Neem Leaf SAP

Neem (*Azadirachta indica*) based preparations have been widely used for centuries as traditional medicine for its antimicrobial, antiulcer, anti-inflammatory, antihelminthic, antidiabetic, anticancer and sedative properties. Substantial pre-clinical evidence supports the antimicrobial applications of neem leaf preparations. Neem preparations have been widely used to treat skin conditions such as psoriasis, acne, scabies and fungal infections. Neem leaf extract is rich in phytochemicals that are known to exert pleiotropic effects including inhibition of angiogenesis, cancer cell growth and induction of apoptosis. Neem leaf preparations have been also extensively studied for their applications in the management of gastric ulcers and diabetes. **Neem Leaf SAP** provides high quality neem leaf powder that can be used to foster immunity and optimal digestion, improve diabetic symptoms and blood lipid profile and as an adjunctive support in cancer therapy.

ACTIVE INGREDIENTS

Each vegetable capsule contains:

Neem (Azadirachta indica) leaf 650 mg

OTHER INGREDIENTS: Vegetable magnesium stearate and Silicon dioxide in a vegetable capsule composed of carbohydrate gum and purified water.

Contains no: Gluten, soy, wheat, corn, eggs, dairy, yeast, citrus, preservatives, artificial flavour or colour, starch, or sugar.

This product is non-GMO and vegan friendly.

Neem Leaf SAP contains 90 capsules per bottle.

DIRECTIONS FOR USE

Adults: Take 2-4 capsules daily or as directed by your health care practitioner.

INDICATIONS

Neem Leaf SAP can be used as an adjunctive support in cancer therapy, and can help:

- Improve digestive health and alleviate gastric ulcers.
- Manage diabetic symptoms and improve blood lipid profile.
- Alleviate anxiety.

CAUTIONS & WARNINGS

Consult a healthcare practitioner prior to use if you are pregnant or breastfeeding or if you have diabetes. Do not use if seal is broken. Keep out of reach of children.

PURITY, CLEANLINESS & STABILITY

All ingredients listed for each product lot number of **Neem Leaf SAP** have been tested by an ISO 17025 accredited third-party laboratory for identity, potency, and purity.



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Neem Leaf SAP

Digestive Support Soutien digestif

NPN 80077535

90 CAPSULES

Scientific Advisory Panel (SAP):

adding nutraceutical research

to achieve optimum health

Science-based digestive support

Research Monograph

INTRODUCTION

Neem (Azadirachta indica), is an evergreen tree that is native to India, Pakistan, and Bangladesh ^[1]. Neem based preparations have been widely used as traditional medicine for centuries known for their antifungal, anti-inflammatory, anti-malarial, antihelmintic, antibacterial, antiviral, antidiabetic, anticancer and sedative effects ^[2,3]. Especially, pre-clinical evidence supports the efficacy of neem leaf extracts in antimicrobial applications and cancer therapy ^[2]. Multiple chemical constituents, such as azadirachtin, gedunin, nimbidin, nimbidol, nimbin, salannin and quercetin, present in neem have been associated with these aforementioned health benefits. ^[1,3] Neem phytochemicals have been shown to suppress proliferation and growth of cancer cells, inhibit angiogenesis, induce apoptosis and decrease tumor cell invasion and migration.^[1,2]

ANTIMICROBIAL PROPERTIES

Neem extracts exhibit strong antimicrobial effects against bacteria (planktonic forms), bacterial biofilm; *Candida albicans*; viruses and parasites such as *Plasmodium sp.* that cause malaria. A recent *in vitro* study demonstrated the antimicrobial potential of neem leaf extract against Methicillin-resistant *Staphylococcus aureus* (MRSA) biofilm and planktonic aggregation and *Schistosoma mansoni* worms.^[4] In another study, neem leaf extract exhibited profound dose-dependent antibacterial activity against periodontophatic bacterium *Porphyromonas gingivalis*, along with strong antioxidant activity.^[5] A number of studies have shown the potential antimicrobial efficacy of neem leaf extract against *Candida albicans*, *Streptococcus mutans*, *Enterococcus faecalis*, *Plasmodium berghei*, *Pseudomonas aeruginosa* and *Leishmania donovani* infections.^[6-9] Topical neem leaf and bark preparations have been widely used to treat skin conditions such as psoriasis, acne, scabies and fungal infections. Oral supplementation with neem leaf extracts could potentially confer similar skin health benefits.

CANCER

The anticancer properties of neem have been extensively investigated in preclinical studies against a wide variety of human cancer cell lines and animal models for human cancers including gastrointestinal, hematological, Ehrlichs carcinoma, lung, liver, skin, oral, prostate and gynecological cancers.^[10-15] Neem components are known to modulate tumor microenvironment through various mechanisms including attenuation of angiogenesis and induction of selective cytotoxicity towards cancer cells compared to normal cells during cancer therapy ^[11, 12]. Besides inhibiting cancer cell proliferation, neem components exert anticancer effect by induction of apoptosis as well as other forms of cell death including autophagy.^[10]

A clinical study evaluated the potential of neem leaf extract to induce apoptosis in cervical cancer cells and estimated caspase activity and TNF- α and IFN- γ levels in monocytes from cervical cancer patients. It was found that neem treated monocytes displayed elevated activity capase-3, caspase-8 and caspase-9 activities along with increased apoptosis exhibited by neem-exposed cervical cancer cells. ^[15] In another study neem oil suppressed acute skin toxicity in pateints with head and

neck cancer undergoing radio or chemo-radiotherapy.^[16]

Another unique aspect of neem leaf preparations is that it has been observed to potentiate the antitumor activities of certain chemotherapeutic drugs in addition to protecting against deleterious side effects of these drugs.^[2] Pre-treatment of an experimental animal model with neem leaf extract reduced leucopenia and neutropenia and potentiated the antitumor activities of cyclophosphamide.^[107] Neem leaf extracts have been observed to positively modulate phase-I and phase-II xenobiotic-metabolizing enzymes, lipid and protein oxidation and antioxidant defense enzymes leading to attenuation of the dimethylbenz[a]anthracene induced carcinoma in the animal model.^[107] Administration of neem leaf extracts attenuate oxidative stress by decreasing lipid peroxidation levels and enhance reduced glutathione contents and activities of various antioxidant enzymes.^[2] Alt these evidence suggest that neem leaf extract may be used as a potent preventive and adjuvant therapy against cancer.^[2]

ANTIULCER

Neem leaf extract have been shown to inhibit restraint-stress induced gastric lesions and ulcers at a dose of 100 mg/kg in animal models^[19]. Oral administration of 500 mg/kg for 6 days resulted in 65% and 76% protection of stress and aspirin-induced damage respectively in an experimental animal model [20]. Neem leaf extract dose-dependently reduced gastric lesions by 85%, 75% and 88% at doses (i.p.) of 20, 24 and 32 mg/kg, respectively and proved to be more potent than ranitidine.^[19] These preclinical studies provide encouraging results which need to be validated using well controlled clinical studies. Nevertheless, neem leaf extract evidently holds potential as a safe therapeutic option for the management of gastric ulcers.^[19]

ANTIDIABETIC AND LIPID LOWERING EFFECTS

Hypoglycemic effects of neem leaf extracts have been reported in various models of

diabetic animals in addition to their anti-lipid peroxidative, anti-hypercholesterolemic and triglyceride lowering activities ^[21] Oral supplementation with neem leaf powder (1 g daily) in diabetic animals reduced symptoms of polydipsia and polyphagia.^[22] Oral administration of nimbidin demonstrated significant hypoglycaemic effect in fasting animal models. ^[23] Phytochemicals in neem leaves possess α -amylase and α -glucosidase inhibitory activities resulting in anti-hyperglycemic and anti-lipidemic effects.^[21, 24]

A new tetranortriterpenoid meliacinolin isolated from neem leaves was found to effectively reduce insulin resistance, improve renal function, lipid abnormalities, and oxidative stress, suggesting the multiple therapeutic benefits of meliacinolin in diabetes pathogenesis.^[21] Overall, neem leaf extract can be used as an effective therapeutic strategy to improve post prandial hyperglycemia for diabetes management.

ANTI-ANXIETY

Pharmaceutical interventions using benzodiazepines for managing anxiety are effective in the short term, but may lead to impaired motor function. In an animal study, neem leaf extract dosed at 7 mg/kg dosage was found to induce anxiolysis without motor deficiency.^[25]

SAFETY

Normal consumption of neem preparations are known to be safe as they have been consumed for several millennia.^[11] Aqueous extracts of neem leaves have been reported to be non-toxic to mice and LD50 was >2.5 g/kg body weight. Pure azadirachtin has been shown to have low toxicity in humans at a daily dose of 15 mg/ kg body weight.^[11]

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