

Artemisinin SAP

Science-based *Artemisia annua* extract for optimal health

Commonly known as sweet wormwood, 'Qinghao', *Artemisia annua* has been used as a staple ingredient in Chinese traditional medicine due to its numerous therapeutic properties, with descriptions in texts from 168BC. Artemisinin, the primary component of *Artemisia annua*, has been widely used as an anti-malarial drug. Recent evidence however has proven Artemisinin to have anti-tumor activity and shown its beneficial impact on tumor cell growth regulation. Interestingly, Artemisinin has also been found to be useful in pain relief and osteoarthritis management. Its unique anti-microbial, anti-helminthic and anti-protozoal properties combined with anti-inflammatory and antioxidant benefits suggest potential applications of Artemisinin on general digestive health.

Artemisinin SAP helps regulate cancer cell growth and have anti-tumor effects. **Artemisinin SAP** can also be used to alleviate chronic pain in osteoarthritis and improve osteoarthritis, in addition to its anti-bacterial, anti-helminthic and anti-inflammatory properties.

ACTIVE INGREDIENTS

Each vegetable capsule contains:

Sweet wormwood extract 500 mg
(*Artemisia annua* herb top) 10% Artemisinin

Other ingredients : Vegetable magnesium stearate and silicon dioxide in a vegetable capsule composed of vegetable 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.

Artemisinin SAP contains 60 capsules per bottle.

DIRECTIONS FOR USE

Adults: Take 1 capsule one to two times daily or as directed by your healthcare practitioner. Consult a healthcare practitioner for use beyond 7 days. For occasional use only.

INDICATIONS

Artemisinin SAP can be used as an antimicrobial and an anti-helminthic to improve digestive disorders, and can help:

- Regulate cell growth and have an anti-tumor effect.
- In the management of osteoarthritis and alleviate pain.

CAUTIONS AND WARNINGS

Consult a healthcare practitioner if symptoms persist or worsen.

Contraindications: Do not use if you are pregnant or breastfeeding.

Known adverse reactions: May cause gastric upset, dizziness, or headache, in which case discontinue use and consult a healthcare practitioner. Hypersensitivity/allergy has been known to occur, in which case, discontinue use.

Do not use if seal is broken. Keep out of reach of children.

PURITY, CLEANLINESS, AND STABILITY

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



Scientific Advisory Panel (SAP):
adding nutraceutical research
to achieve optimum health



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INTRODUCTION

Artemisinin is the active component of the plant *Artemisia annua*, a plant native to temperate areas of Vietnam, China, Brazil, United States, East Africa, Russia and India.^[1] *Artemisia annua* has been described in traditional medicine since 168 BC and has been used primarily as an anti-malarial against resistant strains of *Plasmodium*, as well as *Toxoplasma gondii* and *Pneumocystis carinii*.^[2] Recent studies however, have provided new insights into the potential anti-tumor activity of Artemisinin.^[3] Several clinical trials support the increasing evidence of cell growth regulation and control following administration of Artemisinin.^[4, 5, 6] Interestingly, Artemisinin has proven to be useful in the management of pain and symptoms related to osteoarthritis. Artemisinin being a well-known anti-malarial upon being tested shows promising results as an anti-microbial and anti-helminth in addition to its anti-inflammatory and antioxidant properties, which could prove to be a useful therapeutic agent against digestive tract disorders.

CANCER AND TUMOR PROGRESSION

Artemisinin and various derivatives of artemisinin have been tested in clinical trials for their efficacy in regulation of tumor cell growth. In a study conducted with a derivative of dihydroartemisinin, patients suffering from abnormal cervical cell growth were administered 100 mg/day in the first week and 200 mg/day in the second week of treatment. The treatment showed a marked decrease in expression of tumor markers such as tumor suppressor protein p53, epidermal growth factor receptor (EGFR), Ki-67 antigen and von Willebrand factor (CD31), with an improvement in clinical symptoms such as pain and vaginal discharge.^[3] A randomized controlled trial administering 120 mg/day of artemisinin derivative, artesunate for 8 days in 21 day treatment cycle combined with vinorelbine and cisplatin improved the short-term survival rate and slowed the time to progression of malignant growth in lung cells.^[4] Artesunate has also shown a disease control rate of 27% in dose limiting toxicity studies, which looked at doses 8 mg/kg to 45 mg/kg given on days 1 and 8 of a 21 day cycle. The maximum tolerated dose was 18 mg/kg, with the treatment being well tolerated in 19 patients suffering from advanced solid tumor malignancies.^[6] Artemisinin derivatives have an anti-proliferative activity on malignant cell growth in colon and rectum, where one out of 9 patients post treatment developed recurring malignancy, against 6 out of 11 patients in the placebo group. Patients were administered 200 mg/day of artemisinin derivative for 14 days and based on immunohistochemistry a downregulation of Ki67 predicted a reduction of tumor markers.^[5]

Various cell culture studies have been conducted to investigate the mechanism of action of artemisinin and its derivatives on cell growth and proliferation. Artemisinin derivative induced ferroptosis by increasing lipid peroxidation and decreasing glutathione levels selectively in malignant cells.^[7] In malignant ovarian cell growth, it was found that dihydroartemisinin binds to platelet-derived growth factor receptor- α (PDGFR α), thereby reducing protein stability and inhibiting growth and metastasis in malignant cells. [8] Mechanisms of action of artemisinin on gastric and colon abnormal cell growth include increased expression of p53, inhibition of negative cell cycle regulators, increased apoptosis of malignant cells by suppression of janus kinase 2 (JAK2) and signal transducer and activator of transcription 3 (STAT3).^[9, 10] Over 300 artemisinin-specific targets have been identified via proteomics which specifically target malignant cells and increase malignant cell death.^[11]

PAIN MANAGEMENT

Recent studies have explored the use of Artemisinin in management of pain and inflammation in osteoarthritis. *Artemisia annua* extract was administered to 42 patients at doses of 150 mg twice daily or 300 mg twice daily for 12 weeks. Patients with lower artemisinin doses showed an improvement in osteoarthritis index and visual analog for pain, indicating the potential analgesic and anti-inflammatory

activity of artemisinin.^[12] A follow up to this study showed maintained improvement in these patients with artemisinin treatment for further six months, and the treatment was well tolerated for up to 9 months.^[13]

DIGESTIVE SUPPORT

Apart from the ability of *Artemisia annua* to regulate cell growth and its anti-malarial properties, recent evidence suggests its beneficial effects on the digestive tract. The *Artemisia annua* plant apart from artemisinin, contains other bioactives such as sesquiterpene lactones, which could have antihelminthic properties, with less risk of toxicity to mammals.^[14] Several clinical trials conducted with an artemisinin derivative point to the beneficial antihelminthic properties of artemisinin as well. In a double blind, randomized controlled trial providing a combination therapy of artemisinin derivative artemether and praziquantel, administration of 40 mg/kg body weight artemether twice four weeks apart, followed by 6 mg/kg dose every 3 weeks for 5 cycles reduced prevalence of infection by half in 913 children.^[15] Several other studies have shown that artemisinin plays a supportive role in management of several forms of schistosomiasis.^[16, 17, 18] *In vitro* studies have shown that artemisinin inhibits calcium dependent ATPase activity of *Trypanosoma cruzi* membranes, thus inhibiting growth of cultured *T.cruzi* and *Trypanosoma brucei rhodesiense*.^[19]

In addition to their antihelminthic properties, artemisinin derivatives have shown potent anti-fungal activity when tested against *Candida albicans* and *Cryptococcus neoformans*.^[20] Animal studies have shown artemisinin administration to have anti-leishmanial activity, as well as induction of a host protective response.^[21, 22] Artemisinin and its precursor isolated from *Artemisia annua* inhibited the growth of gram positive and gram negative bacteria, with antimicrobial activity comparable to that of antibiotic streptomycin.^[23] Additionally, *Artemisia annua* extracts were shown to have anti-inflammatory, antioxidant, and antimicrobial activity against periodontopathic microorganisms.^[24]

REFERENCES

- Lapkin, AA, et al. Comparative assessment of technologies for extraction of Artemisinin. J Nat Prod. 2006 Nov; 69(11):1653-64.
- Efferth, T, et al. Wilmer Schwabe Award 2006: antiplasmodial and antitumoractivity of artemisinin-from bench to bedside. Planta Med. 2007 Apr; 73(4):299-309.
- Jansen, FH, et al. First study of oral Artemimol-R in advanced cervical cancer: clinical benefit, tolerability and tumor markers. Anticancer Res. 2011 Dec; 31(12):4417-22.
- Zhang, ZY, et al. Artesunate combined with vinorelbine plus cisplatin in treatment of advanced non-small cell lung cancer: a randomized controlled trial. Zhong Xi Yi Jie He Xue Bao. 2008 Feb;6(2):134-8.
- Krishna, S, et al. A randomized, double-blind, placebo-controlled pilot study of oral Artesunate therapy for colorectal cancer. EBioMedicine. 2015 Jan;2(1):82-90.
- Deeken, JF, et al. A phase I study of intravenous artesunate in patients with advanced solid tumor malignancies. Cancer Chemother Pharmacol. 2018 Feb;71.
- Roh, JL, et al. Nrf2 inhibition reverses the resistance of cisplatin-resistant head and neck cancer cells to artesunate-induced ferroptosis. Redox Biol. 2017 Apr;11:254-262.
- Xiaoguang, L, et al. Dihydroartemisinin selectively inhibits PDGFR α -positive ovarian cancer growth and metastasis through inducing degradation of PDGFR α protein. Cell Discov. 2017; 3:17042.
- Zhang, HT, et al. Artemisinin inhibits gastric cancer cell proliferation through upregulation of p53. Tumour Biol. 2014; 35(2):1403-9.
- Wang, D, et al. Dihydroartemisinin increases apoptosis of colon cancer cells through targeting Janus kinase 2/signal transducer and activator of transcription 3 signaling. Oncol Lett. 2018; 15(2):1949-1954.
- Wang, J, et al. Mechanistic investigation of the specific anticancer property of Artemisinin and its combination with Aminolevulinic acid for enhanced anticancer cancer activity. ACS Cent Sci. 2017; 3(7):743-750.
- Stebbing, S, et al. A pilot randomized, placebo-controlled clinical trial to investigate the efficacy and safety of an extract of *Artemisia annua* administered over 12 weeks, for managing pain, stiffness and functional limitation associated with osteoarthritis of the hip and knee. Clin Rheumatol. 2016 Jul;35(7):1829-36.
- Hunt, S, et al. An open label six-month extension study to investigate the safety and efficacy of an extract of *Artemisia annua* for managing pain, stiffness and functional limitation associated with osteoarthritis of the hip and knee. N Z Med J. 2016 Oct;129(1444):97-102.
- Kerboeuf, D, et al. Flavonoids and related compounds in parasitic disease control. Mini Rev Med Chem. 2008; Feb; 8(2):116-28.
- Elmorshedy, H, et al. Prophylactic effect of artemether on human schistosomiasis mansoni among Egyptian children: A randomized controlled trial. Acta Trop. 2016; Jun, 158:52-8.
- Inyang-Etoh, PC, et al. Efficacy of a combination of praziquantel and artesunate in the treatment of urinary schistosomiasis in Nigeria. Trans R Soc Trop Med Hyg. 2009; Jan, 103(1):38-44.
- Li, YS, et al. A double-blind field trial on the effects of artemether on *Schistosoma japonicum* infection in a highly endemic focus in southern China. Acta Trop. 2005; Nov-Dec, 96(2-3):184-90.
- N'Goran, EK, et al. Randomized, double-blind, placebo-controlled trial of oral artemether for the prevention of patent *Schistosoma haematobium* infections. Am J Trop Med Hyg. 2003; Jan, 68(1):24-32.
- Mishina, YV, et al. Artemisinins inhibit *Trypanosoma cruzi* and *Trypanosoma brucei rhodesiense* in vitro growth. Antimicrob Agents Chemother. 2007 May; 51(5):1852-4.
- Galal, AM, et al. Antifungal activity of artemisinin derivatives. J Nat Prod. 2005 Aug; 68(8):1274-6.
- Sen, R, et al. Efficacy of Artemisinin in experimental visceral leishmaniasis. Int J Antimicrob Agents. 2010 Jul; 36(1):43-9.
- Wang, MY, et al. Therapeutic efficacy of artemisinin-loaded nanoparticles in experimental visceral leishmaniasis. Colloids Surf B Biointerfaces. 2015 Jun; 130:215-21.
- Kim, WS, et al. Antimicrobial activity of artemisinin and precursor derived from in vitro plantlets of *Artemisia annua* L. Biomed Res Int. 2014 2014;215872.
- Kim, WS, et al. Anti-inflammatory, antioxidant, and antimicrobial effects of Artemisinin extracts from *Artemisia annua* L. Korean J Physiol Pharmacol. 2015 Jan;19(1):21-7.