

## 10 Reasons to Add Andrographis to Your Medicine Cabinet

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*Andrographis has the potential to replace a whole host of pharmaceutical drugs, and to improve autoimmune disorders, cancer, metabolic disease, and infection*

Although it is native to China, the small shrub known as *Andrographis paniculata* Nees is revered in traditional Indian folk medicine where it goes by the namesake kalmegh (1). Belonging to the Acanthaceae family, the so-called king of bitters exhibits broad-spectrum medicinal activity in the scientific literature, rendering it an essential tool to harness from nature's pharmacopeia. Widely cultivated in southern Asia, andrographis is regarded as an ethno-pharmacological treasure trove, given its myriad therapeutic effects.

Growing "wild as weeds by the roadsides" in India, Indonesia, Java, Malaysia, Pakistan, and Sri Lanka (2), its stems and leaves contain a bitter taste from which its nickname "king of bitters" is derived (3). Growing erect "in moist shady places with glabrous leaves and white flowers with rose-purple spots on the petals," its aerial leaves and stems are used for medicinal purposes (2).

The therapeutic efficacy of andrographis is attributed to its polyphenol, flavonoid, and diterpene lactone content, the last of which are bioactive constituents which mediate the anti-inflammatory effects of andrographis through their collective action on the adrenal glands (1, 4, 5). In particular, the diterpene lactone andrographolide "exhibits a extraordinarily vast range of biological activities" (6). Most prominently, however, andrographis is known for its antimicrobial properties, rendering it a potent natural tool against infection (1).

## 1. Anti-Viral

Scandinavian countries commonly use andrographis for cold prevention and treatment (5). A double-blind, placebo-controlled study of fifty patients using standardized Andrographis paniculata extract showed that the herb significantly decreased the duration and subjective severity of the common cold (1). Studies have also revealed that standardized andrographis preparations significantly improve signs and symptoms of both the common cold and sinusitis relative to placebo (1). In vitro investigations exemplify that aqueous and ethanolic extracts of Andrographis are also effective against highly pathogenic avian influenza viruses (7).

Impressively, systematic literature searches have concluded that andrographis is a safe and effective agent for the treatment of upper respiratory tract infections (8). In fact, andrographis standardized to andrographolide alleviates several symptoms of uncomplicated upper respiratory tract infections including muscular pain, earache, cough, sore throat, and headache (9, 10).

## 2. Anti-Fever

Andrographis has been venerated as a fever-reducing herb since time immemorial, used by populations in the south Asian sub-continent as a potent anti-pyretic (11). In Traditional Chinese Medicine (TCM), andrographis is known as a cold property herb, and is used to expel excess heat from the body (12). Andrographis restores body temperature to normal range in under forty-eight hours (1). Modern science is confirming its anti-fever effects, as andrographis has been shown to be equivalent to paracetamol, the analgesic drug also known as acetaminophen, in fever reduction (13).

## 3. Anti-Parasitic

Xanthone compounds isolated from the roots of Andrographis paniculata demonstrate anti-parasitic activity. In addition, andrographis exhibits efficacy against roundworms and threadworms such as *Dipetalonema reconditum*, reducing the population of larvae in blood by more than 85% (14). Another study showed that alcohol extracts of the andrographis rhizome possess antihelmintic activity against the large human roundworm *Ascaris lumbricoides*, one of the most common parasitic worms in humans that infects over a billion people worldwide (15).

Andrographis may be a viable natural alternative to conventional treatments, since some of the principal pharmaceuticals used to treat parasite infections such as trypanosomiasis and leishmaniasis can lead to severe cardiac and renal toxicity and the development of drug resistance (16).

## 4. Anti-Malarial

In 2012, malaria accounted for over a million deaths globally and was endemic in over a hundred countries, with the poorest countries disproportionately afflicted (17). Ethnographic

studies discuss how the traditional Kadazan tribal group of east Malaysia boil the leaves of the andrographis plant in water and then consume the infusion as an herbal remedy for this mosquito-borne protozoan (3). Herbal remedies for malaria are important, since Plasmodium falciparum, one of the microorganisms responsible for malaria, has become resistant to chloroquine and other drugs which are the standard of care for this tropical disease (18).

Methanolic and chloroform extracts of andrographis show significant activity against malaria (3, 11). The means by which andrographis exerts its anti-malarial effects appear to be through up-regulation of the antioxidant defense enzyme, superoxide dismutase (SOD) (19).

## **5. Anti-Cancer**

Preliminary in vitro examinations show that andrographolide, one of the primary bioactive constituents of andrographis, “presents a strong candidature as a therapeutic anticancer pharmacophore as it exhibits a dual property, acting both directly and indirectly on the cancer cells” (12). In numerous cancer cell lines including those that are drug-resistant, andrographis induces cell cycle arrest or apoptosis, stimulating the tumor cell to commit suicide through extrinsic death receptor pathways (12, 20).

For instance, andrographis is cytotoxic (cell-killing) against cell lines of lymphocytic leukemia and human epidermoid leukemia (21) and almost completely inhibits replication of human colorectal carcinoma cells (22). In another study on breast, cervical, and hepatoma cancer cell lines, treatment with andrographolide increased levels of caspase proteins by eight-fold, which are known to be involved in inducing cell suicide (23). Another anti-cancer mechanism of andrographis is that it increases levels of a protein known as TRAIL, or tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) related apoptosis inducing ligand, an anti-cancer agent which can preferentially target cancer cells over healthy cells (24, 25).

Not only does andrographis suppress cancer cell division and induce programmed cell death in cancer cells, but it also promotes anti-angiogenic effects in neoplastic tissues, which prevents the creation and growth of tumor-specific blood vessels that feed the tumor (Varma et al., 2009). By reducing levels of angiogenic factors such as vascular endothelial growth factor (VEGF) and nitric oxide (NO), andrographis prevents the sprouting of new capillaries to supply the tumor without harming the pre-existing vasculature (12). Andrographolide treatment also significantly decreases the expression of proteins associated with an aggressive phenotype in many cancers (12). Lastly, andrographolide can induce differentiation of multiplying cancer cells into specialized non-cancer cells (26).

## **6. Anti-Diarrheal**

Due to intermittent water supply in developing countries, waterborne diarrhea illnesses are still associated with significant morbidity and mortality (27). In fact, diarrhea is the second leading cause of death in children under five years of age (28). Traditionally, andrographis has been used by indigenous cultures as a folk remedy for bacterial dysentery and acute diarrhea, and

has even been shown to be effective for each of these afflictions in a double-blind study (29). Andrographis has moreover proven to be effective against *Escherichia coli* (E.coli)-associated diarrhea and to have comparable efficacy to the most common antidiarrheal drug loperamide (2).

## **7. Immunomodulatory**

Andrographis can up-regulate both the first-line, non-specific defenses of the innate immune system and the antigen-specific, targeted responses of the adaptive immune system, actions which partly mediate its anti-infectious and anti-oncogenic effects. By enhancing the activity of the immune system, andrographis increases the number and efficacy of our own cancer-killing lymphocytes and natural killer (NK) cells and improves clinical outcomes when taken in late-stage cancer (30, 31). Preliminary trials even show that andrographis increases the level of CD4(+) T cells in HIV infected individuals, an immune cell subtype which is depleted in this condition (32).

Not only that, but both the plant extract of andrographis and andrographolide in particular exhibit potent anti-inflammatory effects, preventing the formation of free radicals called reactive oxygen species (ROS). In fact, one of the metabolites of andrographolide is reported to have identical chemical composition to the anti-inflammatory drug Lian-bi-zhi which is used in clinical practice in China (33). Most importantly, andrographolide interferes with the binding of nuclear factor kappa B (NF- $\kappa$ B) to our genetic material, and therefore prevents expression of the downstream inflammatory cascade governed by this master transcription factor (12). NF- $\kappa$ B is perhaps the best characterized pro-inflammatory mediator, as it recruits immune cells and induces synthesis of inflammation-generating cellular messengers known as chemokine and cytokines (34).

Because dysregulation in NF- $\kappa$ B signaling contributes to chronic inflammation and autoimmune diseases such as type one diabetes, multiple sclerosis, inflammatory bowel disease, and systemic lupus erythematosus (35), using andrographis to reduce NF- $\kappa$ B signaling may be therapeutic in these conditions.

## **8. Liver Support**

Andrographis is officially listed in the Indian Pharmacopoeia as an ingredient in twenty-six traditional Ayurvedic formulations for maladies of the liver (12). This is consistent with the fact that administration of andrographis prevents liver damage secondary to chemical liver toxins including hexachlorocyclohexane, carbontetrachloride, galactosamine, and paracetamol in animal studies (2).

Researchers note that andrographolide confers protection against a wide range of hepatotoxins, owing to its ability to augment antioxidant defenses which neutralize liver-damaging oxidants (12). Andrographis also promotes high levels of glutathione, the master antioxidant which is necessary to remove chemical toxins and mitigate toxin-induced damage

(36). Hepatitis-infected guinea pigs administered andrographis show dramatic improvement, including recovery from jaundice, restoration of liver function tests, and reduction of fever (37). Remarkably, the hepatoprotective effect of andrographolide have been found to be equivalent to silymarin, the active principle in milk thistle (38, 39).

## **9. Cardiometabolic Benefits**

In rat models of diabetes, andrographolide treatment improves diabetic hyperglycemia, oxidative stress, and insulin deficiency in a dose-dependent manner, with a higher dose eliciting a greater benefit (40). Thus, andrographis may be useful in both diabetes and other conditions with an element of insulin resistance such as polycystic ovarian syndrome (PCOS). Because of the potent hypolipidemic effects of andrographis, it may also be a viable adjunctive approach for metabolic syndrome (41). A high dose of andrographis was shown to significantly reduce triglyceride levels to the same extent as treatment with gemfibrozil, a fibrate drug used to lower lipid levels (41).

Andrographis may also have utility in cardiovascular disease, as it decreases damage to the heart muscle and activates fibrinolysis, or the break down of blood clots, after animal models of heart attack (2). Research also indicates that this botanical agent produces blood pressure lowering effects by relaxing the smooth muscle wall of blood vessels, suggesting its application in hypertension (2).

## **10. Autoimmune Disease Benefits**

Rates of autoimmune disorders such as inflammatory bowel disease (IBD) are increasing at epidemic proportions, yet the pharmaceutical standard of care poses significant toxicity (42). It merits exploration, then, that andrographis has been used as a treatment for inflammatory bowel disease in Asian countries (43). In a mouse model of colitis, the animals treated with Andrographis exhibited extremely mild intestinal inflammation and had significant decreases in their expression of inflammatory markers (43).

More promising, however, is that a recent randomized, double-blind, placebo-controlled trial elucidated that a proprietary extract of andrographis had comparable efficacy to mesalazine in treating ulcerative colitis, suggesting that andrographis may be a safe and effective alternative to the pharmaceutical standard of care, mesalazine (43). In another study, andrographis was well-tolerated and produced significant clinical responses in subjects with mild-to-moderate ulcerative colitis (44).

Rheumatoid arthritis (RA), another autoimmune condition of the joints, can progress into joint deformity and disablement despite pharmacologic treatment with nonsteroidal anti-inflammatory drugs, corticosteroids, and disease-modifying antirheumatic drugs (DMARDs) (45). When co-administered with the pharmaceutical agent etoricoxib in a rat model, andrographis extract demonstrated synergistic anti-arthritic activity (46). Andrographis has likewise been shown to diminish tender and swollen joints of rheumatoid arthritis patients in a

prospective, randomized, double-blind, placebo-controlled trial (45) The herb likewise diminished levels of rheumatoid factor (Rf), immunoglobulin A (IgA), and C4, immunological parameters associated with RA (45).

The gut-healing effects of andrographis may extend to autoimmune diseases more broadly, since a single dose of andrographis produces activation of brush-border disaccharidases such as maltase, lactase, and sucrase in three regions of the small intestine (47). Many of these digestive enzymes are compromised in celiac disease due to atrophy of the small intestinal villi, and their production may be impaired in other autoimmune disorders as well. By promoting proper degradation and assimilation of foodstuffs, the constant antigenic stimulation of the immune system by improperly digested food can be reduced, which quenches the fires of autoimmunity.

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