

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.

Dinh lang (*Polyscias fruticosa*)

Evidence Summary

Preclinical studies on cognitive improvement and lifespan extension are compelling but limited in number. It is used in Asia for various indications but is not readily available elsewhere.

Neuroprotective Benefit: Dinh lang root extract treatment significantly improved cognitive functions in senescent mice, but the mechanisms are unclear and these findings have not been extended to humans.

Aging and related health concerns: Dinh lang extends lifespan while decreases tumors in mice, but no studies in humans exist.

Safety: A rodent study has suggested that dinh lang is tolerable at high doses without toxicity, but no studies in humans corroborate this finding.

Availability: Not commonly available in supplement form. Grows in southeast Asia.	Dose: No clinical studies have tested dinh lang in humans. In rodents, 10 mg/kg/day was typically used.	Chemical formula: e.g., $C_{49}H_{78}O_{19}$ MW: e.g., 969.5011
Half life: Unknown	BBB: Unknown	
Clinical trials: None	Observational studies: None	

What is it? Dinh lang (*Polyscias fruticosa*), an evergreen shrub, is widely cultivated in southeast Asia and the tropical islands of the Pacific region [1]. It can also be called *Panax fruticosa*, *Nothopanax fruticosam*, *Parsley panax*, *Ming aralia*, or *Indian polyscias* [2]. In Asian countries, the leaves are used as a tonic, anti-inflammatory, antitoxin, antibacterial, and digestive aid. The root is also used as a diuretic, antipyretic, anti-dysentery, and treatment for neuralgia and rheumatic pain [1; 3]. In Vietnam, it is used for the treatment of ischemia and inflammation [4]. Triterpenoid saponins are considered the main active compounds that contribute to these purported effects [1]. Dinh lang treatment appears to prolong lifespan in mice based on a few studies [5], but these findings have not been extended to humans.

Neuroprotective Benefit: Dinh lang root extract treatment significantly improved cognitive functions in senescent mice, but the mechanisms are unclear and these findings have not been extended to humans.

Types of evidence:

- Several laboratory studies

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

None.

Human research to suggest benefits to patients with dementia:

None.

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

Dinh lang root extract treatment (10 mg/kg/day, orally) for 5 weeks restored cognitive ability in a group of senescent (22-24-month-old) rats that were unable to develop conditioned avoidance response [6]. The same treatment for 4 weeks significantly improved the performance of young mice and improved retention in both 5-month-old and 19-20-month-old mice.

In a subsequent study, dinh lang root extract treatment (10 mg/kg/day, orally) in combination with (-)deprenyl (Parkinson's medication) significantly increased memory function [5]. Treatment was started at 12 months of age and continued until the end of life. At the beginning of the experiment, there were equal numbers of mice with retention in all groups. But 7 months later, only 11 (out of 40) saline-treated mice showed retention, whereas 20-21 (out of 40) drug-treated mice retained retention. At 15 months, 50% of dinh lang plus (-) deprenyl-treated rats showed retention whereas none of the saline-treated animals maintained this function.

In a recent 2019 study, two new oleanane-type triterpenoid saponins, named polyscioside J and polyscioside K, along with two known saponins, ladyginoside A and chikusetsusaponin IVa were purified from an ethanol extraction of dinh lang [4]. It is thought that the large amounts of triterpenoid saponins may confer benefits similar to *Panax ginseng*, as ginseng also contains triterpenoid saponins (e.g., ginsenosides)[7](See *Panax ginseng* report). Other saponins that have been isolated from dinh lang include polysciosides A to H, zingibroside RI, and 3-o-[beta-D-glucopyranosyl (1-4)-beta-D glucurono-pyranosyl] oleanolic acid 28-O-beta-D-glucopyranosyl ester [1].

APOE4 interactions: Unknown.

Aging and related health concerns: Dinh lang extends lifespan while decreases tumors in mice, but no studies in humans exist.

Types of evidence:

- Several laboratory studies

Lifespan: POTENTIAL BENEFIT IN MICE. In a study in mice, dinh lang root extract treatment (10 mg/kg, orally, 3 times a week) from 12 months of age (and continued until the end of life) significantly prolonged lifespan [5]. The combined treatment of dinh lang and (-)deprenyl (0.25 mg/kg, s.c.) proved to be the most effective. Animals in the dinh lang- or (-)deprenyl-treated groups showed a slower rate

of body weight loss, thereby preventing age-related loss of body weight. The two drugs did not suppress food intake in aged mice. The saline group had lifespans ranging from 75 to 133 weeks, whereas the dinh lang-treated group had lifespans ranging from 94 weeks to 171 weeks. The longest-living mouse in the dinh lang plus (-)deprenyl-treated group lived 180 weeks. Longer lifespan was also correlated with better cognitive functions (retention).

Cancer: POTENTIAL BENEFIT IN MICE. In mice, dinh lang root extract treatment (10 mg/kg, orally, 3 times a week) alone or combined with (-) deprenyl treatment (0.25 mg/kg, s.c.) significantly lowered the numbers of tumor-bearing mice compared to saline treatment [5]. Deprenyl alone was less effective in lowering tumors, suggesting that the tumor-lowering effects were driven by dinh lang. Mechanisms underlying this tumor-lowering effect have not been studied, though it is possible the triterpenoid saponins play a role.

Diabetes: POTENTIAL SMALL BENEFIT. In mice fed a high-sucrose diet, pretreatment with a major saponin from dinh lang (PFS; full name, 3-O-[β -d-glucopyranosyl-(1 \rightarrow 4)- β -d-glucuronopyranosyl] oleanolic acid 28-O- β -d-glucopyranosyl ester) at 100 mg/kg dose (orally, 30 min before sucrose administration) significantly decreased postprandial blood glucose levels [8]. This effect on glucose lowering is due to PFS's ability to strongly inhibit α -amylase and α -glucosidase, which in turn lowers the level of postprandial hyperglycemia by controlling starch breakdown into glucose. However, this effect was not as robust as acarbose, an anti-diabetic medication that inhibits α -glucosidase.

Inflammation: POTENTIAL BENEFIT IN RATS. In a study in rats, treatment with dinh lang leaf extract (500 mg/kg, orally) significantly reduced paw edema induced by egg white [3]. And the same dose also showed fever-reducing effects in response to a vaccine. The magnitude of fever reduction was comparable to 100 mg/kg of paracetamol.

In preclinical studies, saponins have been shown to have anti-inflammatory and mast cell stabilizing activities by inhibiting the synthesis of prostaglandins, thromboxanes, arachidonic acid, histamine, bradykinin and serotonin [9]. However, none of these observations have been confirmed in humans.

Body weight: PREVENTS AGE-RELATED WEIGHT LOSS IN MICE. In mice, dinh lang root extract treatment (10 mg/kg, orally, 3 times a week) alone or combined with (-) deprenyl treatment (0.25 mg/kg, s.c.) from 12 months of age (and continued until the end of life) resulted in a lower rate of weight loss than saline treated mice [5]. This study suggests that these treatments prevent age-related weight loss. However, the two drugs did not suppress food intake in aged mice.

Safety: A rodent study has suggested that dinh lang is tolerable at high doses without toxicity, but no studies in humans corroborate this finding.

Types of evidence:

- 2 laboratory studies

In a study in mice, an extract of dinh lang leaves (ethanol-, then chloroform-, then ethylacetate-, then n-butanol-extracted) was considered safe up to a dose of 2.5 g/kg [3]. No toxic symptoms or mortality were observed, and no behavioral or autonomic changes were seen. In an unusual fish toxicity test, 250 mg/mL of dinh lang root n-butanol extract killed 60% of the fish; and 500 mg/mL of the leaf extract killed 60% of the fish [2]. It is not clear how this fish toxicity test results can be extrapolated to safety for human use.

Drug interactions: Drug and supplement interactions with dinh lang have not been studied.

Sources and dosing: Dinh lang (*Polyscias fruticosa*), an evergreen shrub, is widely cultivated in southeast Asia and the tropical islands of the Pacific region [1]. It is not commonly available in supplement form. All studies in mice have used extract from dinh lang roots or leaves—typically the roots/leaves were ethanol-extracted, filtered, and dried [5]. A 50 mg extract was equivalent to 1 g of dried roots. In mice, dinh lang extract treatment at a dose of 10 mg/kg improved cognitive functions and prolonged lifespan [5; 6].

Research underway: There are no ongoing clinical trials testing dinh lang based on ClinicalTrials.gov. There are also no NIH-funded ongoing research evaluating dinh lang.

Search terms:

Pubmed, Google: Dinh lang or *Polyscias fruticosa* or *Ming aralia*

Websites visited for Dinh lang:

- Clinicaltrials.gov (o)
- Examine.com (o)
- Treato.com (o)
- DrugAge (o)
- Geroprotectors (o)
- Drugs.com (o)

- WebMD.com (o)
- PubChem (o)
- DrugBank.ca (o)
- Labdoor.com (o)
- ConsumerLab.com (o)

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