



Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Boswellia

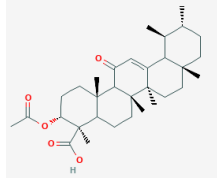
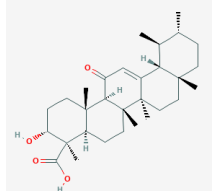
Evidence Summary

Boswellia may modestly reduce cellular damage associated with inflammatory and oxidative stressors. It has a good safety record, but bioavailability is low and varies with formulation.

Neuroprotective Benefit: Boswellia may reduce inflammatory and oxidative stress-mediated damage in the brain, but benefits are tempered by low bioavailability.

Aging and related health concerns: Boswellia can reduce inflammatory pain associated with osteoarthritis, and may also mitigate radiotherapy-related cerebral edema, and modulate blood glucose and lipid levels.

Safety: Boswellia has a long history of safe use in traditional medicine, with no major adverse events reported in clinical studies. New formulations may enhance bioavailability and efficacy.

<p>Availability: OTC</p>	<p>Dose: Varies with formulation 300 to 500 mg 2-3X/day for standard extracts 100 to 250 mg 1x/day for complexed formulations</p>	<p>Major boswellic acids AKBA Chemical formula: C₃₂H₄₈O₅ MW: 512.7 g/mol</p>
<p>Half-life: ~6 hours</p>	<p>BBB: Penetrant</p>	
<p>Clinical trials: RCTs have been conducted for osteoarthritis, inflammatory bowel disease, cerebral edema, diabetes, RRMS, AD, stroke, TBI, and photoaging. Most trials were small, underpowered pilot/ proof-of-concept studies.</p>	<p>Observational studies: None</p>	<p>Source: PubChem</p> <p>KBA Chemical formula: C₃₀H₄₆O₄ MW: 470.7 g/mol</p>  <p>Source: PubChem</p>

What is it?

Boswellia is an herbal extract derived from the bark of the Boswellia tree, which is part of the Burseraceae family [1]. The gum resin contains the bioactive boswellic acids and is used to make the extract. There are a variety of species of Boswellia, and each contains a different combination of boswellic acids, thus each has slightly different medicinal properties, though all generally fall in the category of being anti-inflammatory agents. *Boswellia serrata* is the most commonly used species, and it is also referred to as frankincense (or Indian frankincense), or olibanum. These trees are native to the mountainous regions of India, North Africa, and the Middle East. Boswellia has been used as part of traditional Indian and Persian medicine for centuries, primarily for its anti-inflammatory properties. The gum resin is comprised of volatile oils (5-15%), pure resin (55-65%), and mucus (12-23%), and typically contains about 30% boswellic acids [2]. The four major pentacyclic terpenoids in *Boswellia serrata* resin are β -boswellic acid, acetyl β -boswellic acid, 11-keto- β -boswellic acid (KBA), and acetyl-11-keto-



boswellic acid (AKBA). Pharmacokinetic studies have demonstrated the low bioavailability of these bioactive compounds in traditional extract preparations, which has led to the formulation of new standardized complexed formulations, which show increased bioavailability and efficacy in clinical trials. It has been tested in a variety of small proof-of-concept RCTs, but has been most extensively evaluated in the context of osteoarthritis.

Neuroprotective Benefit: Boswellia may reduce inflammatory and oxidative stress-mediated damage in the brain, but benefits are tempered by low bioavailability.

Types of evidence:

- 1 pilot RCT of *Boswellia serrata* + *Mellisa officinalis* for age-related memory decline
- 2 pilot RCTs for Boswellia (*Boswellia serrata* and *Boswellia papyrifera*) for multiple sclerosis
- 1 pilot RCT for *Boswellia serrata* in mild-to-moderate Alzheimer's disease
- 1 pilot RCT for *Boswellia serrata* in ischemic stroke
- 1 pilot RCT for *Boswellia serrata* in traumatic brain injury clinical trials
- Numerous laboratory studies

Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function:

In traditional Ayurvedic medicine, Boswellia has commonly been used as a memory boosting agent. Preparations of Boswellia have shown potential toward mitigating some aspects of cognitive decline in small pilot studies. The effects were modest across studies. This may be related to the low bioavailability of most preparations of Boswellia, and suggest that Boswellia may have utility as an adjunct to other neuroprotective agents, but is unlikely to exert significant clinical benefits on its own.

In a small RCT (n=70), older adults (aged 60–74 years) treated with a tablet containing 290 mg dried extract of *Mellisa officinalis* and 27 mg of dried extract *Boswellia serrata* for 30 days showed significant improvements on some components of the Wechsler Memory Scale-Revised (WMS-R) relative to placebo [3]. The Boswellia extract used in this study was standardized to contain 70% boswellic acid, 4.67% 11-keto- β -boswellic acid (KBA) and 1.85% acetyl-11-keto-boswellic acid (AKBA). The active group showed significant improvements on the total memory score (Active: 227.58 ± 40.22 vs Placebo: 194.36 ± 27.61 , $p < 0.0001$), the auditory immediate score (48.25 ± 12.88 vs 34 ± 6.55 , $p < 0.0001$), the visual immediate score (57.25 ± 8.95 vs 54.54 ± 15.71 , $p < 0.0001$), the immediate memory score (102.38 ± 20.51 vs 85.45 ± 15.71 , $p < 0.0001$), and working memory score (19.67 ± 4.44 vs 20.36 ± 2.8 , $p < 0.0001$).



Two small pilot RCTs were conducted in patients with relapsing-remitting multiple sclerosis (RRMS) to test the effect of Boswellia on MS-related cognitive decline, which is generally attributed to neuroinflammation and neurodegeneration. In one study (n=60, mean age 30.83 ± 8.16 years), capsules containing 450 mg of *Boswellia serrata* taken twice a day for two months led to significant differences on several tests within the minimum assessment of cognitive function in MS (MACFIMS) battery relative to placebo [4]. Boswellia-treated patients showed improvements on the brief visuospatial memory test (BVRT) (Boswellia: 17.1 ± 7.5 to 21.36 ± 6.34 p<0.01 vs Placebo: 16.44 ± 8.4 to 18.25 ± 7.9) and the California verbal learning test (CVLT) second edition (Boswellia: 44.70 ± 11.38 to 49.34 ± 10.61 p<0.01 vs Placebo 45.10 ± 10.32 to 46.16 ± 10.63). However, there were no significant differences on the paced auditory serial addition test, symbol digit modalities test, controlled oral word association test, judgment of line orientation test and Delis-Kaplan executive function system tests. Similarly, a study (n=80, mean age 36.58 ± 8.50 years) testing a capsule containing 300 mg of *Boswellia papyrifera* twice a day for two months found a significant improvement on the BVRT-revised test relative to placebo [5]. Improvements were also seen on the CVLT and symbol digit modality tests, but the effects were not significantly better than in the placebo group.

Human research to suggest benefits to patients with dementia:

A small clinical study was conducted in 85 patients with mild to moderate Alzheimer's disease (AD) ([IRCT2015051822306N1](#)) testing a standardized extract of *Boswellia serrata*. The results have not yet been published, but the [website](#) of the sponsor (Kondor Pharma) indicates that there was a 1.65 unit reduction on the Clinical Dementia Rating-Sum of Boxes (CDR-SOB) after 6 months of treatment. A reduction in plasma inflammatory markers was also mentioned, but no data was shown.

Mechanisms of action for neuroprotection identified from laboratory and clinical research:

The neuroprotective properties of Boswellia are primarily derived from its anti-inflammatory and antioxidant activities. There are a variety of boswellic acids in Boswellia, and the composition varies by species. 11-keto-β-boswellic acid (KBA) and acetyl-11-keto-boswellic acid (AKBA) are projected to be the most potent bioactive boswellic acids in *Boswellia serrata*, as these show anti-inflammatory activity, namely inhibition of the leukotriene 5-lipoxygenase (5-LOX) in *in vitro* studies [1]. However, pharmacokinetic studies *in vivo* indicate that plasma concentrations of these boswellic acids are very low after oral administration (<0.33 μmol/L for KBA and <0.1 μmol/L for AKBA) due to the poor intestinal absorption of AKBA and extensive 1st pass metabolism of KBA [2]. Due to their high lipophilicity, these compounds are BBB penetrant with brain-plasma ratios of 0.8 for AKBA and 0.5 for KBA [2]. However, due to the low plasma levels, the concentrations in the brain and systemically tend to be lower than the



IC₅₀ for leukotriene inhibition determined *in vitro*. Since modest beneficial effects have been seen throughout clinical and preclinical studies, it suggests that either local tissue concentrations are higher than circulating ones and reach therapeutic values, alternative mechanisms mediate the anti-inflammatory effects, and/or other boswellic acids are important in mediating the therapeutic effects. Due to the poor bioavailability, some of the disparities across studies stem from the differential bioavailability of different preparations of *Boswellia*.

Aging-related cognitive decline: POTENTIAL BENEFIT

Studies in rodents suggest that *Boswellia* has memory protective benefits across the lifespan. When administered to pregnant rats, an aqueous extract of *Boswellia* improved spatial memory performance on the Morris water maze and increased hippocampal expression of CaMKII in the offspring [6]. In the context of aging (24 months old) male rats treated with an extract of *Boswellia serrata* gum resin (100 mg/kg for 8 weeks) improved spatial learning on the Morris water maze, which was associated with increased dendritic complexity in the hippocampus [7]. The hippocampal volumes in the CA1 region were also larger in the *Boswellia*-treated aged rats [8]. These studies suggest that *Boswellia* preserves cognition by maintaining dendritic structure, thereby preserving the framework for synaptic plasticity.

Alzheimer's disease: POTENTIAL BENEFIT

Boswellia serrata (90 mg/kg) was found to be protective in both prevention and therapeutic treatment regimens in a male rat model of AlCl₃-induced cognitive impairment. *Boswellia* treatment was associated with improved performance on the T-maze and higher levels of acetylcholine in the brain [9]. A methanolic extract of *Boswellia* resin (137.5 mg/kg for 3 months) also reduced A β plaques, and pro-inflammatory markers (CRP, NF-kB, MCP-1, LTB₄) in this model [10]. Similarly, *Boswellia serrata* gum extract (400 mg/kg oral for 8 weeks) reduced learning and memory impairments on the passive avoidance and Morris water maze tests in a male rat model (streptozotocin + high fat/fructose diet) of type 2 diabetes-induced cognitive decline [11]. The behavioral effects occurred in conjunction with a reduction in deposition of A β and p-tau, a reduction in pro-inflammatory mediators (TNF- α , IL-1 β , IL-6), less insulin resistance, and enhanced antioxidant capacity (GSH, SOD). In cell culture, incense acetate, which is a major component of *Boswellia carterii*, was shown to protect human olfactory bulb neural stem cells from A β ₂₅₋₃₅ mediated cell death by mitigating A β -induced oxidative stress and inflammation [12].

Neuroinflammation: In the LPS-induced model of neuroinflammation, acetyl-11-keto- β -boswellic acid (AKBA), a major brain-penetrant component of *Boswellia serrata*, protected against memory



impairments on the passive avoidance and Morris water maze tests when administered as a pre-treatment in male rats [13]. The effect was associated with a decrease in pro-inflammatory mediators (IL-6, TNF- α , GFP) and oxidative stress markers (MDA), along with an increase in anti-inflammatory mediators (IL-10), antioxidant enzymes (SOD), and brain derived neurotrophic factor (BDNF). Similar protective effects on behavioral measures, oxidative stress markers, amyloid, and inflammatory mediators were seen when AKBA was administered after lipopolysaccharide (LPS) injection [14].

Excitotoxicity: Preclinical studies suggest that *Boswellia* contains a variety of compounds which protect against seizures and excitotoxic cell death. In male rats, 11-keto- β -boswellic acid (KBA), an active brain penetrant component of *Boswellia serrata*, inhibited kainic acid-induced increases in glutamate and cell death in the hippocampus when administered as a pre-treatment [15]. Cell culture experiments suggest that the protective mechanism involves the suppression of N- and P/Q-type Ca²⁺ channels and protein kinase A (PKA) activity [15]. An aqueous extract of *Boswellia* led to a preservation of learning and memory behavior and neurons in the hippocampal CA1 region in the pentylene-tetrazol kindling model of temporal lobe epilepsy in male rats [16]. Incensole derivatives isolated from *Boswellia papyrifera* also delayed the onset and reduced the duration of pentylene-tetrazol-induced seizures in mice [17].

Ischemic stroke: POTENTIAL BENEFIT

Boswellia was shown to improve neurological outcomes, while reducing inflammation and oxidative stress in a pilot RCT (n=80) in the context of ischemic stroke (NIHSS score 4-20) when administered within 72 hours [18]. Two capsules containing 400 mg of boswellic acids (Strowell™) three times per day for one month in conjunction with standard of care significantly improved neurological function based on the NIHSS evaluation relative to placebo during the one-month follow-up period (*Boswellia*: baseline 7.29 ± 5.50 to 1.86 ± 2.78 vs Placebo: baseline 7.43 ± 3.85 to 3.95 ± 3.64 , $p=0.021$). The *Boswellia*-treated group also showed significant reductions in plasma markers of inflammation (TNF α , IL-1 β , IL-6, IL-12p70, PGE2, MCP-1, IP-10, IL-8), and oxidative stress (8-isoprostanes) within seven days.

Preclinical studies indicate that *Boswellia* protects against ischemic injury via its anti-inflammatory and antioxidant activities. In the middle cerebral artery occlusion (MCAO) stroke model, *Boswellia serrata* extracts reduce neurological deficits in male rats [19]. The neurological effects are accompanied by a reduction in brain infarct size, neuronal cell death, and oxidative stress. The protective effects are thought to be mediated, at least in part, by AKBA, as similar benefits are achieved with preparations of AKBA [19]. Due to the poor bioavailability of AKBA, its efficacy can be enhanced by encapsulation in nanoparticles [20]. Cell culture studies indicate that AKBA engages the endogenous Nrf2 antioxidant pathway, and dampens inflammatory mediators NF- κ B and 5-lipoxygenase (5-LOX), resulting in greater

cell viability in the context of ischemic stress [20]. AKBA may exert some of its anti-inflammatory effects by acting on endothelial cells to reduce the expression of complement receptors and cell adhesion molecules [21]. KBA can also reduce infarct volumes and neurological deficits in the MCAO model by reducing oxidative stress, via activation of the Nrf2 antioxidant pathway [22].

Traumatic brain injury: POTENTIAL MINOR BENEFIT WITH EARLY INTERVENTION

Trends to improvement were seen in patients with diffuse axonal injury (Glasgow coma scale ≤ 12) in a small (n=38) 12-week cross-over RCT testing capsules containing 360 mg *Boswellia serrata* (60% Boswellia gum resin, 20–23% mucilage and 5–9% essential oils) taken three times per day [23]. Both groups showed improvement on the disability rating scale over the course of the study, but there were trends toward greater improvement on cognitive function related items during the period taking Boswellia, relative to the placebo period. The lack of significant benefit may stem from the treatment starting too late following injury and the low bioavailability of the projected bioactive boswellic acids in this preparation. Since the protective effects are expected to be related to the anti-inflammatory activity, early administration which can dampen the initiation of the damage-inducing inflammatory response is likely to be the most effective.

In a preclinical closed head injury model, male mice treated with incensole acetate within one hour of the injury induction showed reduced neurological and cognitive deficits [24]. There was also a reduction in hippocampal neurodegeneration and pro-inflammatory mediators (TNF α , IL-1 β , GFAP) in the brain.

APOE4 interactions: Not established

Ageing and related health concerns: Boswellia can reduce inflammatory pain associated with osteoarthritis, and may also mitigate radiotherapy-related cerebral edema, and modulate blood glucose and lipid levels.

Types of evidence:

- 1 meta-analysis and systematic review of RCTs for supplements in osteoarthritis
- 1 meta-analysis of RCTs for Boswellia in osteoarthritis
- 2 systematic reviews of RCTs of supplements for inflammatory bowel disease
- 2 RCTs for different Boswellia formulations in osteoarthritis
- 1 RCT of a Boswellia complex formulation in irritable bowel syndrome
- 2 pilot clinical studies of Boswellia for radiation-induced cerebral edema
- 1 pilot RCTs of Boswellia-containing creams for skin damage



- 4 clinical studies of Boswellia for type 2 diabetes
- Numerous laboratory studies

Osteoarthritis: BENEFIT FOR REDUCING PAIN

Boswellia has been extensively studied in the context of osteoarthritis, and systematic reviews demonstrate that this indication has the strongest evidence for clinical benefit. In a systematic review and meta-analysis involving 69 studies (n=11,586 participants) examining 20 supplements used for osteoarthritis, Boswellia serrata was identified as one of seven supplements that showed evidence for clinically important short-term pain relief (Standardized mean difference [SMD] -1.61, 95% CI -2.10 to -1.13, based on 3 trials n=186) [25]. Boswellia serrata was also the only supplement in this study to show evidence for clinically important short-term improvement of joint stiffness (SMD -0.94, 95% CI -1.26 to -0.62). A meta-analysis of seven RCTs (n=545 participants) testing Boswellia for osteoarthritis found that relative to the placebo or western medicine control groups, Boswellia treatment was associated with significant improvements in pain based on the visual analog scale (Weighted mean difference [WMD] -8.33, 95% CI -11.19 to -5.46, p<0.00001) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain score (WMD -14.22, 95% CI -22.34 to -6.09; p = 0.0006) [26]. There were also significant improvements for WOMAC stiffness (WMD -10.04, 95% CI -15.86, to -4.22; p = 0.0007), WOMAC joint function (WMD -10.75, 95% CI -15.06 to -6.43; p<0.00001); and the Lequesne severity index: (WMD -2.27, 95% CI -3.08 to -1.45; p<0.00001). The efficacy in clinical studies varies depending on the formulation used. Studies with formulations that involve complexing with lipids have higher efficacy. One study testing a solid lipid Boswellia serrata particles formulation (WokVida®) with a standard Boswellia extract showed that the particle formulation use led to a lower dependence on rescue analgesics at the of the two-month study (92 vs. 76%, p < 0.05), and a decrease in the inflammatory mediators IL-2 and IL-4, which was not seen with the standard extract [27]. It should be noted that radiographic analysis indicated that while Boswellia provided symptomatic pain relief, it did not affect clinical radiographic features of osteoarthritis, suggesting that it may not significantly impact disease progression.

Inflammatory bowel disease: POTENTIAL BENEFIT

Boswellia has been tested in clinical trials for a variety of inflammatory bowel diseases, and the results have been modest and mixed, depending on the bowel disease. A systematic review of 21 RCTs examining herbal therapies for inflammatory bowel disease concluded that *Boswellia serrata* gum resin was as effective as the anti-inflammatory drug mesalazine for ulcerative colitis [28]. Meanwhile a systematic review of 10 RCTs for inflammatory bowel disease interventions concluded that *Boswellia*



serrata was ineffective for collagenous colitis [29]. In patients with mild irritable bowel syndrome (IBS) (n=69), treatment with a *Boswellia serrata* lecithin-based delivery form (Casperome®, 1 tablet/day) for six months resulted in lower mean score values for self-assessed IBS symptoms (recurrent abdominal pain, abdominal pain at pressure, altered bowel movements, meteorism, spontaneous cramps of the abdomen) [30]. There was also a significant reduction in evidence of air plus peristalsis and loops dilatation during ultrasound (17.14% vs 58.82%, p<0.05), as well as a reduction in oxidative stress with *Boswellia*.

The beneficial effects are related to the anti-inflammatory activity of *Boswellia*. Despite its low systemic bioavailability following oral administration, local concentrations of the major bioactive boswellic acids are expected to be significantly higher than plasma levels, and with levels in the range of those demonstrating inhibition toward 5-LOX and NF-κB *in vitro* [2]. The exact anti-inflammatory mechanisms mediating its effects have not been fully elucidated, and may also involve the suppression of prostaglandin E2 (PGE2) and cathepsin G, and the downregulation of immune cell activating cell adhesion molecules on endothelial cells.

Radiation-induced cerebral edema: POTENTIAL BENEFIT

Boswellia serrata dry resin extract was granted orphan drug designation for peritumoral brain edema by the EMA in 2002 [2]. However, to date, only a couple of pilot clinical trials have been conducted assessing the efficacy of *Boswellia* for this indication. The studies suggest that *Boswellia* has the potential to reduce radiotherapy-related brain edema in at least a subset of patients. The characteristics of the patients most likely to benefit have not yet been established.

In one RCT, patients with malignant cerebral tumors treated with radiotherapy (n=44) were treated with the H15 preparation of *Boswellia serrata* (4200 mg/day) or placebo throughout the duration of radiotherapy [31]. In the *Boswellia*-treated group, 60% of patients showed a reduction in edema to <25% of baseline values, compared to 26% in the placebo group. Notably, the patient with the highest serum levels of boswellic acids also had one of the largest reductions in edema. The reduction in edema may have been partially related to anti-tumor activity, as preclinical studies indicate that *Boswellia* has the potential to exert anti-cancer effects [32]. In this study, fewer *Boswellia*-treated patients continued to show disease progression relative to placebo (0% vs 18%), however, there were no significant differences in progression-free survival. A separate study assessed a phytosome-based delivery form of boswellic acids extract (Monoselect AKBA™, 4500 mg/day) in patients with glioblastoma undergoing radiochemotherapy and surgery (n=20) [33]. A reduction (>75%) or stabilization of edema was seen in 33% at 12 weeks post-surgery and in 50% at 22 weeks. By 34 weeks, 25% did not require steroid

treatment (dexamethasone), while 37.6% were on a stable or reduced dose. In two patients, the reduced edema allowed for a successful surgical resection of the tumor.

Diabetes: POTENTIAL TO LOWER GLUCOSE AND TRIGLYCERIDE LEVELS

Clinical studies have been mixed with respect to the ability of *Boswellia* to modulate glucose parameters in the context of type 2 diabetes. The efficacy may be influenced by the formulation and dosing of *Boswellia*. In a six-week study, patients with type 2 diabetes (n=60) taking *Boswellia serrata* (300 mg 3x/day) showed a significant reduction in blood glucose levels (173.71±10 vs 147.57±8 mg/dl, p<0.01) and an increase in plasma insulin levels (13.3±1.5 vs 24.54±3.7 mIU/ml, p<0.01) [34]. There was also a reduction in the insulin resistance index relative to the placebo group. In another RCT (n=70), *Boswellia* gum resin (400 mg 2x/day) taken for 12 weeks decreased the fasting blood sugar level (-17.6% vs -1.4%, p<0.001), glycated hemoglobin (HbA1c) (-4.95% vs -0.13%, p<0.001), and insulin (-24.7% vs -6.8%, p<0.001) in type 2 diabetics, relative to placebo [35]. *Boswellia* treatment was also associated with decreases in cholesterol (-6.3% vs +1.92%, p=0.003), LDL (-13.1% vs -1.4%, p<0.001) and triglycerides (-6.53% vs +0.81%, p<0.001). An herbal combination containing *Boswellia* (olibanum 200 mg, silymarin 200 mg, and nettle 200 mg capsule 3x/day) taken for 90 days, led to a significant reduction in the fasting blood glucose level relative to placebo (152.13 ± 44.63 vs 124.68 ± 21.94 mg/dL, p = 0.003), as well as a reduction in HbA1c (-19% vs -7%, p<0.01) and triglycerides (148.89 ± 37.60 vs 171.96 ± 47.90 mg/dL, p=0.04) [36]. In an RCT (n=56) testing *Boswellia serrata* gum resin (250 mg 2x/day) for 8 weeks, reductions were seen in fasting blood sugar (171.82 ± 60.78 to 149.86 ± 26.19 mg/dL, p=0.04), HbA1c (8.17 ± 1.88 to 7.60 ± 1.34, p=0.02), and triglycerides (162.13 ± 53.53 to 135.93 ± 31.92 mg/dL, P=0.01) relative to baseline, but the differences were not significant relative to placebo [37]. The lack of significance may stem from the lower dose and shorter duration of this trial relative to the ones that showed benefit. The protective mechanisms may be related to its antioxidant, anti-inflammatory, and hypolipidemic properties [38].

Skin aging: POTENTIAL BENEFIT

There have been a couple of clinical trials testing *Boswellia*-containing creams for protection from photoaging or radiotherapy-induced skin damage. In a small RCT, women (n=15) treated with a cream containing 0.5 % boswellic acids (5-Loxin®) showed statistically significant reductions (p < 0.05) of tactile roughness (1.46 ± 1.20 to 1.08 ± 0.95) and fine surface lines (2.23 ± 0.83 to 1.69 ± 0.18) within 30 days [39]. There was also a significant increase in skin thickness based on echographic measurements (1.36 ± 0.12 mm to 1.58 ± 0.26 mm). Similarly, women (n=114) with mammary carcinoma undergoing radiation therapy treated with a cream containing 2% boswellic acids (Bosexil®) were less likely to

experience erythema (22% vs 49%) and skin damage (10.1% vs 13.3%), and to require the use of cortisone (25.0% vs 63.0%) [40]. These studies suggest that Boswellia-containing creams may help protect against some forms of skin damage.

Safety: Boswellia has a long history of safe use in traditional medicine, with no major adverse events reported in clinical studies. New formulations may enhance bioavailability and efficacy.

Types of evidence:

- 3 meta-analyses or systematic reviews
- 14 clinical trials
- 3 pharmacokinetic clinical studies
- Numerous laboratory studies

Boswellia has been safely used for hundreds of years as part of traditional Ayurvedic and Persian medicine [2]. Clinical trials of standardized formulations also show evidence that it is generally well-tolerated, with side effects similar to placebo in the vast majority of studies. Most studies reported no adverse events with treatment, and where it was measured Boswellia treatments did not alter kidney parameters, liver enzymes, or routine blood laboratory test measures [36; 41; 42]. Some studies reported minor gastrointestinal events including, diarrhea, abdominal pain, and nausea [43]. A case of contact dermatitis was also reported in a topical formulation ([MSKCC](#)).

Pharmacokinetic studies indicate that the oral bioavailability of the presumed major bioactive boswellic acids in Boswellia is low [44]. New formulations are being developed and tested, which show enhanced bioavailability [45]. These include complexing with phospholipids (phytosome technology) and nano-encapsulation. In a pharmacokinetic study, phytosome complexed Boswellia (Casperome[®]) showed faster absorption (by 1.5 to 2 hours), and higher concentrations, with C_{max}'s that were four-fold higher for AKBA, two-fold higher for the boswellic acids α BA, β BA, α BA, and α BA, and 10% higher for KBA, relative to un-complexed Boswellia [46]. These concentrations were within the range of the IC₅₀ for inhibition of major inflammatory mediators including cathepsin G.

Drug interactions: There are no known drug interactions with Boswellia ([rxlist](#)). However, mass-spectroscopy analysis indicates that *Boswellia serrata* compounds are substrates of cytochrome P450 (CYP-450) 1A2, 2C8, 2C9, 2C19, 2D6, and 3A4, and P-glycoprotein in the gastrointestinal tract, thus drugs that use these enzymes may be impacted ([Drugs.com](#)). Additionally, Boswellia may have anti-platelet effects, and may show an interaction with anticoagulants, such as warfarin.

Sources and dosing:

Boswellia is available as an OTC herbal supplement. Preparations of *Boswellia serrata* gum resin should be standardized for the major bioactive boswellic acids KBA and AKBA. According to European Pharmacopeia 6.0, air dried gum resin should contain a minimum of 1% KBA and AKBA, each [2]. The dosing can vary up to six-fold, depending on the manufacturer, as formulations vary in their bioavailability and potency. Dosing recommendations are typically on the order of 300 to 500 mg taken two to three times per day, but doses tend to be lower, on the order of 100 to 250 mg, for branded standardized formulations ([rxlist](#), [Examine.com](#)). Boswellia should be taken with food, as a study found that the bioavailability of the major boswellic acids could be increased three-fold when consumed with a high-fat meal, due to the lipophilic nature of these compounds [47].

[5-Loxin®](#), a *Boswellia serrata* extract enriched to contain 30% AKBA has shown efficacy in clinical trials, however, the [Aflapin®](#) formulation was found to have higher oral bioavailability for AKBA and better efficacy in the context of osteoarthritis in clinical studies [48]. Solid lipid *Boswellia serrata* particles ([WokVida®](#)) showed superior clinical efficacy over standardized *Boswellia* extract in osteoarthritis, due to its enhanced bioavailability [27]. The [Strowell®](#) formulation of *Boswellia serrata* was used a clinical trial showing benefit in the context of ischemic stroke [18]. The *Boswellia serrata* lecithin-based delivery form ([Casperome®](#)) using phytosome technology, or the complex of an active ingredient with a phospholipid (lecithin) has also been tested in several clinical trials. This preparation, which is formulated by Indena S.p.A. (Milan, Italy), has been established to have good bioavailability and pharmacokinetic properties.

Research underway:

According to Clinicaltrials.gov, there are active clinical studies involving *Boswellia* for cancer, postoperative pain, and COVID-19. There are additional clinical trials registered on the [Cochrane trials database](#), but is unclear how many are active.

Search terms:

Pubmed, Google: *Boswellia*; Frankincense

- Alzheimer's disease, neurodegeneration, stroke, aging, cancer, arthritis, diabetes, clinical trial, safety, systematic review, meta-analysis



Websites visited for Boswellia:

- [Clinicaltrials.gov](https://clinicaltrials.gov)
- [Examine.com](https://www.examine.com)
- [Rxlist.com](https://www.rxlist.com)
- [Drugs.com](https://www.drugs.com)
- PubChem ([AKBA](https://pubchem.ncbi.nlm.nih.gov/compound/AKBA), [KBA](https://pubchem.ncbi.nlm.nih.gov/compound/KBA))
- [DrugBank.ca](https://pubchem.ncbi.nlm.nih.gov/compound/DrugBank.ca)
- [ConsumerLab.com](https://www.consumerlab.com)
- [MSKCC](https://www.mskcc.org)

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