling CBD



Cannabis Derivative May Help Treat Form of Epilepsy

Researchers complete first large-scale, double-blind clinical trial on the effects of cannabidiol on people with Dravet syndrome.

CBD PRODUCTS FOR SALE

Made with 99% pure CBD, Medterra's products are guaranteed to be THC free and can be shipped to all 50 states and most international countries.

INTRODUCING BUNDLE & SAVE!

SAVE NOW

99% PURE CBD **THC FREE** **100% NATURAL**

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CBD: Safety

- Oral form Possibly Safe in adults at doses of up to 300mg for up to 6 months or 1200-1500mg daily for up to 4 weeks. Epidiolex safely used at 10-20mg/kg/day
- Oral form Possibly Safe in children at prescription doses up to 20mg/kg/day. Greater than 15mg/kg/day associated with increased side effects of diarrhea, weight loss, somnolence
- Possibly Unsafe in pregnancy and lactation
- Insufficient evidence for topical CBD

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Slide 20

- 1 2 problems - limiting the insufficient evidence data. other parts of the monograph contain what looks like potentially promising data on anticancer activity and more.
Secondly- I have natural database access through IFM and am having trouble getting my references copied. links are not working. will try tomorrow.

Tonya Sweezer, 1/6/2020

CBD: Evidence Likely Effective

Epilepsy

- Adults and Children: CBD oil Epidiolex dosage of 2.5mg/kg/twice daily for one week, then increased to 5mg/kg/twice daily effective in Dravet syndrome and Lennox-Gestaut syndrome. Reduction in seizure
- Dravet syndrome: Reduction in seizure frequency by 39% (placebo 13%)
- Lennox-Gestaut syndrome: reduction in seizure frequency by 37-43%
- Other research -Tonic clonic seizures (91% reduction), epileptic spasms (88% reduction), complex partial seizures (59%)

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CBD Insufficient Reliable Evidence

- Dystonia: Cannabidiol 100-600mg daily for 6 weeks improved dystonia by 20% to 50% in some patients but study lacked adequate control
- Fragile X syndrome: Applying topical CBD gel to skin BID for 12 weeks at dose from 50mg to 250mg improved anxiety, compulsiveness, hyperactivity and social avoidance but not depressed mood. Study lacks a comparator group.
- Insomnia: 160mg before bed improves sleep duration but not induction. 40 and 80mg doses not effective. May reduce dream recall
- **GVHD *****
- **Opioid Withdrawal *****
- Conflicting evidence for social anxiety disorder, schizophrenia

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CBD: Drug Interactions

- Generally not to be used with the anticonvulsants Brivaracetam and Clobazam due to increasing serum levels
- Avoid use with CNS depressants due to concurrent sedative effects
- Avoid use with Cytochrome P450 CYP2C19 - PPI, Protonix, Prevacid, Valium, Soma, Nelfinavir
- Use with Valproic acid increases risk of elevated liver transaminases

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Take Home Message on CBD

- High use and prevalence of CBD containing products
- Possibly safe for use in adults and children (studied as prescription drug Epidiolex)
- Most evidence supports use for epilepsy and seizure disorder
- Insufficient evidence for multiple other concerns, some evidence for use in insomnia, fragile x syndrome, dystonia, GVHD
- Avoid use with CNS depressants, anticonvulsants and valproic acid

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Turmeric: Background

- Spice commonly used in Asian food
- Derived from root of turmeric plant
- Perennial herb and member of the Zingiberaceae (ginger) family



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Turmeric: Background

- Curcuminoids, specifically, curcumin is the yellow-colored primary active constituent derived from turmeric.
 - Used to color foods and in cosmetics



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Curcumin

- Powerful anti-inflammatory properties
- Powerful antioxidant properties
- Poorly absorbed in blood stream.
- Absorption enhanced by 2000% when take black pepper (piperine) with turmeric
- Best supplements will have piperine in them

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Reported Uses

OA	Crohn's disease	Liver disease	Allergic rhinitis	Alzheimer's
RA	Ulcerative Colitis	Gallbladder disease	Hyperlipidemia	Topical analgesia
Dyspepsia	CABG	Common cold	Radiation dermatitis	Topical inflammatory skin conditions
Abdominal pain	Diarrhea	Respiratory infections	Fibromyalgia	Topical infected wounds

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Turmeric: Safety

- Likely safe when used orally or topically. Clinical trials have shown safety upto 12 months.
- Possibly safe when used as enema, short term.
- Pregnancy: likely safe when used in amounts commonly found in foods. Likely unsafe when used in medicinal doses. Might stimulate menstrual flow and the uterus.
- Lactation: safe in foods but insufficient evidence for medicinal amounts during lactation.

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Turmeric: Evidence Possibly Effective

Allergic Rhinitis: 500mg daily for 2 months significantly reduced nasal symptoms compared with placebo in people with allergic rhinitis.

Wu S, Xiao D. Effect of curcumin on nasal symptoms and airflow in patients with perennial allergic rhinitis. *Ann Allergy Asthma Immunol.* 2016;117(6):697-702.e1.

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Turmeric: Evidence Possibly Effective

Osteoarthritis

- Some extracts can improve OA symptoms
- Specific 500mg tablets (100mg curcumin) BID seems to reduce pain and improve functionality in patients with OA of knee after 2-3 months of treatment.
- Reduced use of analgesics

Belcaro G., Cesarone M. R., Dugall M., Pellegrini, L., Ledda, A., Grossi, M. G., Togni, S., and Appendino, G. Product-evaluation registry of Meriva(R), a curcumin-phosphatidylcholine complex, for the complementary management of osteoarthritis. *Panminerva Med* 2010;52(2 Suppl 1):55-62.

Belcaro G, Cesarone MR, Dugall M, et al. Efficacy and safety of Meriva, a curcumin-phosphatidylcholine complex, during extended administration in osteoarthritis patients. *Alt Med Rev* 2010;15:337-4.

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Turmeric: Evidence Possibly Effective

Nonalcoholic fatty liver disease (NAFLD)

- Taking curcumin daily reduces severity of NAFLD.
- Decreases liver enzyme levels and reduces severity in 75-78% of patients compared to 4.7-27% of patients receiving placebo
- Decreases additional fat deposition in liver (upto 4.5% compared to upto 25% in those taking placebo)

Rahmani S, Asgary S, Askari G, et al. Treatment of non-alcoholic fatty liver disease with curcumin: a randomized placebo-controlled trial. *Phytother Res.* 2016 Sep;30(9):1540-8.

Panahi Y, Kinpour P, Mohtashami R, Jafari R, Simental-Mendia LE, Sahebkar A. Efficacy and safety of phytosomal curcumin in non-alcoholic fatty liver disease: a randomized controlled trial. *Drug Res (Stuttg).* 2017 Apr;67(4):244-51.

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Turmeric: Evidence Insufficient Evidence to Rate

Ulcerative colitis: studied as an add-on to traditional treatments. Clinical research in adults with mild to moderate, active ulcerative colitis shows taking a specific turmeric extract 3 grams daily for 1 month along with mesalamine improves overall symptoms 65.3% of patients compared to 12.5% for patients on mesalamine alone.

- The addition of turmeric led to clinical remission in 53.8% of patients and endoscopic remission in 36.3% of patients compared to no remission on mesalamine alone.

Lang A, Salomon N, Wu JC, et al. Curcumin in combination with mesalamine induces remission in patients with mild-to-moderate ulcerative colitis in a randomized controlled trial. *Clin Gastroenterol Hepatol.* 2015 Aug;13(8):1444-9.

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Drug Interactions

- Antiplatelet/Anticoagulants
- Antidiabetic drugs
- Theoretically reduces efficacy of camptothecin and cylophosphamide.
- Sulfasalazine (can increase blood levels of sulfasalazine by 3.2 fold which could increase effect and adverse effects of sulfasalazine)

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Googling Turmeric

10 Proven Health Benefits of Turmeric and Curcumin

Healthline and our partners may receive a portion

Turmeric may be the most effective nutrit

Many high-quality studies show that it ha:

Here are the top 10 evidence-based heal

IT'S UBER ANTI-INFLAMMATORY AND A POWERHOUSE ANTIOXIDANT.

One of the biggest selling points on turmeric is that it's anti-inflammatory by nature, says Robin Foroutan, RD, an integrative dietitian at the [Morrison Center](#) in New York. "Since most diseases are all about runaway inflammation, using herbs and foods that help the body balance inflammation is pretty exciting."

<https://www.healthline.com/nutrition/top-10-evidence-based-health-benefits-of-turmeric#section9>
<https://www.womenshealthmag.com/health/a27562416/turmeric-benefits/>

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Take Home Message on Turmeric

Relatively safe.

Sufficient evidence that it is useful in Allergic Rhinitis, NAFLD, and Osteoarthritis.

Consider as add-on treatment for Ulcerative Colitis.

Use cautiously with diabetes medications and antiplatelet/anticagulants.

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Elderberry

- Dark purple berry of the European or Black elder, a deciduous tree found in warmer areas of North America, Europe, Asia and Northern Africa
- Cooked fruit is made into pies, jams and flavorings.
- Also used medicinally

Also known as....Arbre de Judas, Baccae, Black-Berried Alder, Black Elder, Black Elderberry, Boor Tree, Bountry, Common Elder, Elder, Eder Berry, Ellanwood, Ellhorn, European Alder, etc...

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Elderberry: How it Works

- Applicable part is the ripe fruit
- Contains several flavanoids (part of polyphenol class of phytonutrients) which have antioxidant effects
- Extract has both antiviral and immunomodulating effects, inhibits hemagglutinin activity and replication of several strains of influenza A and B
- Increases production of inflammatory cytokines and tumor necrosis factor

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Elderberry: Evidence Possibly Effective

Constipation

- Research has shown improvement in colonic transit time and increase number of daily evacuations compared to placebo.
- Tea from elderberry flowers, anise fruit, fennel fruit, and senna flowers 150ml TID for 5 days

Picon PD, Picon RV, Costa AF, et al. Randomized clinical trial of a phytotherapeutic compound containing Pimpinella anisum, Foeniculum vulgare, Sambucus nigra, and Cassia augustifolia for chronic constipation. *BMC Complement Altern Med.* 2010;10:17.

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Elderberry: Possibly Effective

- Influenza
 - Elderberry fruit extract (sambucol, nature's way) 15ml QID reduces symptoms and duration when given within 48 hours of initial symptoms.
 - Significant symptom relief occur within 2-4 days of treatment.
 - On average, reduces duration of symptoms by about 56%.

Zakay-Rones Z, Thom E, Wollan T, Wadstein J. Randomized study of the efficacy and safety of oral elderberry extract in the treatment of influenza A and B virus infections. *J Int Med Res* 2004;32:132-40.

Zakay-Rones Z, Varsano N, Zlotnik M, et al. Inhibition of several strains of influenza virus in vitro and reduction of symptoms by an elderberry extract (*Sambucus nigra* L.) during an outbreak of influenza B Panama. *J Altern Complement Med* 1995;1:361-9.

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Elderberry: Possibly Effective

- Influenza
 - Elderberry extract lozenge 175mg QID for 2 days, starting within 24 hours of initial symptoms, improves flu-like symptoms compared to placebo. Substantial symptom relief within 48 hours.

Kong F. Pilot clinical study on a proprietary elderberry extract: efficacy in addressing influenza symptoms. *Online Journal of Pharmacology and Pharmacokinetics* 2009;5:32-43.

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Elderberry: Insufficient Evidence to Rate

Cardiovascular disease

Common Cold

Gingivitis

Hyperlipidemia

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Elderberry: Drug interactions

- Immunosuppressants
 - Theoretically, elderberry might interfere with immunosuppressant therapy because of its immunostimulating activity.

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Googling Elderberry

The Surprising Health Benefits Of Elderberry

By Danielle L'Ecuyer



Elderberries: A Potent Cold and Flu Remedy?

OCTOBER 19, 2017

https://healthprep.com/cold-flu-cough/health-benefits-of-elderberry/?utm_source=google&utm_medium=search&utm_campaign=1648305011&utm_content=65965708707&utm_term=elderberry&gclid=CjwKCAjw8qjnBRA-EiwAaNvhwPtZ--Ydfqj9tHM8ifixyqC-z7m_fAm75oefMUAY99GyEERSpjOfxoChWQQAvD_BwE
<https://www.pharmacytimes.com/contributor/cate-sibley-pharmd/2017/10/elderberries-a-potent-cold-and-flu-remedy>

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Take Home Message on Elderberry

Safe.

Use for non-high risk patients with influenza.

Sometimes, I use it if tamiflu is too expensive.



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Wheatgrass: Background

- Freshly sprouted shoot of the common wheat plant, *Triticum aestivum*.
- Native to Southwest Asia and Mediterranean regions, although it is cultivated all over the world.

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Wheatgrass: People Use This For

- Used as concentrated source of nutrients
- To increase hemoglobin
- Diabetes
- Preventing tooth decay
- Improve wound healing
- Preventing bacterial infections
- Preventing gray hair
- Help digestion
- Topical for plantar heel pain

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Wheatgrass: Safety

Safe when consumed in foods

Safe when wheatgrass juice is taken orally up to 18 months

Pregnancy and Lactation: Insufficient, avoid using

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Wheatgrass: Evidence Insufficient Reliable Evidence to Rate

- Beta-Thalassemia (prelim evidence 100ml juice for 18 months can reduce blood transfusion requirements in some children with transfusion-dependent beta-thalassemia)
- Hypercholesterolemia
- Plantar heel pain (no more effective than placebo)

Marawaha, R. K., Bansal, D., Kaur, S., and Trehan, A. Wheat grass juice reduces transfusion requirement in patients with thalassemia major: a pilot study. *Indian Pediatr.* 2004;41(7):716-720.

Kumar N, Iyer U. Impact of wheatgrass (*Triticum aestivum* L.) supplementation on atherogenic lipoproteins and menopausal symptoms in hyperlipidemic south asian women - a randomized controlled study. *J Diet Suppl.* 2017;14(5):503-513. doi: 10.1080/19390211.2016.1267063.

Ben-Arye E, Golden E, Wengrower D, et al. Wheat grass juice in the treatment of active distal ulcerative colitis a randomized double-blind placebo-controlled trial. *Scand J Gastroenterol* 2002;4:444-9..

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Wheatgrass: Evidence Based Use

Insufficient Reliable Evidence to Rate

- Ulcerative colitis (prelim evidence suggests drinking freshly extracted wheatgrass juice might reduce overall disease activity and the severity of rectal bleeding in patients with active distal ulcerative colitis.

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Wheatgrass: Drug Interactions

Moderate: Be Cautious

- Antidiabetes drugs (some animal research - lowers blood glucose and stimulates the release of insulin from beta-cells)

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Take Home Points - Wheatgrass

No great data to promote use. More data is needed.

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Flaxseed: Background

- Food and fiber crop native to Europe, Asia, and the Mediterranean
- Golden yellow to reddish brown seeds of flax
- Contains phytoestrogen, soluble fiber, and an oil
 - Flaxseed oil is 55% alpha-linoleic acid, an essential omega-3 fatty acid, one of the richest food sources of alpha-linoleic acid.

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Flaxseed: People Use This For

Constipation

Acne

Diarrhea

Benign prostatic hyperplasia

Diverticulitis

Diabetes

Irritable bowel syndrome

Prediabetes

Gastritis

Menopausal symptoms

Mastalgia

And much more...

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Flaxseed: Safety

Likely safe except in raw or unripe form.

Raw flaxseed contains potentially toxic cyanogenic glycosides;

Unripe flaxseed are also thought to be poisonous when consumed due to cyanide content.

Pregnancy - possibly unsafe, mild estrogenic effects. Avoid use.

Lactation - insufficient reliable information available; avoid using.

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Flaxseed: Evidence Possibly Effective

Diabetes (whole flaxseed, in those with higher baseline glucose and insulin levels).

Hypercholesterolemia (seems to significantly reduce total cholesterol and LDL cholesterol)

- 30-50 mg/day lowers cholesterol by 5%-15%, LDL by 8-18%

Mohammadi-Sartang M, Sohrabi Z, Barati-Bodaji R, Raeisi-Dehkordi H, Mazloom Z. Flaxseed supplementation on glucose control and insulin sensitivity: a systematic review and meta-analysis of 25 randomized, placebo-controlled trials. *Nutr Rev.* 2018 Feb 1;76(2):125-39.

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Flaxseed: Evidence Possibly Effective

Hypertension - meta-analyses show effectiveness for reducing blood pressure

Mastalgia (25gm daily for 2 months reduces breast pain by about 72% and duration of pain by 60% compared to baseline healthy women with cyclic mastalgia)

Khalesi S, Irwin C, Schubert M. Flaxseed consumption may reduce blood pressure: a systematic review and meta-analysis of controlled trials. *J Nutr.* 2015 Apr;145(4):758-65.

Goss PE, Li T, Theriault M, et al. Effects of dietary flaxseed in women with cyclical mastalgia. *Breast Cancer Res Treat* 2000;64:49

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Flaxseed: Drug Interactions

Moderate: Be cautious

Acetaminophen, Antibiotic drugs, Anticoagulant/Antiplatelet drugs,

Anti-diabetes drugs, Antihypertensive drugs, Estrogens, Furosemide, ketoprofen, metoprolol

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Take Home Points - Flaxseed

Can use flaxseed for:

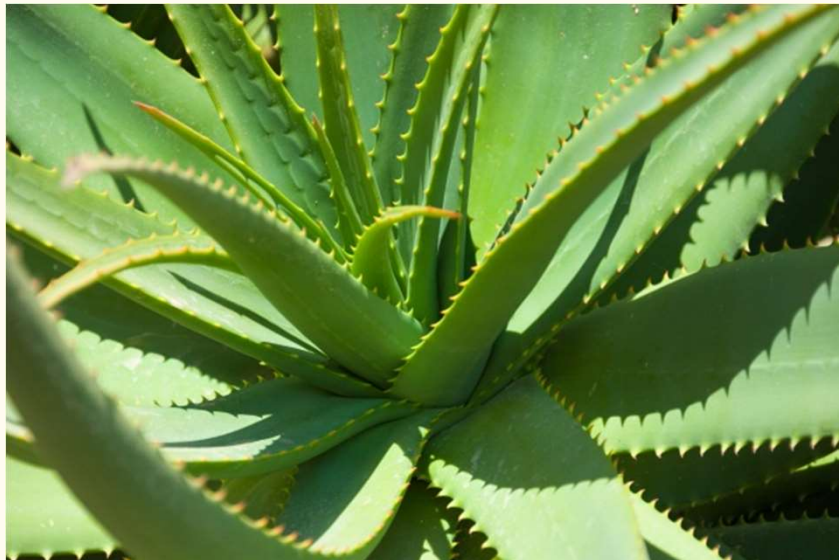
Diabetes

Hypercholesterolemia

Blood pressure

Mastalgia

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Aloe vera: Background

- Cactus -like plant that grows in hot, dry climates
- Cultivated in Florida, Texas and Arizona
- Commonly used in cosmetics and as medicine

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Aloe vera: People Use This For

- Weight loss
- Diabetes
- Hepatitis
- Inflammatory bowel disease
- Osteoarthritis
- GI ulcers
- Asthma
- Dry skin
- General tonic

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Aloe vera: Safety

Likely safe when used topically

Possibly safe when used orally, short term upto 8 weeks

Possibly unsafe when aloe latex is used orally. Some evidence that anthraquinones in aloe latex are carcinogenic or promote tumor growth, although data is conflicting.

Aloe whole-leaf extract is classified as human carcinogen.

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Aloe: Mechanism of Action

Applicable part is the leaf.

From the leaf, multiple components can be extracted.

Most aloe-containing products use aloe gel or aloe latex.

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Aloe: Mechanism of Action

Aloe gel

- Clear, jelly-like substance from the thin-walled mucilaginous cells in the center of the leaf.
- Often found in topical formulations and in cosmetics
- Mono and poly-saccharides - acemannan, aloeride, tannins, sterols, amylase, lipase, alkphos, etc.
- Might inhibit synthesis of thromboxane A₂, a potent vasoconstrictor and thereby increase microcirculation and prevent ischemia in wounds.

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Aloe

Aloe latex

- Intensely bitter, yellow sap or juice produced in the peripheral bundle sheath cells just beneath the leaf skin
- Drains from cut leaves and dries to form solid granules, sometimes referred to as “aloes.”
- Contains anthraquinones and glycosides

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Aloe vera: Evidence Possibly Effective

Acne

- Topical application with 50% aloe gel in the morning and evening with tretinoin gel 0.025% and twice daily cleansing with a medical soap, improves acne lesions by approximately 35% over the same treatment without the aloe.

Hajheydari Z, Saeedi M, Morteza-Semnani K, Soltani A. Effect of Aloe vera topical gel combined with tretinoin in treatment of mild and moderate acne vulgaris: a randomized, double-blind, prospective trial. *J Dermatolog Treat* 2014;25(2):123-9.

71

Aloe vera: Evidence Possibly Effective

Burns

- superficial/partial thickness → aloe gel or cream bid reduces healing time compared to silver sulfadiazine, decreases wound size compared to silver sulfadiazine

Khorasani G, Hosseinimehr SJ, Azadbakht M, et al. Aloe versus silver sulfadiazine creams for second-degree burns: a randomized controlled study. *Surg Today*. 2009;39:587-91.

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Aloe vera: Evidence Possibly Effective

Diabetes

- Most clinical research shows reduction of fasting blood glucose by 30-46.6 mg/dL and HbA1c by 0.41% to 1.05% in adults with prediabetes and diabetes.
- Heterogeneity between studies, small sample sizes, wide variability in dose and form limit the validity and ability to identify effective dose.

Vogler BK, Ernst E. Aloe vera: a systematic review of its clinical effectiveness. *Br J Gen Pract* 1999;49:823-8.

73

Aloe vera: Evidence Possibly Effective

Psoriasis

- Apply aloe extract 0.5% cream TID for 4 weeks significantly improves and increases the resolution of psoriatic plaques compared to placebo.
- Seems to reduce desquamation, erythema, and infiltration.
- Other prelim research shows 70% aloe mucilage bid for 8 weeks improves psoriasis severity more effectively than triamcinolone 0.1% cream, although both treatments has similar effects on dermatology-specific quality of life.

Syed TA, Ahmad SA, Holt AH, et al. Management of psoriasis with Aloe vera extract in a hydrophilic cream: a placebo-controlled, double-blind study. *Trop Med Int Health* 1996;1:505-9.
Choonhakarn C, Busaracome P, Sripanidkulchai B, et al. A prospective, randomized clinical trial comparing topical aloe vera with 0.1% triamcinolone acetonide in mild to moderate plaque psoriasis. *J.Eur.Acad.Dermatol.Venereol.* 2010;24:168-72.

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Aloe vera: Evidence Based Use

Possibly effective

- Weight loss (147 mg bid for 8 weeks → decreased body weight by 0.6kg)
- Psoriasis
- Lichen planus
- Constipation - taking Aloe latex orally as stimulant laxative

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Aloe vera: Drug Interactions

- Anticoagulant/Antiplatelet
- Antidiabetes Drugs
- Digoxin (MAJOR INTERACTION) **overuse of aloe latex increases the risk of adverse effects from the cardiac glycoside drugs due to potassium depletion. Overuse of aloe, along with cardiac glycoside drugs, can increase the risk of toxicity
- Diuretic Drugs (increase risk of hypokalemia)
- Warfarin

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Aloe vera: Interaction with diseases

Diabetes

GI conditions (contraindicated with intestinal obstruction)

Kidney disorders: high dose of aloe latex linked to nephritis and renal failure.

Surgery - affect blood glucose level

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Take Home Points

Evidence supports use in acne, burns, diabetes, psoriasis.

Be cautious with aloe latex.

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Ashwagandha: Background

- *Withania somnifera*
- Small evergreen shrub that grows to 4-5 feet tall.
- Found in dry areas of India and Middle East, parts of Africa.
- “Adaptogen” - coined by Russian researchers.
 - Tonic, describes class of botanicals that increase resistance to physical, chemical, and biological stress and build up general vitality, including the physical and mental capacity for work.

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Reported Uses

Arthritis

Boost testosterone

Fatigue

Increase muscle mass

Nervous Exhaustion

Anxiety

Insomnia

GI disorders

Stress

Memory

Depression

Cholesterol

Anti-cancer

Male infertility

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Ashwagandha: Evidence Possibly Effective

- Stress
 - 300mg BID after food for 60 days reduces perceived stress by 33-44% and decreases cortisol levels by 22%-28%.
 - Also seems to prevent stress related weight gain compared to placebo

Chandrasekhar K, Kapoor J, Anishetty S. A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of ashwagandha root in reducing stress and anxiety in adults. *Indian J Psychol Med.* 2012;34(3):255-62.

Choudhary D, Bhattacharyya S, Joshi K. Body weight management in adults under chronic stress through treatment with ashwagandha root extract: a double-blind, randomized, placebo-controlled trial. *J Evid Based Complementary Altern Med.* 2017 Jan;22(1):96-106

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Ashwagandha: People also use this for...but insufficient reliable evidence to rate

Arthritis

Fatigue

Nervous Exhaustion

Anxiety

Insomnia

GI disorders and other uses

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Ashwagandha: Safety

Safe, short-term. Trials show safe for up to 12 weeks.

Pregnancy: Likely Unsafe (Abortifacient effects)

Lactation: Insufficient reliable evidence. Avoid use.

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Ashwagandha: Drug Interactions

- Antidiabetic drugs
- Antihypertensive drugs
- BZDs
- CNS depressants
- Immunosuppressants
- Thyroid Hormone** potentially increases thyroid hormone levels
 - Several studies have looked at the effects of ashwagandha in mice, where extract 1.4g/kg/d increased T4 and T3 and there is one case report of a woman who developed thyrotoxicosis after taking this. Quality of case was poor. More recent RCT showed small increase in T4 but no cases of hyperthyroidism were seen after 8 weeks of treatment.

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Take Home Point on Ashwagandha

Can use for stress reduction.

- Also evidence for guided imagery, lemon balm, massage for stress treatment

Do NOT use in pregnant women.

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Milk Thistle: Background

- Native to Europe, introduced to North America by early colonists
- Found throughout eastern US, California, South America, as well as Africa, Australia, and Asia
- Mature plant grows up to 2 meters high, has large bright purple flowers and many stout spines
- Also known as: Blessed Milk Thistle, Cardo Lechoso, Chardon Argente, Silybum, Mary Thistle, etc...

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Milk Thistle: Background

The white veins on the plants' spiked green leaves are fabled to carry the milk of the Virgin Mary. This legend is also the derivation of the name "milk thistle."



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Reported Uses - Milk Thistle

Liver disorders

Amanita phalloides (death cap)
mushroom poisoning

Jaundice

Cirrhosis

Loss of appetite

Gallbladder complaints

Ulcerative colitis

Diabetes

Diabetic nephropathy

Hangover

And more...

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Milk Thistle: Mechanism of Action

Silymarin seems to decrease insulin resistance and have protective effect on pancreas in rats with experimentally induced diabetes.

Antioxidant effects - oxidative stress can contribute to pancreatic beta-cell dysfunction, reduced insulin resistance

Anti-inflammatory effect - decreases production of tumor necrosis factor (TNF)-alpha and interleukin-1beta, regulates inflammatory mediators, downregulates synthesis of prostaglandin and leukotrienes as well as inhibits cyclooxygenase (COX)11.

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Milk Thistle: Evidence Possibly Effective

Diabetes

- Research shows taking 140 mg TID for 45 days reduces fasting blood glucose by 11%, reduces insulin by 14% and improves insulin resistance by 26% compared to baseline in patients with Type 2 DM.
- These improvements were statistically significant compared to placebo group, which showed an 8% increase in blood glucose and 26% increase in insulin, 36% increase in insulin resistance.
- Improvements noted in HDL but not LDL

Ebrahimpour-Koujan S, Gargari BP, Mobasseri M, Valizadeh H, Asghari-Jafarabadi M. Lower glycemic indices and lipid profile among type 2 diabetes mellitus patients who received novel dose of *Silybum marianum* (L.) Gaertn. (silymarin) extract supplement: A Triple-blinded randomized controlled clinical trial. *Phytomedicine*. 2018;44:39-44.

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Milk Thistle: Evidence Based Use

Diabetes

- Some research looked at combo product with milk thistle (210mg) and tree turmeric (1176mg) daily for 12 months → reduced HbA1c by 18% compared to baseline in obese patients with Type 2 DM and metabolic syndrome. Placebo only showed 5.3% reduction. Statistically significant.

Guarino G, Strollo F, Carbone L, et al. Bioimpedance analysis, metabolic effects and safety of the association *Berberis aristata/Bilybum marianum*: a 52-week double-blind, placebo-controlled study in obese patients with type 2 diabetes. *J Biol Regul Homeost Agents*. 2017;31(2):495-502.

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Milk Thistle: Insufficient Reliable Evidence to Rate

Liver disease

- Conflicting evidence. Some data shows some improvement in liver function tests, liver histology. However, other studies with similar dose of same product is not associated with any benefit over placebo.

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Milk Thistle: Drug Interactions

Anti-diabetes drugs - may need to adjust doses of medications, can cause hypoglycemia

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Milk Thistle: Disease interactions

Cross-allergenicity: members of family include ragweed, chrysanthemums, marigolds, daisies, and many other herbs

Diabetes: monitor glucose levels closely

Hormone Sensitive Cancers/Conditions: Milk thistle constituent, silymarin, can bind to estrogen receptor beta. Avoid use in breast cancer, uterine cancer, ovarian cancer, endometriosis, and uterine fibroids.

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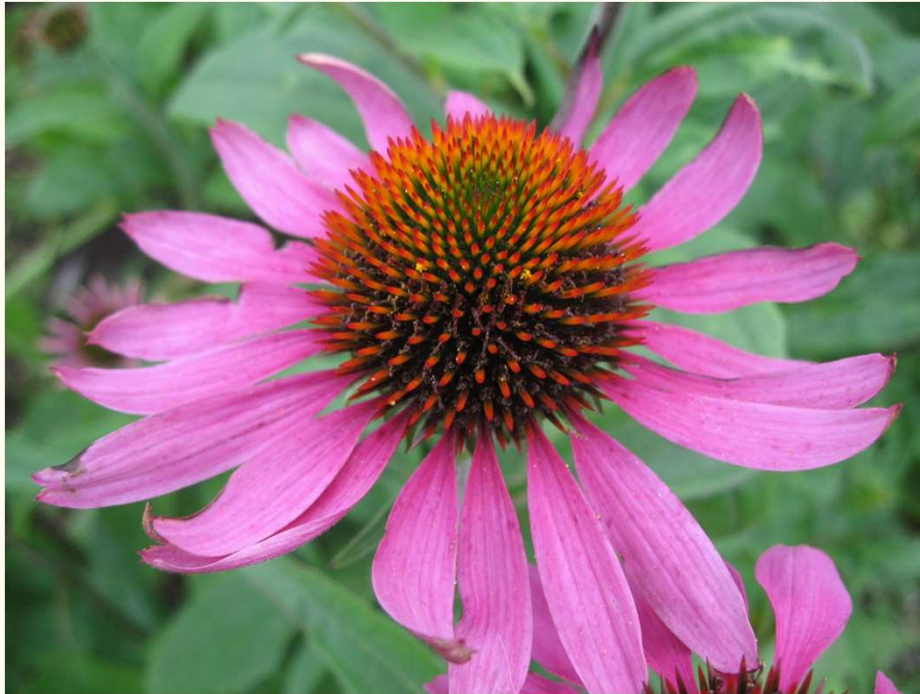
Take Home Message on Milk Thistle

Consider use in Diabetes.

140mg to 200mg three times a day in patients with Type 2 Diabetes.

You will likely need to decrease any insulin use by your patient.

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Echinacea purpurea: Background

- Perennials closely related to sunflowers, daisies, and ragweed
- Indigenous to Rocky Mountains in US but are now cultivated for medicinal use in western US, Canada, and Europe.
- 9 species - but 3 used for medicinal purposes Echinacea angustifolia, purpurea, and pallida.

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Echinacea: Mechanism of Action

Induce anti-inflammatory effects.

Anti-oxidant effects

Immunologic effects - immunostimulatory properties appear to target both nonspecific and specific immune function.

Wound healing effects: animal research suggests extracts can speed wound healing, enhance epithelialization, and reduce inflammation. A constituent may have activity against bacterial hyaluronidase which is necessary for bacteria to spread through skin and mucous membranes.

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Reported Uses

- Common Cold - treat and prevent
- Influenza and Other URI
- Immunostimulant for fighting variety of other infections (OM, UTI, etc)
- Chronic Fatigue Syndrome
- Leukopenia
- Anxiety
- RA
- Migraines
- And more...

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Echinacea: Safety

Likely safe when used orally and short-term

Children - possibly safe in children over 12 years of age and older. There is concern for severe allergic reaction in children less than 12 years of age.

Pregnancy - not enough data. Advise pregnant patients to avoid echinacea.

Lactation - not enough data. Advise against.

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Echinacea purpurea: Evidence Possibly Effective

Might have a small beneficial effect if taken soon after onset of cold symptoms.

However, data on use of echinacea for prevention and treatment of common colds are conflicting. Many studies have methodological problems, which limit the usefulness of their results.

May reduce duration of cold from 9 days to 7 days. On day 7, the daily symptom score is 50% less than placebo.

In children, taking extract of Echinacea purpurea (2-5 year olds) twice a day for up to 10 days did not reduce cold symptoms duration or severity, but was associated with increase in skin rash.

Linde K, Barrett B, Wolkart K, et al. Echinacea for preventing and treating the common cold. Cochrane Database Syst Rev 2006;(1):CD000530.

Schulten B, Bulitta M, Ballering-Bruhl B, et al. Efficacy of Echinacea purpurea in patients with a common cold. A placebo-controlled, randomised, double-blind clinical trial. *Arzneimittelforschung* 2001;51:563-8.

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Echinacea: Drug Interactions

Caffeine - increases caffeine concentration by 30%

Cytochrome P450 1A2 (CYP1A2) Substrates

- Echinacea appears to inhibit CYP1A2 enzyme in humans. This may increase levels of drugs metabolized by CYP1A2. (tylenol, amitriptyline, clopidogrel, clozapine, diazepam, estradiol, olanzapine, ondansetron, propranolol, verapamil, theophylline, warfarin and more...

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Echinacea: Disease Interactions

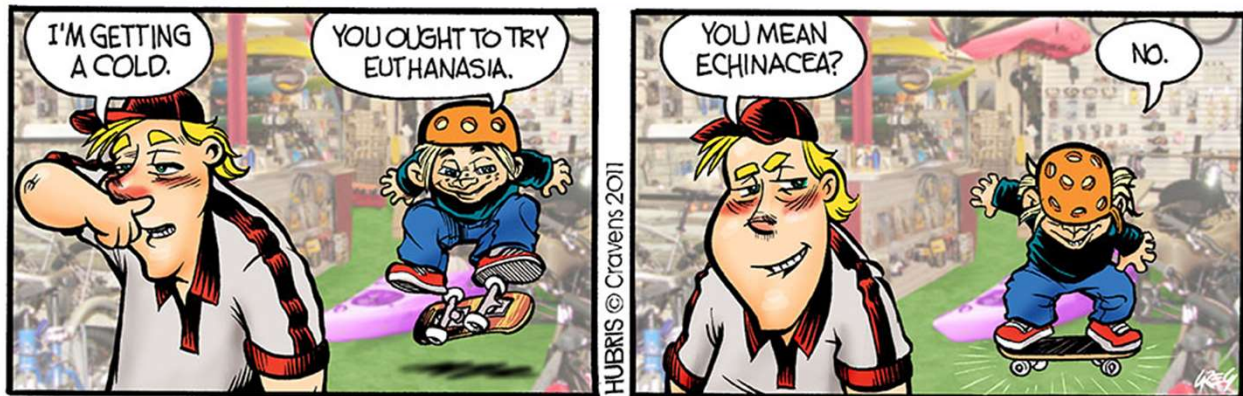
Avoid in atopy, can worsen asthma symptoms

Avoid in autoimmune diseases

Pemphigus vulgaris - one case report with well controlled PV took echinacea and within 1 week developed disease flare including blisters on his trunk, head and oral mucosa. When echinacea was discontinued, symptoms decreased but did not entirely resolve.

*The immunostimulatory effects of echinacea are thought to exacerbate this and other autoimmune disorders.

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Take Home Points on *Echinacea purpurea*

- Small effect on cold symptoms
- Do not use in children less than 12 years old

Consider *pelargonium sidoides* for bronchitis, common cold. Considered safe in children 6-10 years old for use up to 7 days. There is evidence that it is effective in both bronchitis and common cold.

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Oregano Background

- Perennial herb which grows between 1-3 feet tall and has olive green leaves and purple flowers
- Lamiaceae family - closely related to mint, thyme, basil, sage and lavender
- Native to warm-temperate western and southwestern Europe and Mediterranean region
- Turkey is one of the largest exporters of oregano

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Oregano Background

- Widely cultivated and grows on most continents
- Countries known for producing high-quality oregano essential oils include Greece, Israel, and Turkey.
- Leaves are used dry or fresh as culinary herb for flavoring

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Oregano: How it works

- Leaves and above ground parts are used medicinally
- Essential oil is extracted from above ground parts
- Oregano essential oil and its constituent carvacrol have bactericidal activity against many organisms in vitro (including MSSA and MRSA)
- Oils rich in phenolic compounds (carvacrol and thymol) have the greatest antibacterial activity.
- These phenolic compounds accumulate in the lipid bilayer of the bacterial cell membrane, disrupting its structure and function.
- Oregano has not been studied in human infections

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Reported Uses of Oregano

Influenza	Common Cold	Croup
Cough	Asthma	Allergies
Sinusitis	Bronchitis	dyspepsia
bloating	Intestinal parasites	dysmenorrhea
RA	UTI	headaches
diabetes	Heart conditions	hyperlipidemia
acne	Athlete's foot	rosacea
ringworm	Varicose veins	toothache

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Oregano Safety

Safe in foods.

Safe if use medicinal doses orally or topically. Avoid oil concentration over 1% - it can be irritating.

Pregnancy: AVOID medicinal use. Thought to be abortifacient.

Lactation: avoid, no evidence

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Oregano Evidence Insufficient to Rate

- Intestinal infections and infestations
 - Small, uncontrolled study, emulsified oregano leave oil product 200mg TID with meals for 6 weeks resulted in eradication of *Blastocystitis hominis*, *Entamoeba hartmanni*, and *Endolimax nana* from the stool in 10 or 13 patients.
 - Clinical significance is unclear - CDC considers *Entamoeba hartmanni* and *Endolimax nana* to be nonpathogenic. And blastocystosis caused by *Blastocystitis hominis* is self limiting and does not require treatment.

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Oregano Evidence Insufficient to Rate

- Wound Healing
 - Prelim evidence that applying ointment with 3% concentration of water-soluble fraction of oregano plant twice daily for 10-14 days after minor dermatological surgery might reduce infection rates and improve scar formation compared to petrolatum ointment.

Need more evidence

Force M, Sparks WS, Ronzio RA. Inhibition of enteric parasites by emulsified oil of oregano in vivo. *Phytother Res* 2000;14:213-4.

Ragi, J., Pappert, A., Rao, B., Havkin-Frenkel, D., and Milgraum, S. Oregano extract ointment for wound healing: a randomized, double-blind, petrolatum-controlled study evaluating efficacy. *J.Drugs Dermatol.* 2011;10(10):1168-1172.

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Oregano Drug Interactions

Anticoagulant/Antiplatelets

Anti-diabetes Drugs

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Oregano Interactions with Diseases

Bleeding disorders (component of oregano leaves has antithrombin activity in vitro, theoretically might increase risk of bleeding, use with caution)

Cross-Allergenicity (plants in Lamiaceae family)

Diabetes (might lower blood sugar)





Surgery (might increase risk of bleeding, patients should discontinue oregano 2 weeks before elective surgery)

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Take Home Point

Lack of evidence for medicinal use of oregano.

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	 CONSUMERLAB.COM	 NSF INTERNATIONAL	 U.S. PHARMACOPEIA (USP)	 UL
Does it buy initial test samples in stores or are they provided by the manufacturer?	Purchased in stores.	Provided by the manufacturer.	Provided by the manufacturer.	Provided by the manufacturer.
How often does it retest or spot-check?	Once per year using samples purchased in stores.	Once per year using samples provided by manufacturer and occasionally purchased in stores.	One to six times per year using samples purchased in stores.	Twice per year using samples purchased in stores.
How much do manufacturers pay to have each product certified?	\$3,000 to \$5,000 per product.	\$3,000 to \$5,000 per product plus an audit fee of about \$13,000.	\$3,000 to \$15,000 per product plus an initial audit fee of \$15,000 and a label fee of 1 cent per bottle.	\$2,000 to \$8,000 per product plus an audit fee of \$4,000 to \$7,000.
Are there products it won't test?	Products containing ingredients known to be unsafe.	Products marketed for weight loss or sexual enhancement.	Products known to contain unsafe ingredients and those marketed for erectile dysfunction, weight loss, or sports.	Products containing ingredients known to be unsafe or those not recognized as dietary ingredients by the FDA.

<https://www.consumerreports.org/vitamins-supplements/what-usp-verified-and-other-supplement-seals-mean/>

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Resources for you

- Herb List App – by National Center for Complementary and Integrative Health
- <https://nccih.nih.gov/>
- Natural Medicines Database

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Thank you.
Questions?

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<http://www.nutritionaloutlook.com/herbs-botanicals/us-herbal-supplement-sales-77-2016>

<https://www.nutraingredients-usa.com/Article/2018/09/12/US-botanical-sales-top-8-billion-notch-8.5-growth-ABC-report-says#>

Natural Medicine Database : <https://naturalmedicines.therapeuticresearch.com/>

University of Arizona Center for Integrative Medicine's Integrative Medicine in Residency curriculum

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