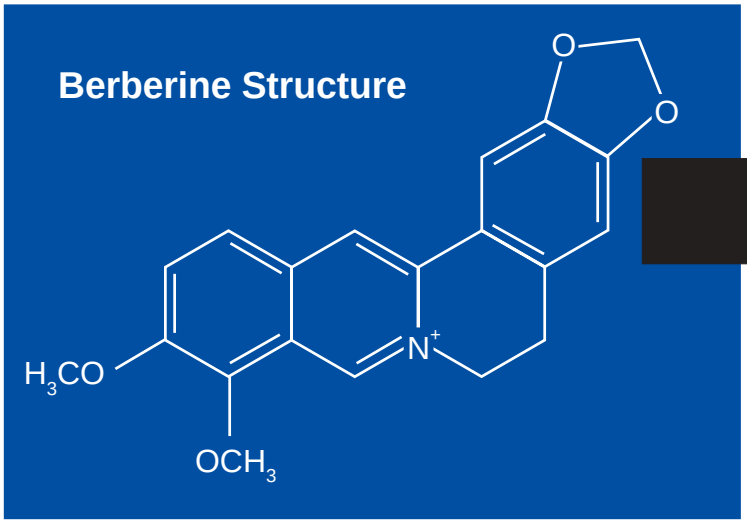

Monograph

Berberine

Introduction

Berberine is a plant alkaloid with a long history of medicinal use in both Ayurvedic and Chinese medicine. It is present in *Hydrastis canadensis* (goldenseal), *Coptis chinensis* (Coptis or goldenthread), *Berberis aquifolium* (Oregon grape), *Berberis vulgaris* (barberry), and *Berberis aristata* (tree turmeric). The berberine alkaloid can be found in the roots, rhizomes, and stem bark of the plants. Berberine extracts and decoctions have demonstrated significant antimicrobial activity against a variety of organisms including bacteria, viruses, fungi, protozoans, helminths, and chlamydia. Currently, the predominant clinical uses of berberine include bacterial diarrhea, intestinal parasite infections, and ocular trachoma infections.[1]

Pharmacology

The pharmacologic actions of berberine include metabolic inhibition of certain organisms, inhibition of bacterial enterotoxin formation, inhibition of intestinal fluid accumulation and ion secretion, inhibition of smooth muscle contraction, reduction of inflammation, platelet aggregation inhibition, platelet count elevation in certain types of thrombocytopenia, stimulation of bile and bilirubin secretion, and inhibition of ventricular tachyarrhythmias.[1,2]

Clinical Applications

Bacterial Diarrhea

Diarrhea caused by *Vibrio cholera* and *Escherichia coli* has been the focus of numerous berberine studies, and results indicate several mechanisms which may explain its ability to inhibit bacterial diarrhea. An animal study found berberine reduced the intestinal secretion of water and electrolytes induced by cholera toxin.[3] Other studies have shown berberine directly inhibits some *V. cholera* and *E. coli* enterotoxins,[4] significantly reduces smooth muscle contraction and intestinal motility,[2] and delays intestinal transit time in humans.[5] Berberine sulfate has also been found to be directly bacteriocidal to *V. cholera*.[6] In the case of *E. coli*, *in vitro* research indicated berberine sulfate was capable of inhibiting bacterial adherence to mucosal or epithelial surfaces, the first step in the infective process. This may be a result of berberine's inhibitory effect on fimbrial structure formation on the surface of the treated bacteria.[7]

Intestinal Parasites

Berberine extracts and salts have demonstrated growth inhibition *of Giardia lamblia, Entamoeba histolytica, Trichomonas vaginalis*,[8] and *Leishmania donovani*,[9] with crude extracts being more effective than berberine salts.[10]

In tropical climates *Giardia lamblia* infestation (giardiasis) is a common occurrence, particularly in pediatric populations.[11] Clinical trials conducted in India showed berberine administration improved gastrointestinal symptoms and resulted in a marked reduction in Giardia-positive stools. In comparison to metronidazole (Flagyl), another popular giardiasis medication, berberine was nearly as effective at half the dose.[12]

Both *in vivo* and *in vitro* studies of berberine's effects on *E. histolytica* indicated berberine sulfate was rapidly amoebicidal and caused encystation, degeneration, and eventual lysis of the trophozoite forms.[13]

Berberine sulfate rapidly inhibited the growth of *Trichomonas vaginalis* via formation of large autophagic vacuoles that eventually result in lysis of the trophozoite forms.[8]

Studies have shown berberine markedly decreased parasitic load and rapidly improved hematologic parameters in infected animals. *In vitro* results indicated berberine inhibited multiplication, respiration, and macromolecular biosynthesis of amastigote forms of the parasite, interfered with the nuclear DNA of the promastigote form, and inhibited organism maturation.[9]

Ocular Trachoma Infections

A clinical study of aqueous berberine versus sulfacetamide for the treatment of *Chlamydia trachomatis* infection was conducted on 51 subjects in an outpatient eye clinic. It was determined that while sulfacetamide eye drops produced slightly better clinical results, conjunctival scrapings of these patients remained positive for the infective agent and relapses occurred. In contrast, the conjunctival scrapings of patients receiving the berberine chloride eye drops were negative for *C. trachomatis* and there were no relapses, even one year after treatment. It was also concluded that, while berberine chloride had no direct anti-chlamydial properties, it seemed to cure the infection by stimulating some protective mechanism in the host.[14] A second clinical study found berberine chloride superior to sulfacetamide in both the clinical course of trachoma and in achieving a drop in serum antibody titers against *C. trachomatis*.[15]

Cardiovascular Effects

Both clinical trials and animal research have indicated berberine administration prevented ischemia-induced ventricular tachyarrhythmia, stimulated cardiac contractility, and lowered peripheral vascular resistance and blood pressure.[16,17] The mechanism for berberine's antiarrhythmic effect is unclear, but an animal study indicated it may be due to suppression of delayed after-depolarization in the ventricular muscle.[18] An animal study suggested, in addition to affecting several other parameters of cardiac performance, berberine may have a vasodilatory/hypotensive effect attributable to its potentiation of acetylcholine.[16]

Anti-inflammatory Effects

In vitro studies utilizing human cell lines demonstrated that berberine inhibited activator protein 1 (AP-1), a key transcription factor in inflammation and carcinogenesis.[19] Another study, utilizing human peripheral lymphocytes, showed berberine to exert a significant inhibitory effect on lymphocyte transformation, concluding that its anti-inflammatory action may be due to inhibition of DNA synthesis in activated lymphocytes.[20] A third study concluded that during platelet activation in response to tissue injury, berberine had a direct affect on several aspects of the inflammatory process. It exhibited dose-dependent inhibition of arachidonic acid release from cell membrane phospholipids, inhibition of thromboxane A2 from platelets,[21] and inhibition of thrombus formation.[22]

Other Effects

Berberine has demonstrated a number of other beneficial effects, including immunostimulation via increased blood flow to the spleen, macrophage activation, elevation of platelet counts in cases of primary and secondary thrombocytopenia, and increased excretion of conjugated bilirubin in experimental hyperbilirubinemia.[1] In addition, berberine may possess anti-tumor promoting properties as evidenced by inhibition of COX-2 transcription and N-acetyltransferase activity in colon and bladder cancer cell lines,[23,24] and transient, but marked, inhibitory action on the growth of mouse sarcoma cells in culture.[25]

Dosage and Toxicity

Berberine is not considered toxic at doses used in clinical situations, nor has it been shown to be cytotoxic or mutagenic. Side-effects can result from high dosages and may include gastrointestinal discomfort, dyspnea, lowered blood pressure, flu-like symptoms, and cardiac damage. Berberine usage should be avoided in pregnancy, due to potential for causing uterine contractions and miscarriage, and in jaundiced neonates because of its bilirubin displacement properties. The therapeutic dosage for most clinical situations is 200 mg orally two to four times daily.[1]

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