



# Andrographis

*Andrographis paniculata*

## Common names

King of bitters, Indian echinacea, chiretta

## Family

*Acanthaceae* (acanthus)

## Part used

Aerial parts

## Background and traditional uses

Andrographis is an erect annual with four-angled branches that grows between 30-110cm in height. It has simple, glabrous, lanceolate leaves that grow up to 8cm long and 2.5cm wide. Its flowers are small and white, borne in panicles or terminal racemes that give way to linear-oblong seed pods. It is found commonly growing in the wild, in the plains and forest undergrowths of India, from the base of the Himalayas towards Sri Lanka in the south.<sup>1</sup>

Ayurvedic texts refer to andrographis as the 'king of bitters' for its ubiquitous use as a digestive stimulant, indicated for a wide range of health issues thought to originate in the gut. It is believed to be included in at least half of the combination remedies used in the Ayurvedic tradition. In traditional Chinese medicine (TCM), andrographis is considered to be an energetically 'cold' medicine, used to dispel heat and toxicity in the lungs, throat and urinary tract.<sup>2</sup> TCM also uses andrographis to dry systemic 'dampness' and ease diarrhoea.<sup>3</sup> Because it grows so abundantly, andrographis has widespread use as a household remedy throughout its native habitats, particularly in the treatment of the common cold.<sup>4</sup>

## Actions

### Primary:<sup>4</sup>

- Immune modulating
- Anticancer
- Antimicrobial
- Antimalarial
- Cardioprotective
- Hypoglycaemic
- Hepatoprotective
- Choleric
- Bitter tonic
- Anti-inflammatory
- Antipyretic
- Antiplatelet
- Antithrombotic

### Secondary:<sup>4</sup>

- Antioxidant
- Vulnerary

## Applications and indications

- The World Health Organization (WHO) recognises the use of andrographis for bacillary dysentery, bronchitis, burns, carbuncles, chickenpox, colic, colitis, common cold, convalescence, coughs, dyspepsia, eczema, fevers, hepatitis, malaria, mouth ulcers, otitis media, pelvic inflammatory disease, sores, tuberculosis, vaginitis, and venomous snake bites.<sup>5</sup>
- Other indications include pharyngotonsillitis and rheumatoid arthritis.<sup>4</sup>

## Active constituents and pharmacodynamics

The main active constituents of andrographis are considered to be the **bitter diterpene lactones**, a group known as **andrographolides**.<sup>4,5</sup> The group includes andrographolide, deoxyandrographolide, 11,12-didehydro-14-deoxyandrographolide, neoandrographolide, andrographiside, deoxyandrographiside and andropanoside.<sup>5</sup> Andrographis also contains a spectrum of diterpenoid glycosides, diterpene dimers, flavonoids and xanthenes.<sup>6</sup>

Several *in vivo* studies suggest that andrographolides are easily absorbed with up to 91% bioavailability at small doses (equivalent to an upper limit of 1mg/kilogram of andrographolides), with bioavailability progressively reducing at higher doses (to just 21.4% at a dose of 10mg/kilogram). This information supports the reputation of andrographis as having a high toxicity threshold and wide safety buffer zone.<sup>7</sup>

## Summary of clinical evidence

### Immunity

In a randomised, double-blind, placebo-controlled study, 158 adult participants were administered either a dried extract of andrographis or placebo and instructions for dosing daily from the onset of a common cold.<sup>8</sup> Symptoms were evaluated at days two and four after onset and showed that andrographis was significantly effective in reducing headaches, tiredness, earaches, sleeplessness, sore throat, nasal secretion, phlegm, frequency and intensity of cough when compared to placebo. No adverse reactions were seen in the study group.<sup>8</sup>

One randomised, controlled trial recruited 152 patients with pharyngotonsillitis to compare andrographis to paracetamol for improving relief of fever and sore throat.<sup>9</sup> The patients received a low or high dose of andrographis (3g/day or 6g/day respectively), or paracetamol (3.9g/day) for seven days. Efficacy was evaluated in terms of disappeared, improved, not improved or worse symptoms of fever and sore throat. On days three and seven, assessments were made, and there were significant differences in favour of high dose andrographis and paracetamol over low dose andrographis. At day three, high dose andrographis had greater scores for eradication of fever than paracetamol (68.1% and 67.3% respectively) and achieved comparable results for reducing sore throat (29.7% and 30.6% respectively). This study shows that andrographis has the potential to be a substitute for paracetamol in the treatment of pharyngotonsillitis symptoms.<sup>9</sup>

In a randomised, double-blind, placebo-controlled trial, 223 patients with uncomplicated upper respiratory tract infections were split into two groups and administered either KalmCold™ (each capsule containing 100mg of andrographis and 200 mg of micro crystalline cellulose) at a dose of 200mg/day of andrographis (two capsules) or placebo.<sup>10</sup>

Participants were assessed using a self-evaluation tool that measured cough, expectoration, nasal discharge, headache, fever, sore throat, earache, fatigue and sleep disturbances. The mean symptoms scores for both groups showed very similar decreasing trends for days one to three, but symptoms were unchanged in the placebo group for the remaining two days of the study. The study group, on the other hand, showed significant continued symptom improvement for the remainder of the treatment period.<sup>10</sup>

One systematic review highlighted the benefits of andrographis for the symptomatic relief of acute respiratory tract infections (ARTI) in adults and children.<sup>11</sup> The study reviewed 33 randomised, controlled trials, and found that andrographis improved coughs and sore throats when compared with placebos. It showed statistically significant results in improving overall ARTIs when compared to placebo, usual care or other herbal therapies while also shortening the duration of cough, sore throat and sick leave/time to resolution when compared to usual care. No major adverse events were reported; supporting the use of andrographis as a sole or adjuvant therapy to treating ARTIs with low risk of side effects.<sup>11</sup>

### Ulcerative colitis

In an eight-week comparative, randomised, double-blind, multi-centre trial, 120 participants with mild to moderately active ulcerative colitis were split into two groups and received either 1.2g/day of HMPL-004, a standardised andrographis extract, or 4.5g/day of a slow-release mesalazine medication.<sup>12</sup> At the conclusion of the trial, both groups were shown to have experienced similar rehabilitative effects as a result of their treatments, leading researchers to conclude that andrographis may be an efficacious in alleviating the symptoms of ulcerative colitis.<sup>12</sup>

A follow-up randomised, double-blind, placebo-controlled trial recruited 224 adults with mild to moderate ulcerative colitis and split them into three groups, who received either placebo or 1.2g or 1.8g of the same andrographis extract, HMPL-004, for eight weeks.<sup>13</sup> At the conclusion of the trial, 38% of the andrographis groups were in clinical remission compared to 25% in the placebo group. Interestingly, adverse events developed in 60% of the placebo group compared to 53% of the combined study groups. Additionally, the higher dose of andrographis was determined to be more clinically effective than the lower dose.<sup>13</sup>

### Rheumatoid arthritis

In a prospective, randomised, double-blind and placebo controlled study, 60 women with rheumatoid arthritis were treated with either placebo or Paractin (an andrographis extract standardised to contain 30mg andrographolides) three times daily.<sup>14</sup> At the conclusion of the 14-week trial, a significant reduction in tenderness and swelling of joints was experienced by the study group when compared to placebo.<sup>14</sup>

## Cancer

Treatment of cancer cells *in vitro* with andrographalides has been associated with the upregulation of Death-Receptor 4 (DR4), thus enhancing TRAIL-mediated apoptosis.<sup>17</sup> TRAIL is a selectively tumour cytotoxic agent from the immune system and a therapeutic target in cancer research.<sup>15</sup> Andrographolide has also been shown to have antiproliferative effects in leukaemic cells at regular concentrations, with apoptosis being induced at higher concentrations.<sup>16</sup> Andrographolides have also been shown to inhibit the proliferation of ovarian cancer, prostate cancer, CNS cancer and lung cancer cells *in vitro*.<sup>17</sup>

## Diabetes

In an *in vivo* experiment, mice with alloxan-induced diabetes were treated with an andrographis extract, which was shown to lower blood glucose, increase insulin production, prevent the dysfunction and loss of beta cells and stimulate transport proteins.<sup>18</sup> The hypoglycaemic and cell protective effects of the extract led the researchers to conclude that andrographis could potentially be used in the treatment of diabetes.<sup>18</sup>

## Dosage summary

**Liquid extract (1:2):** 20-40mL weekly<sup>4,19</sup>

**Dried herb equivalent:** 5g three times daily in divided doses<sup>4,18</sup>

## Safety information

Andrographis appears to have a very low toxicity risk.<sup>4</sup> The lack of controlled studies over a significant time period means that interactions and contraindications are theoretical rather than evidential:

- Avoid prescribing in pregnancy and lactation as safety parameters are unknown.<sup>4</sup> Avoid prescription for patients with known *Acanthaceae* plant family allergies.<sup>4</sup>
- Because andrographis appears to have antiplatelet and anticoagulation activity, it is best avoided for patients taking antiplatelet or anticoagulation drugs.<sup>4</sup>
- Andrographis may theoretically interact beneficially with hepatotoxic drugs due to its hepatoprotective effects.<sup>4</sup>
- Use with caution for patients taking immunosuppressant therapies as andrographis appears to stimulate immunity.<sup>4</sup>
- Andrographis may potentiate the effects of barbituates, hypoglycaemic agents and drugs metabolised by the cytochrome P450 system – prescribe with care.<sup>4</sup>

## References

1. Caldecott T. Ayurveda: the divine science of life. Philadelphia: Mosby Elsevier, 2006.
2. Bensky D, Gamble A, Kaptchuk TJ, et al. Chinese herbal medicine: materia medica. Seattle: Eastland Press, 1993.
3. Chen JK, Chen TT, Crampton L. Chinese medical herbology and pharmacology. City of Industry: Art of Medicine Press, 2004.
4. Braun L, Cohen M. Herbs and natural supplements: an evidence-based guide, vol. 2, 4th ed. Sydney: Elsevier, 2014.
5. World Health Organization (WHO). *Herba andrographidis*. Monographs on selected medicinal plants, vol. 2. Geneva: WHO, 2004.
6. Joselin J, Jeeva S. *Andrographis paniculata*: a review of its traditional uses, phytochemistry and pharmacology. *Med Aromat Plants* 2014;3:169.
7. Pan Y, Abd-Rashid BA, Ismail Z, et al. *In vitro* modulatory effects of *Andrographis paniculata*, *Centella asiatica* and *Orthosiphon stamineus* on cytochrome P450 2C19 (CYP2C19). *J Ethnopharmacol* 2011;133(2):881-887.
8. Cáceres, DD, Hancke JL, Burgos RA, et al. Use of visual analogue scale measurements (VAS) to assess the effectiveness of standardized *Andrographis paniculata* extract SHA-10 in reducing the symptoms of common cold - a randomized double blind-placebo study. *Phytomedicine* 1999;6(4):217-223.
9. Poolsup N, Suthisisang C, Prathanturug S, et al. *Andrographis paniculata* in the symptomatic treatment of uncomplicated upper respiratory tract infection: systematic review of randomized controlled trials. *J Clin Pharm Ther* 2004;29:37-45.
10. Saxena RC, Singh R, Kumar P, et al. A randomized double blind placebo controlled clinical evaluation of extract of *Andrographis paniculata* (KalmCold) in patients with uncomplicated upper respiratory tract infection. *Phytomedicine* 2010;17(3-4):178-185.
11. Hu XY, Wu RH, Logue M, et al. *Andrographis paniculata* (Chuan Xin Lian) for symptomatic relief of acute respiratory tract infections in adults and children: a systematic review and meta-analysis. *PLoS One* 2017;12(8):e0181780.
12. Tang T, Targan SR, Li ZS, et al. Randomised clinical trial: herbal extract HMPL-004 in active ulcerative colitis - a double-blind comparison with sustained release mesalazine. *Aliment Pharmacol Ther* 2010;33(2):194-202.
13. Sandborn WJ, Targan SR, Byers VS, et al. *Andrographis paniculata* extract (HMPL-004) for active ulcerative colitis. *Am J Gastroenterol* 2013;108(1):90-98.
14. Burgos RA, Hancke JL, Bertoglio JC, et al. Efficacy of an *Andrographis paniculata* composition for the relief of rheumatoid arthritis symptoms: a prospective randomized placebo-controlled trial. *Clin Rheum* 2009;28(8):931-946.
15. Zhou J, Lu GD, Ong CS, et al. 2008. Andrographolide sensitizes cancer cells to TRAIL-induced apoptosis via p53-mediated death receptor 4 up-regulation. *Mol Cancer Ther* 2008;7(7):2170-2180.
16. Cheung HY, Cheung SH, Li J, et al. Andrographolide isolated from *Andrographis paniculata* induces cell cycle arrest and mitochondrial-mediated apoptosis in human leukemic HL-60 cells. *Planta Med* 2005;71(12):1106-1111.
17. Rajagopal S, Kumar RA, Deevi DS, et al. Andrographolide, a potential cancer therapeutic agent isolated from *Andrographis paniculata*. *J Exp Ther Oncol* 2003;3(3):147-158.
18. Zhang Z, Jiang J, Yu P, et al. Hypoglycemic and beta cell protective effects of andrographolide analogue for diabetes treatment. *J Transl Med* 2009;7(1):62.
19. Indian Drug Manufacturer's Association (IDMA). *Indian Herbal Pharmacopeia* (rev ed). Mumbai: IDMA, 2002.



