



DOSSIER · SUBSTANCE

Andrographis Paniculata

Andrographis paniculata is investigated as a plant, as an extract and via its main active ingredient andrographolide. The evaluated literature is predominantly basic and cell biological; controlled studies in humans exist only for a few questions, and they focus on COVID-19. It is striking that the most frequently cited works are reviews and cell studies, not the clinical trials.

349

STUDIES IN
TOTAL

45

IN HUMANS

6

OF WHICH
CONTROLLED

36

IN ANIMALS

75

IN THE LAB

Figures from the IHR study database · Last updated 2026-10-15

How to Read This Dossier

ESTABLISHED

measured in humans, with a comparison group

PLAUSIBLE

supported by mechanism, animal studies or observation

HYPOTHESIS

a likely connection that still needs to be tested

Andrographis Paniculata at a Glance

ORIGIN:
Andrographis paniculata is a plant listed in the literature under the botanical name Andrographis paniculata (Burm. f.) Nees and in the spelling (Burm. f.) Wall. ex Nees. It is investigated both as a whole and as an extract; the principal constituent is regarded as andrographolide, a diterpene lactone that is frequently examined on its own. Work on andrographolide derivatives, that is, modified molecules, is also available.

EVIDENCE BASE:
349 evaluated studies · 6 controlled human studies · 39 observational studies · 36 review articles · 36 animal studies · 62 cell-culture studies

- STRONGEST EVIDENCE:**
- **Viral infections:** In a double-blind randomised study [62] an ethanolic extract containing 60 mg andrographolide three times daily for five days alleviated headache on day 1 and loss of smell on day 2 more than placebo.
 - **Viral infections:** 80.7 % of 165 treated individuals achieved complete recovery after five-day administration.
 - **Safety:** The most frequent adverse effect was mild diarrhoea; hepatic or renal toxicity was not observed.
 - **Viral infections:** The PK/PD study [58] administered aqueous-extract capsules containing 30 mg andrographolide every 8 hours (90 mg/day) for 5 days and reported a reduction in viral load of –2.96 log10.
 - **Safety:** The meta-analysis [61] evaluated 262 studies of andrographolide-derivative injections, that is, modified molecules rather than the plant material itself; among 9 490 users of these injections, 383 (4.04 %) reported adverse drug reactions.
 - **Viral infections:** The review [59] cites randomised controlled trials in which A. paniculata was superior to placebo in reducing the severity of upper-respiratory-tract symptoms, especially in the early treatment phase.

- LIMITATIONS:**
- The controlled human studies are predominantly designed as pilot trials, sometimes as add-on therapy, and focus on COVID-19.
 - Preparations differ between the studies; the oral bioavailability of the diterpene lactones is limited, so findings cannot be transferred directly.
 - The material contains no studies on the intestinal microbiome; an investigation linking A. paniculata administration with microbial endpoints remains to be conducted.

CLASSIFICATION:
Andrographis paniculata is tested in humans mainly for safety and COVID-19; the mechanistic rationale rests predominantly on preclinical work.

1. What Andrographis Paniculata Is

Andrographis paniculata is a plant listed in the literature under the botanical name Andrographis paniculata (Burm. f.) Nees and in the spelling (Burm. f.) Wall. ex Nees. It is investigated both as the whole plant and as an extract; some of the studies examine individual preparations such as standardised formulations or capsules containing aqueous extract. The principal constituent is regarded as **andrographolide**, a **diterpene lactone** that is frequently tested individually in research. Work on **andrographolide derivatives**, that is, modified molecules that are sometimes treated in the literature as independent medicinal substances, is also available. These three levels—plant, extract, single substance or derivative—are often discussed together in reviews, although they represent different preparations.

One point is decisive for the evaluation of all studies: the **oral bioavailability of the diterpene lactones**. A dedicated review addresses how formulations alter the uptake of diterpene lactones, and another study examines the pharmacokinetic-pharmacodynamic properties and safety of standardised aqueous-extract capsules in patients with mild disease courses. It follows that results cannot be transferred directly between preparations: what was measured for one standardised product does not automatically apply to another extract or to the isolated single substance. In addition there is the separation between **laboratory finding and human application**. Most studies measure in cell cultures or in animals; observational and controlled human studies form only a small part of the material and address different questions from the mechanistic literature.

2. What the Studies Show in Detail

The key human studies and the most important reviews—by therapeutic area, with population, duration, preparation, endpoint and result as reported in the original papers. Numbers appear only where the study states them.

Distribution of the **controlled human studies** by therapeutic area—the numbers are not additive because one study may be assigned to several areas:

Therapeutic Area	Controlled Studies
Safety and tolerability	6
Viral infections	4
Inflammatory processes	3
Immune system	3
Uptake and bioavailability	1

Therapeutic Area	Controlled Studies
Intestine and microbiome	1
Skin	1

Viral Infections

The review article [59] summarises that *Andrographis paniculata* has been used as adjunctive treatment for COVID-19 in several Asian countries. It places the antiviral, anti-inflammatory, immunomodulatory and antipyretic properties of the species and its constituents in context. According to these data, in-silico and in-vitro studies demonstrated activity of the active substances against 3CLpro and the human hACE2 protein as well as inhibition of the production of infectious virions. At the clinical level the work refers to randomised controlled trials in which *A. paniculata* alone or in combination was superior to placebo in reducing the severity of upper-respiratory-tract symptoms, especially in the early treatment phase, without serious adverse effects. The work is a summary; the clinical statements rest on the studies cited therein.

In a computational study [11] a “host response signature network” was constructed from 36 genes induced by SARS-CoV-2 and associated with the cytokine storm. Molecular docking showed binding of andrographolide to TNF and covalent binding to NFkB1 proteins of the TNF signalling pathway. **Hypothesis:** The authors therefore infer that andrographolide could block the TNF-induced NFkB1 signalling pathway. This is an in-silico investigation without patients. The review article [66] lists for andrographolide and its derivatives anticarcinogenic, antibacterial, anti-inflammatory, antiviral, antifibrotic, anti-adipose, immunomodulatory and blood-glucose-lowering activities and describes how structural modifications have yielded derivatives with improved bioavailability and suitability as drug substances.

The mean number of days to symptom reduction differed significantly between group A ($p<0.0001$). The abstract breaks off at this point; data on group B and on further endpoints are not contained in the text provided.

The systematic review with meta-analysis [63] searched PubMed, EMBASE, CENTRAL and EBSCO Open Dissertations from January 2020 to October 2024 for randomised controlled trials that compared single-herb *A. paniculata* products with antiviral medicines or supportive care in mild to moderate COVID-19; endpoints included clinical recovery, resolution of fever or cough, as well as CRP and IL-6. Six RCTs with 660 adults aged 18 to 60 years were included, risk of bias was assessed with Cochrane RoB 2.0, and pooled effects were calculated as relative risk and mean difference with 95% confidence intervals. The present abstract ends before reporting the pooled results. In the exploratory PK/PD study [58], patients with mild COVID-19 received aqueous *A. paniculata* extract capsules containing 30 mg andrographolide every 8 hours (90 mg/day) for 5 consecutive days; the analysis showed rapid absorption and elimination with limited systemic exposure, a sigmoidal, saturable exposure-response relationship and a reduction in viral load of $-2.96 \log_{10}$, after which the abstract breaks off.

Gut and Microbiome

The systematic review with meta-analysis [61] evaluated clinical studies on adverse drug reactions of andrographolide-derivative medicines and herbal *A. paniculata* preparations. A total of 262 studies were included: 125 randomised controlled trials, 23 non-randomised controlled trials, 6 case series and 108 case reports. Among 9490 users of andrographolide-derivative injections, 383 (4.04 %) reported adverse drug reactions. The meta-analysis yielded an incidence of 5.48 % [95% CI (4.47 %, 6.72 %)] for andrographolide sulfonate and 3.69 % for potassium sodium dehydroandrographolide succinate for the three most frequently used injections; the abstract breaks off before reporting the corresponding confidence interval and the third injection.

The review [50] addresses the oral bioavailability of the diterpene lactones from *A. paniculata*. Andrographolide is the principal diterpene and the main active constituent of the species. The work lists low water solubility, slow dissolution rate, low gastrointestinal absorption, high chemical and metabolic instability and rapid elimination as limiting factors. It describes the use of self-microemulsifying drug delivery systems as a strategy to improve dissolution and bioavailability after oral administration of an *A. paniculata* extract formulation.

The present material contains no studies on questions of the gut microbiome. The studies assigned here address tolerability and absorption, not the composition or function of the intestinal flora. A study linking *A. paniculata* administration with microbial endpoints remains to be conducted.

Safety and Tolerability

In a prospective, double-blind randomised controlled trial [62], patients with asymptomatic or mildly symptomatic COVID-19 received either an ethanolic *A. paniculata* extract containing 60 mg andrographolide three times daily for five days or placebo. 165 participants completed the study, 83 in the extract group and 82 in the placebo group. The highest score reached on the WHO progression scale was 4. COVID-19 symptoms were significantly alleviated on the final day of intervention in both groups, with no significant difference between the groups.

The extract alleviated headache on day 1 and loss of smell on day 2 significantly more than placebo. Global assessment showed complete recovery in 80.7 % of patients after five-day treatment. The most frequent adverse effect at high dose was mild diarrhoea, which resolved within a few days. No hepatic or renal toxicity was observed; the abstract breaks off at this point.

What is missing: The study recorded five treatment days in asymptomatic to mildly symptomatic COVID-19. The present text contains no information on longer use, higher doses or other patient groups. Recording of adverse effects beyond the treatment period remains to be done.

Inflammatory Processes

The review [65] describes andrographolide as a labdane diterpene and principal active constituent from *A. paniculata* with anti-inflammatory, antioxidant and antineoplastic properties. It names the transcription factors NF- κ B, AP-1 and HIF-1 as well as the signalling pathways PI3K/Akt, MAPK and JAK/STAT as targets; in addition, enhancement of the Nrf2 pathway is cited as the basis of the antioxidant and anti-inflammatory effect. The work points out that andrographolide targets can influence glucose metabolism and discusses this metabolic effect as a possible common explanation for the actions described in preclinical and clinical studies.

The review [7] classifies andrographolide as the main constituent of *A. paniculata* and lists anti-inflammatory, antioxidant, anticarcinogenic, antimicrobial and antihyperglycaemic effects. Traditional use in Chinese medicine includes colds and fever, sore throat, burning tongue and snake bites. The work explicitly draws attention to safety issues that are easily overlooked in clinical practice, including nephrotoxicity and reproductive toxicity, and calls for scientific examination of the efficacy-safety balance.

The review [67] addresses andrographolide in atherosclerotic cardiovascular disease. It describes that andrographolide, in addition to its use in sore throat, can also be employed for the prevention and treatment of atherosclerotic diseases, thereby influencing obesity, diabetes, hyperlipidaemia and atherosclerosis itself via various targets and signalling pathways, including lipid accumulation, inflammation, oxidative stress and cellular changes. The work identifies the pharmacological mechanisms of this application as an open question. The review [10] summarises the anticarcinogenic properties of andrographolide and names molecular targets in breast, lung, colon, kidney and cervical cancer as well as in leukaemia and hepatocellular carcinoma.

The review [69] summarises neuropharmacological properties of andrographolide. Neuroprotective, analgesic and antifatigue effects are listed; the most pronounced findings concern neuroinflammation, cerebral ischaemia, Alzheimer's and Parkinson's disease, multiple sclerosis and brain tumours in mice and rats. According to these data, andrographolide and its derivatives can improve memory and learning ability in experimental animals without toxicity in the brain. Work [68] provides an overview of analytical methods for determining andrographolide in biological samples, pharmaceutical formulations and plant material, including spectrophotometry, chemiluminescence, electroanalysis, chromatography and coupled techniques.

Immune System

The review [8] evaluates the antimicrobial efficacy of *A. paniculata* and its metabolites. According to these data, andrographolide can inhibit virulence factors of invasive microbes and regulate the host immune response. The work reports that controlled clinical studies showed treatment with *A. paniculata* to be safe and effective in acute respiratory infections such as the common cold and sinusitis. The work positions *A. paniculata*, especially andrographolide, as a candidate for the development of antimicrobial medicines and emphasises inhibition of invasive microbes and biofilm formation.

What is missing: The work is a critical evaluation of secondary metabolites and clinical studies; the review contains no primary data on immunological endpoints such as cytokine profiles or cell populations. A study that prospectively measures the immunomodulatory effect of *A. paniculata* on defined immune parameters remains to be conducted.

Oncology

Study [39] investigated andrographolide in non-small-cell lung carcinoma. Molecular-dynamics simulations showed direct binding of andrographolide to signal transducer and activator of transcription-3 (STAT3) with high affinity. Proteome analyses revealed that andrographolide reduces PD-L1 expression in the tumour via suppression of the JAK2/STAT3 pathway and modulates P62-dependent selective autophagic degradation of PD-L1 by inhibiting STAT3 phosphorylation.

In vivo, andrographolide suppressed tumour growth in H1975 xenograft mice and in Lewis lung-carcinoma cell models, with higher concentrations achieving greater efficacy. It prolonged survival time in the mice and enhanced the efficacy of anti-PD-1 antibody immunotherapy by stimulating infiltration and function of CD8+ T cells. **Hypothesis:** The authors propose the combination of andrographolide with anti-PD-1 immunotherapy. The findings derive from cell and animal models; whether these effects occur in humans has not been investigated.

Bone and Joints

Study [25] examined whether constituents of *A. paniculata* exert a protective effect on cartilage in osteoarthritis via inhibition of fatty-acid-binding protein 4 (FABP4). The starting point was the observation that *A. paniculata* strongly inhibits FABP4 activity. The authors analysed single-cell RNA-sequencing data from joint tissue of osteoarthritis patients (GSE152805, GSE145286), performed docking analyses with AutoDock Vina and measured anti-FABP4 activity in a fluorescence-displacement assay.

In human C28/I2 chondrocytes, bulk RNA sequencing showed that FABP4 increases fatty-acid oxidation and the formation of reactive oxygen species, which was inhibited by andrographolide. Formation of reactive oxygen species activated the NF- κ B pathway. Anti-osteoarthritis activity was tested in rats with monosodium-iodoacetate-induced osteoarthritis. The findings rest on cell-culture and animal models; a clinical trial in humans remains to be conducted.

Overall Picture

Across the fields, two strands stand out: the anti-inflammatory and immunomodulatory action of andrographolide, described in reviews via NF- κ B, AP-1, HIF-1, PI3K/Akt, MAPK, JAK/STAT and Nrf2 [65], and the clinical testing in COVID-19, ranging from individual randomised studies to a meta-analysis of six RCTs with 660 adults [63]. In addition, there are preclinical findings on lung carcinoma [39] and osteoarthritis [25] that rest on cell and animal models.

Clinical testing is at an early stage: the COVID-19 studies include a few hundred participants, short treatment durations of five days and different preparations [52][58][62]. Studies on the gut microbiome, on immunological endpoints in humans and on oncological or joint-related endpoints in humans remain to be conducted. Open questions concern oral bioavailability [50], the transferability of preclinical mechanisms and the dose-response relationship [58].

Methodology of the evidence base

The studies available comprise randomised controlled trials, observational studies, a systematic review with meta-analysis, narrative reviews, a computer-assisted docking study and cell and animal models. The clinical studies in COVID-19 predominantly tested five treatment days, with endpoints such as symptom duration, WHO progression scale, viral load, CRP and IL-6 [52][58][62][63]. Typical limitations are small case numbers, short observation periods and different preparations and doses. What is systematically missing are studies with longer treatment durations, defined immunological endpoints and clinical endpoints relating to oncology and joint diseases.

What is cited is not what was tested in humans

The ranking of the most-cited works does not place a controlled study at the top. At the top are

REVIEWS

, an **observational** study on pharmacology, pharmacokinetics and toxicity, a study in human cells on activity against SARS-CoV-2 and mechanism reviews. Anyone who reads citation counts as a measure of evidential strength overestimates the clinical foundation. The mechanism literature is extensive and widely received; the number of controlled trials in humans, by contrast, remains small and focuses on a few questions. Both have their place, but they are not the same.

A second point concerns the

DISTINCTION BETWEEN THE SUBSTANCES TESTED

. Medicinal products based on andrographolide derivatives are not the same as herbal preparations of Andrographis paniculata. Safety data on derivatives cannot be transferred to extracts, and results from cell culture or animal studies on isolated andrographolide do not justify a statement about an extract. In the literature these levels are frequently mentioned in the same breath. Anyone assessing the evidence must first clarify what was actually investigated: a standardised preparation, an unstandardised extract or a modified single substance.

3. How Robust the Research Is

The evaluated literature is clearly distributed. **Basic research and cell-culture studies** form a large part of the evaluated literature. In humans there are observational studies and a small group of controlled trials. Their fields of application concentrate on a few areas: most frequently **safety**, followed by **antiviral questions, inflammation and the immune system**; individual studies address bioavailability, the gut and the skin. The antiviral studies centre on **COVID-19**, and the most-cited studies are found there: a randomised pilot study on add-on therapy with a standardised formulation in mild to moderate courses, a double-blind placebo-controlled trial of an extract and a systematic review with meta-analysis. The most-cited safety study compares adverse effects of medicinal products based on andrographolide derivatives with herbal preparations.

The methodological situation is divided in two. On one side stands a broad **preclinical** base from cell culture, animals and mechanisms; it contributes to the logic of action but says nothing about the course in humans. On the other side stand the controlled studies, which are predominantly designed as **pilot studies**, sometimes as **add-on therapy** to an existing treatment, in a narrow field of application. The preparations differ between the studies, which makes comparison difficult. Two systematic reviews with meta-analysis are available, but they concern different things: once adverse effects of medicinal products based on andrographolide derivatives, once use in COVID-19. The first thing to clarify, therefore, is which preparation was tested with which endpoint before findings are combined.

4. What Is Frequently Claimed — and What the Data Support

CLAIM	EVIDENCE BASE
Andrographis acts against COVID-19	The controlled studies on this are pilot and adjunct therapy studies in mild to moderate courses; two systematic reviews with meta-analysis are available. Be
Andrographis helps with colds and respiratory infections	No controlled human study on this indication is included in the evaluated literature. COVID-19, safety, inflammation and the immune system were examined;
Andrographolide acts against cancer	For non-small cell lung cancer, studies on cells and in animals are available that investigate autophagy, ferroptosis and the anti-tumour immune response. A
The preparations are interchangeable with one another	Several studies address the oral bioavailability of diterpene lactones and how formulations alter them. Measured concentrations and effects therefore relate

5. Profile: Molecule and Charge

Andrographis paniculata is not a single molecule but a **mixture** — there is no molecular formula and no fixed molecular mass. What can be described are functional groups, charge behaviour and redox properties; that is exactly what the next section addresses.

6. Charge, Electrons, Radicals

Zeta potentials are available for preparations: galactose micelles with RSPPO50 showed a loading of $10.91 \pm 0.19 \%$ and a zeta potential of $-37.17 \pm 0.63 \text{ mV}$ ²⁸. For AND-SLN, particle size of 193.84 nm, a polydispersity index of 0.211, zeta potential of -22.8 mV and 83.70 % encapsulation efficiency were measured ³¹; coating of AGL shifted the values to 375.3 nm and 29.80 mV ³². These figures describe the surface charge of the carrier particles, not a charge of the active substance. Whether the constituents themselves carry charge or participate in cation exchange is not examined in the studies; such a measurement remains to be done.

Reactive oxygen species were determined with H2DCF-DA ¹² and DCFDA ²⁷. In UVB-damaged HaCat cells, Andrographis herba, the aerial plant part, lowered ROS values and increased viability ²⁹. In cancer cell lines, by contrast, ROS rose: ADG caused cell death via ROS, iron accumulation, malondialdehyde and glutathione depletion ²⁵, ubiquitinated GPX4 ²⁵, and andrographolide inhibited TrxR1 with ROS-dependent ER stress in human NSCLC cells ²⁶. For ADE, elevated ROS, malondialdehyde, intracellular iron and lipid-ROS values as well as altered glutathione are described ³⁰. These preclinical redox measurements come from cell cultures and tissue; none of them has been collected in humans. What would need to be clarified is whether ROS, glutathione and the thioredoxin system are measurable there.

7. Interactions with Other Substances

With which other substances on the platform this substance has been jointly investigated or discussed in human studies and reviews — combination, comparison or shared mechanism of action. The number indicates studies in which both appear.

SUBSTANCE	SHARED STUDIES	OF WHICH CONTROLLED IN HUMANS
Chronic inflammation	38	3
Adaptogens	9	6
Stress, Cortisol and Inflammation	9	0
Art Therapy	6	0
Frankincense (Boswellia)	5	2
Turmeric and Curcumin	4	0
Iron	3	0
Ginkgo biloba	2	0
NAC and Glutathione	2	0
Pelargonium sidoides	2	0

For combinations, a study with NSCLC patients describes the administration of Andrographis with anti-PD-1 antibodies as a possible strategy ⁹. In breast cancer cells, andrographolide with TRAIL enhanced cell killing synergistically ³⁵. With a 5-FU dose below the IC50, additive antitumoural effects resulted ($P<0.05$) and a stronger upregulation of HMOX1 ($P<0.05$) than under each individual treatment ³⁴. Flavonoids from A. paniculata bind stably to the HBx protein in calculations, involving Arg138, His139, Lys140 and Trp141 ³⁷. The cytotoxicity was $CC50 = 832.915 \mu\text{g/mL}$ for AP and $CC50 = 593.122 \mu\text{g/mL}$ for TP after 24 h ³⁷.

Regarding absorption, a nonlinear proportionality of the oral bioavailability of andrographolide is shown ³³. Dissolution profiles of different AP products can alter the bioavailability of the diterpenoids ³⁶. A review compares the oral uptake of the diterpene lactones from A. paniculata ³⁸. For COVID-19, research into extraction methods and formulations that increase the bioavailability of andrographolide is called for ³³. Regarding binding, calculations show stable interactions of flavonoids from A. paniculata with the HBx protein ³⁷.

8. Overdosage, Tolerability, Limits

In asymptomatic or mildly symptomatic COVID-19 patients, an ethanolic extract from Andrographis paniculata (APE) was tested double-blind against placebo; 165 patients completed the study, 83 in the APE group and 82 in the placebo group ⁴. Administration was at 180 mg/day over 5 days, with liver and kidney function monitored; no hepatic or renal toxicity occurred ⁴. In an exploratory pharmacokinetic study with standardised aqueous extract capsules, the adverse events were mild, without hepatotoxicity or renal toxicity ⁶.

A systematic review with meta-analysis of clinical studies evaluated adverse drug reactions and adverse events of andrographolide derivative medications and of preparations from Andrographis paniculata ^{2 2}. Another study described mild adverse events, mainly liver enzyme elevations, which resolved without serious complications ⁵. In patients with liver or kidney dysfunction, the respective health status should be taken into account ¹⁵. What would need to be examined is which dose and duration of use triggers the liver enzyme elevations and how tolerability presents in cases of impaired liver or kidney function.

9. The Most Robust Studies

Ordered by strength of evidence, not by familiarity. The complete evaluation comprises considerably more studies; the most robust ones are listed here.

Controlled Studies in Humans

- ¹ A Comprehensive Review of Andrographis paniculata (Burm. f.) Nees and Its Constituents as Potential Lead Compounds for COVID-19 Drug Discovery (2022)
- ² Adverse Effects of Andrographolide Derivative Medications Compared to the Safe use of Herbal Preparations of Andrographis paniculata: Results of a ... (2022)
- ³ A randomized controlled pilot study of add-on therapy of CIM-MEG19 (standardized Andrographis paniculata formulation) in mild to moderate COVID-19 (2023)
- ⁴ Andrographis paniculata extract versus placebo in the treatment of COVID-19: a double-blinded randomized control trial (2023)
- ⁵ Exploring the clinical effects of <i>Andrographis paniculata</i>-derived compounds, its extract, or derivatives for the treatment of ... (2025)
- ⁶ Exploratory pharmacokinetic-pharmacodynamic characterization and safety of standardized <i>Andrographis paniculata</i> aqueous extract ... (2026)

Observational Studies in Humans

- ⁷ Andrographolide: A review of its pharmacology, pharmacokinetics, toxicity and clinical trials and pharmaceutical researches (2022)
- ⁸ Andrographis paniculata (Burm. f.) Wall. ex Nees: An Updated Review of Phytochemistry, Antimicrobial Pharmacology, and Clinical Safety and Efficacy (2021)
- ⁹ Andrographolide suppresses non-small-cell lung cancer progression through induction of autophagy and antitumor immune response (2022)
- ¹⁰ Anti-Cancer Agent: The Labdane Diterpenoid-Andrographolide (2023)
- ¹¹ A Computational Approach Identified Andrographolide as a Potential Drug for Suppressing COVID-19-Induced Cytokine Storm (2021)
- ¹² Identification of Andrographolide as a novel FABP4 inhibitor for osteoarthritis treatment (2023)
- ¹³ A validated LC-MS/MS method for clinical pharmacokinetics and presumptive phase II metabolic pathways following oral administration of Andrographis ... (2023)
- ¹⁴ In silico identification of potential inhibitors against main protease of SARS-CoV-2 6LU7 from Andrographis paniculata via molecular docking ... (2022)
- ¹⁵ Comparative pharmacokinetics and safety evaluation of high dosage regimens of Andrographis paniculata aqueous extract after single and multiple oral ... (2023)
- ¹⁶ Andrographolide Induces Noxa-Dependent Apoptosis by Transactivating ATF4 in Human Lung Adenocarcinoma Cells (2021)
- ¹⁷ Andrographolide induces ferroptosis in colorectal cancer via P53-mediated downregulation of the SLC7A11/GPX4 signaling pathway (2025)
- ¹⁸ The use of Andrographis paniculata and its effects on liver biochemistry of patients with gastrointestinal problems in Thailand during the COVID-19 ... (2022)
- ¹⁹ Use of Andrographis paniculata (Burm.f.) Wall. ex Nees and risk of pneumonia in hospitalised patients with mild coronavirus disease 2019: A ... (2022)
- ²⁰ The Effects of Andrographis paniculata (Burm.F.) Wall. Ex Nees and Andrographolide on Neuroinflammation in the Treatment of Neurodegenerative Diseases (2023)
- ²¹ Andrographolide inhibits Burkitt's lymphoma by binding JUN and CASP3 proteins (2024)
- ²² Identification of active components in Andrographis paniculata targeting on CD81 in esophageal cancer in vitro and in vivo (2022)
- ²³ Andrographolide suppresses the malignancy of pancreatic cancer via alleviating DNMT3B-dependent repression of tumor suppressor gene ZNF382 (2024)
- ²⁴ Creep in nitroimidazole inhibitory concentration among the Entamoeba histolytica isolates causing amoebic liver abscess and screening of ... (2023)

10. Summary

In humans, safety and tolerability have primarily been examined. The double-blind randomised study [62] in 165 persons with asymptomatic to mildly symptomatic COVID-19 showed significant symptom relief in both groups with no difference between extract and placebo, yet greater relief of headache on day 1 and of loss of smell on day 2 under the extract; 80.7 % achieved complete recovery. The meta-analysis [61] on andrographolide-derivative injections covered 262 studies and 9490 users, of whom 383 (4.04 %) reported adverse drug reactions. The PK/PD study [58] demonstrated rapid absorption and elimination with limited systemic exposure together with a viral-load reduction of -2.96 log10 in mild COVID-19.

PLAUSIBLE An inflammation- and immune-related mechanism of action is described via targets such as NF-κB, AP-1 and HIF-1 as well as the signalling pathways PI3K/Akt, MAPK and JAK/STAT, in addition to an enhancement of the Nrf2 signalling pathway [65]. A computational study [11] demonstrated binding of andrographolide to TNF and covalent binding to NFκB1 proteins of the TNF signalling pathway. **Hypothesis:** The authors conclude from this that andrographolide could block the TNF-induced NFκB1 signalling pathway; the work is an in-silico investigation without patients. For clinical use it follows that findings from cell culture and animals cannot be transferred directly to humans.

The meta-analysis [63] compared single-herb A. paniculata products with antiviral medicines or supportive care in mild to moderate COVID-19 and included six randomised controlled trials with 660 adults. A study that prospectively measures the immunomodulatory effect on defined immune parameters is still outstanding, as is an investigation of microbial endpoints. It also remains open how oral bioavailability of the diterpene lactones can be reliably improved by formulations.

11. What Remains Open

- **Bioavailability:** Which formulation achieves an uptake in humans that corresponds to the range examined in studies, and how does this translate into measurable endpoints?
- **Delineation of substances:** Which results for isolated andrographolide and andrographolide derivatives apply to herbal preparations of *Andrographis paniculata* and which do not?
- **Clinical endpoints:** Will future controlled trials examine symptom duration and course rather than laboratory values, and can the COVID-19 findings be transferred to other respiratory infections?

12. Further Paths

Topics, mechanisms of action and chains in which this substance occurs — for all who wish to look beyond the substance.

- Interaction network

Frequently Asked Questions

What was tested in the controlled studies — the plant or individual substances?

Both occur, and the distinction is important. Mentioned are a standardised formulation as add-on therapy, an extract compared to placebo as well as capsules with aqueous extract in a study on uptake and safety. To be distinguished from this are works on medicinal products based on andrographolide derivatives. A safety review with meta-analysis compares exactly these derivative medicinal products with herbal preparations and thereby addresses two different things side by side.

How robust are the COVID-19 findings on *Andrographis*?

The controlled studies are designed as pilot studies, partly as add-on therapy to an existing treatment, and concern mild to moderate courses. In addition, there is a systematic review with meta-analysis that summarises the use of andrographolide-derived substances, extracts and derivatives in COVID-19. The findings therefore relate to individual preparations in defined settings, not to the plant as such; how this translates to other disease courses has not been examined.

What should be considered regarding safety questions?

Safety is the application area with the most controlled studies. The most striking work on this is a systematic review with meta-analysis that contrasts adverse effects of medicinal products based on andrographolide derivatives with experiences with herbal preparations. Anyone wishing to draw a conclusion about extracts from this must consider the preparation: derivative medicinal products and herbal preparations are not interchangeable. Which preparation was tested and to what extent remains the decisive question.

Sources

- 1 A Comprehensive Review of Andrographis paniculata (Burm. f.) Nees and Its Constituents as Potential Lead Compounds for COVID-19 Drug Discovery
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