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Review

Berberine: Alkaloid with wide spectrum of pharmacological activities

[1]Amritpal Singh*, [2]Sanjiv Duggal, [3]Navpreet Kaur, [4]Jaswinder Singh

[1]Dept of Dravyaguna, Sri Dhanwantry Ayurvedic College, Sec 46-C, Chandigarh

[2]Dept of Pharmaceutical Sciences, Lovely Professional University, Phagwara (Pb.)

[3]Dept of Dentistry, Sri Guru Ram Das Institute of Medical Education and Research, Amritsar (Pb.)

[4]Dept of Pharmacology, Sri Guru Ram Das Institute of Medical Education and Research, Amritsar (Pb.)

*Corresponding author

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ABSTRACT

Berberine is an isoquinoline alkaloid, present in roots and stem-bark of *Berberis* species. Berberine based formulations, are widely used in traditional systems of medicine including, Ayurveda and Traditional Chinese Medicine. Berberine has demonstrated wide range of pharmacological activities including; antihypertensive, anti-inflammatory, antioxidant, antidepressant, anticancer, anti-diarrhoeal, cholagouge, hepatoprotective and above all, antimicrobial. Recent studies, have thrown light on antidiabetic and hypolipidemic activities of the alkaloid. Berberine has been tested clinically in the treatment of oriental sore, diarrhea, trachoma diabetes mellitus type-2, hypercholesterolemia, and congestive cardiac failure. The present review, discusses preclinical and clinical investigations on berberine, with potential for drug-development.

Keywords: Berberine, pharmacology, isoquinoline alkaloid, trachoma, diabetes mellitus-2.

INTRODUCTION

Berberine (fig.1) is an isoquinoline alkaloid, with a bright yellow color, that is easily seen in most of the herb materials, which contain any significant amount. Berberine is chief alkaloid from roots and stem-bark of *Berberis* species. It is manufactured mostly from roots of *B.aristata* (5% in roots and 4.2% in stem-bark), *B. Petiolaris* (0.43%), *B.vulgaris, B. aquifolium, B. thunbergii* and *B. asiatica* (Watt, 1972; Nandkarni, 1976; Chopra, Nayar and Chopra, 1996), *C.teeta* (rhizome 8-9%) and *Hydrastis Canadensis* (Gruenwald, et al., 2000). Among Chinese herbs, the primary sources are *B. sargentiana, Phellodendron amurense* and *CoPtis chinensis. CoPtis chinensis* rhizomes and related species used as its substitutes have about 4–8% berberine, while *Phellodendron amurense* bark has about half as much, at 2–4% berberine (Dharmananda, 2005).

With emergence of drug-resistance and cost- effectiveness of synthetic drugs, there is growing interest in medicinal natural products (Wagner, 2006). The present review is dedicated to

pre-clinical and clinical investigations conducted with berberine and potential for drug development

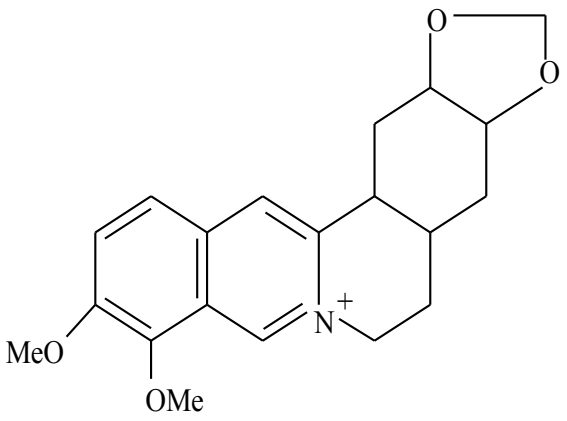

Fig-1: Chemical structure of berberine

Pharmacological studies:

Pre-clinical

(1) Anti-Proliferative and anti-migratory activity: Berberine is capable of inhibiting growth and endogenous platelet-derived growth factor synthesis in vascular smooth muscle cells after *in vitro* mechanical injury. A study, analyzed the effects of berberine on vascular smooth muscle cell growth, migration, and signaling events after exogenous platelet-derived growth factor stimulation *in vitro* in order to mimic a post-angioplasty platelet-derived growth factor shedding condition.

Pretreatment of vascular smooth muscle cells with berberine, inhibited platelet-derived growth factor-induced proliferation. Berberine significantly suppressed platelet-derived growth factor F-stimulated Cyclin D1/D3 and Cyclin-dependent kinase gene expression. Moreover, berberine increased the activity of AMP-activated protein kinase, which led to phosphorylation activation of p53 and increased protein levels of the Cdk inhibitor p21.

Compound C, an AMPK inhibitor, partly but significantly; attenuated berberine-elicited growth inhibition. In addition, stimulation of vascular smooth muscle cells with platelet-derived growth factor led to a transient increase in GTP-bound, active form of Ras, Cdc42 and Rac1, as well as VSMC migration. However, pretreatment with berberine significantly inhibited platelet-derived growth factor F-induced Ras, Cdc42 and Rac1 activation and cell migration. Co-treatment with farnesyl pyrophosphate and geranylgeranyl pyrophosphate drastically reversed berberine-mediated anti-proliferative and migratory effects in vascular smooth muscle cells. The observations offer a molecular explanation for the anti-proliferative and anti-migratory properties of berberine (Liang, et al., 2008).

(2) Antimicrobial activity

Antibacterial: In one experiment, berberine hydrochloride reduced the cholera toxin-induced secretion of water, sodium and chloride in perfused rat ileum. Berberine was also found to inhibit the intestinal secretory response of *Vibrio cholerae* and *Escherichia coli* enterotoxins without causing histological damage to the intestinal mucosa (Sack, 1982).

Berberine is also active against other intestinal infections that cause aute diarrhea such as *Shigella dysenteriae, Salmonella ParatyPhi* and various *Klebsiella sPecies.* Berberine sulphate has been shown to block the adherence of *StrePtococcus Pyrogenes* and *E. coli* to host cells, possibly explaining it's mechanism of action against numerous pathogens (Sun, 1988).

The effects of chlorpromazine (CPZ), berberine and verapamil on intestinal hyper secretion in the rabbit ileal loop model by the heat-labile enterotoxin (LT) of *Escherichia coli* were studied in relation to their ability to inhibit the stimulation of intestinal adenylate cyclase by the heat-labile enterotoxin. Chlorpromazine 5 mg by the intraluminal route and 4 mg/kg by the intramuscular route significantly reduced LT-induced intestinal hyper secretion. Berberine (10 mg) exerted an inhibitory effect, but only after i.l. administration, whereas verapamil did not exert any significant inhibitory effect when administered either (2.5 mg) or i.m. (4 mg/kg).

At concentrations of (0.17-1.34) x 10^{-3} M CPZ, the anti-secretory effect of CPZ correlated with its inhibitory effect on rabbit heat-labile enterotoxin-stimulated intestinal adenylate cyclase. Inhibition of cAMP synthesis was probably not involved in the mechanism of action of the two other substances. These results indicate that chlorpromazine and phenothiazines in general are efficient drugs for reducing heat-labile enterotoxin-induced intestinal hyper secretion and could represent a model for synthesis of new anti-secretory drugs with no tranquiliser side effects (Askri and Scheftel, 1988).

Berberine was found to be the active constituent in an extract of *Hydrastis canadensis* root that demonstrated activity against a multiple drug-resistant strain of *Mycobacterium tuberculosis* (Gentry, 1998). Berberine is reported to inhibit *Helicobacter Pylori* (Bae, 1998).

The growth thermogenic curves of Escherichia coli affected by berberine, coptisine (fig. 2) and palmatine (fig 3) extracted from *CoPtis chinensis* were determined quantitatively by microcalorimetry. The power-time curves of E. coli with and without the three protoberberine alkaloids were acquired; meanwhile the extent and duration of inhibitory effects on the metabolism were evaluated by growth rate constant (k), half-inhibitory ratio (IC50), peak time of maximum heat-output power (tp), total heat-production (Qt) and so on. The inhibitory effects of three protoberberine alkaloids on E. coli revealed that the sequence of their antimicrobial activity was berberine > coptisine > palmatine (Yan, et al., 2007).

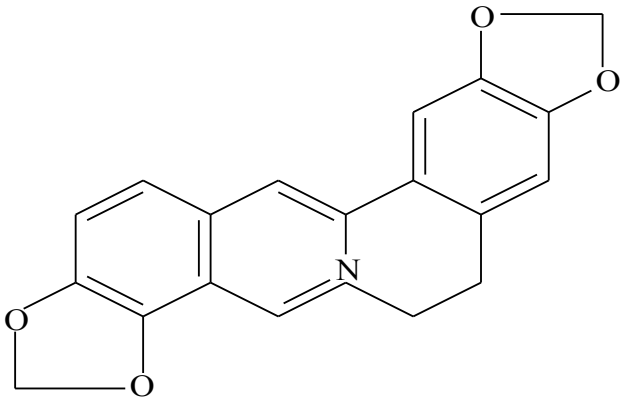

Fig -2: Chemical structure of coptisine

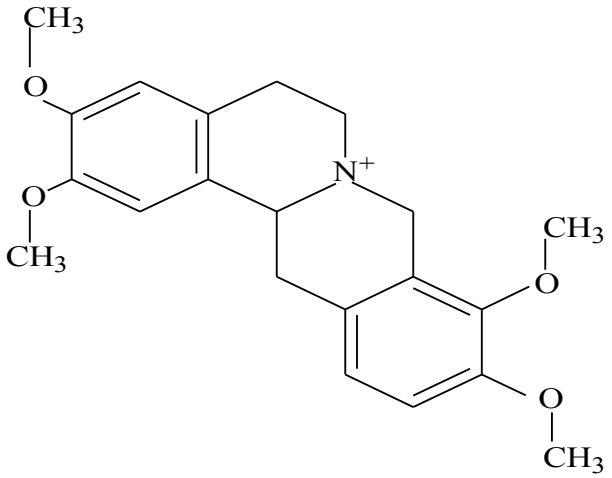

Fig-3: Chemical structure of palmitine

Antibacterial activity of berberine is potentiated by methoxyhydnocarpin (fig 4). This observation has led to the possibility that plants produce both antibacterial compounds and compounds, which target bacterial efflux mechanisms, to inhibit possible resistance to latent plant antibacterial in bacteria in their environment (Wagner, 2000).

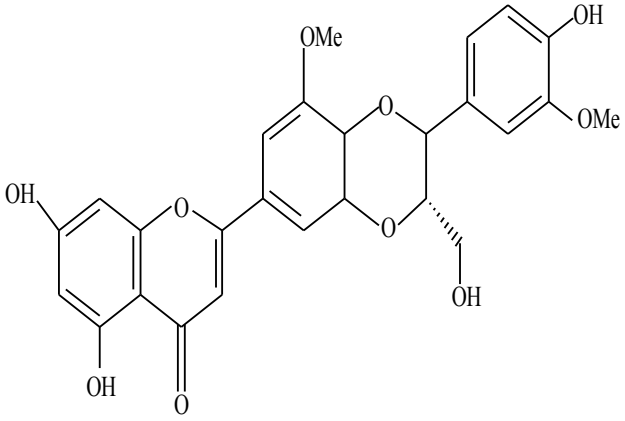

Fig- 4: Structure of 5' methoxyhydnocarpin

Antifungal: The antifungal activity of trial denture cleansers prepared with berberine hydrochloride was examined against *Candida albicans, C. troPicalis,* and *C. glabrata*. A commercial denture cleanser and a trial denture cleanser that exhibited strong antifungal activity were tested for their effects on *Candida* sp., the color stability of the dental material, and the surface roughness of acrylic resin plates. The results of these tests revealed that the trial denture cleanser removed 64% to 89% of adhered cells from acrylic resin surfaces and had little effect on the other physical properties tested (Nakamoto, et al., 1995).

AntiProtozoal: Parenteral administration of berberine has been shown to give rise to a statistically significant prolongation of the lives of rats infected with Trypanosoma equiperdum (Serry and Bieter, 1940).

Berberine sulfate has been shown to inhibit the growth of *Entamoeba histolytica, Giardia lamblia* and *Trichomonas vaginalis, in vitro.* The parasites all exhibited morphological changes after exposure to berberine sulfate (Kaneda, 1991).

Earlier studies shave demonstrated utility of berberine in the treatment of Leishmania donovani infestation (Hanson, Chapman and Kinnamon, 1977; Ghosh, et al., 1983; Ghosh, et al.,

1985). Berberine and several of its derivatives were tested for efficacy against Leishmania donovani and Leishmania braziliensis panamensis in golden hamsters. Tetrahydroberberine was less toxic and more potent than berberine against L. donovani but was not as potent as meglumine antimonate (Glucantime), a standard drug for the treatment of leishmaniasis. Only berberine and 8-cyanodihydroberberine showed significant activity (greater than 50% suppression of lesion size) against L. braziliensis panamensis (Vennerstrom, et al., 1990).

3. Gastrointestinal system

Cholagouge: Extract of *B. vulgaris*, with 80% berberine and additional alkaloids stimulated the bile excretion of rats by 72% (Subbaiah and Amin, 1967). Berberine has been shown to lower bilirubin levels (Chan, 1977).

Anti-diarrheal activity: The motility of the small intestine in unanesthetized rats receiving berberine sulfate (0.2, 2.0, and 20.0 mg/kg i.p.) was investigated. Motility was determined by two methods: myoelectric activity was monitored with indwelling bipolar electrodes, and intestinal transit was measured by the movement of radio chromium (Na51CrO4). The 20.0-mg/kg dose caused a marked inhibition of spike activity for 21.8 +/- 7.0 min and disrupted activity fronts of the migrating myoelectric complex for 212.3 min.

Berberine, 2.0 mg/kg i.p., disrupted migrating myoelectric complexes for 64.6 min but spike inhibition was not observed. Transit of the small intestine was significantly (p less than 0.001) delayed at 15 and 100 min after the highest dose of berberine. Naloxone blocked the spike inhibition noted with 20.0 mg/kg of berberine but failed to improve transit. Phentolamine blocked spike inhibition and was associated with a significantly earlier return of activity fronts of the migrating myoelectric complex.

Animals pretreated with this antagonist tended toward a higher geometric center in transit studies than those injected with berberine alone. Berberine was also administered by various routes (intraperitoneal injection, intravenous injection, orogastric gavage, and intraluminal injection). An intraperitoneal injection was 10-fold more potent than an intravenous injection. Orogastric gavage and intraluminal administration of berberine did not alter intestinal motility. In summary, berberine sulfate significantly inhibits myoelectric activity and transit of the small intestine. This appears to be partially mediated by opioid and alpha-adrenergic receptors. The antidiarrheal properties of berberine may be mediated, at least in part, by its ability to delay small intestinal transit (Eaker and Sninsky, 1989).

HePatoProtective activity: Hepatoprotective effect of Coptidis rhizoma aqueous extract and its possible mechanism were studied in ratsintoxicated with carbon tetrachloride (CCl4) in the present study. SPRAGUE-Dawley (SD) rats aged 7 weeks old were intraperitoneally injected with CCl4 at a dose of 1.0 ml/kg as a 50% olive oil solution. The rats were orally given the Coptidis rhizoma aqueous extract at doses of 400, 600, 800 mg/kg and 120 mg/kg berberine body weight after 6 h of CCl4 treatment. At 24 h after CCl4 injection, samples of blood and liver were collected and then biochemical parameters and histological studies were carried out.

The results showed that Coptidis rhizoma aqueous extract and berberine inhibited significantly the activities of alanine aminotransferase and aspartate aminotransferase and increased the activity of superoxide dismutase. Observation on the hepatoprotective effect of berberine was consistent to that of Coptidis rhizoma aqueous extract. The study demonstrated that Coptidis rhizoma aqueous extract has hepatoprotective effect on acute liver injuries induced by CCl4, and the results suggest that the effect of Coptidis rhizoma aqueous extract against CCl4-induced liver damage is related to antioxidant property (Xing, et al., 2009).

4. Cardiovascular system activity

AntihyPertensive activity: The alkaloid produces long lasting, dose related fall in blood pressure of anaesthetized rabbits (Watt, 1972). Fractions from the root extracts of *B. vulgaris*, which contain 80% berberine and other alkaloids, have been shown to reduce the blood pressure of cats for several hours. With varying doses, both positive and negative inotropic effects on the cats'

hearts were recorded (Lahiri, et al., 1958). Infusion of berberine when given intravenous to rats reduces blood pressure (Anonymous, 1976).

AlPha 2 adrenocePtor antagonist activity: In this study, the interaction of berberine with human platelet alpha 2 adrenoceptor was investigated. Berberine was found to inhibit competitively the specific binding of [3H]-yohimbine. The displacement curve was parallel to those of clonidine, epinephrine, norepinephrine, with the rank order of potency (IC50) being clonidine (0.4 microM) greater than epinephrine (7.5 microM) greater than norepinephrine (14.5 microM) = berberine (16.6 microM).

Increasing concentrations of berberine from 0.1 microM to 10 microM inhibited [3H]-yohimbine binding, shifting the saturation binding curve to the right without decreasing the maximum binding capacity. In platelet cyclic AMP accumulation experiments, berberine at concentrations of 0.1 microM to 0.1 mM inhibited the cAMP accumulation induced by 10 microM prostaglandin E1 in a dose dependent manner, acting as an alpha 2 adrenoceptor agonist. In the presence of L-epinephrine, berberine blocked the inhibitory effect of L-epinephrine behaving as an alpha 2 adrenoceptor antagonist. Thee properties are similar to those of clonidine on human platelets, suggesting that berberine is a partial agonist of platelet alpha 2 adrenoceptors. These findings may account for hypotensive, antisecretory, and sedative effects of berberine (Hui, et al., 1991).

Anti-arrhythmic activity: The study describes cardiovascular effects of berberine and its derivatives, tetrahydroberberine and 8-oxoberberine. Berberine has positive inotropic, negative chronotropic, antiarrhythmic, and vasodilator properties. Both derivatives of berberine have antiarrhythmic activity. Some cardiovascular effects of berberine and its derivatives are attributed to the blockade of K+ channels (delayed rectifier and K (ATP)) and stimulation of Na+ -Ca (2+) exchanger. Berberine has been shown to prolong the duration of ventricular action potential. Its vasodilator activity has been attributed to multiple cellular mechanisms. The cardiovascular effects of berberine suggest its possible clinical usefulness in the treatment of arrhythmias and/or heart failure (Lau, et al., 2001).

AntiPlatelet activity: In the present study, it was demonstrated *ex vivo* that berberine significantly inhibited rabbit platelet aggregation induced by adenosine diphosphate, arachidonic acid, collagen or calcium ionophore A23187. The most potent inhibition was observed in collagen-induced platelet aggregation. Using radioimmunoassay, we show in vitro that berberine significantly inhibited synthesis of thromboxane A_2 in rabbit platelets induced by adenosine diphosphate, arachidonic acid or collagen in which collagen-induced thromboxane A_2 synthesis was also most potently inhibited. In our in vivo study using radioimmunoassay, the plasma prostacyclin level was reduced by 34.6% during a 30-min period after intravenous administration of 50 mg/kg of berberine. The results suggest that berberine might inhibit arachidonic acid metabolism in rabbit platelets and endothelial cells at two or more sites: cyclooxygenase in the arachidonic acid cascade and possibly the enzyme(s) for arachidonic acid liberation from membrane phospholipid(s) (Huamng et al., 2002).

HyPoliPidemic activity: Berberine lowers elevated blood total cholesterol, LDL cholesterol, triglycerides and aterogenic apolipoptoteins (Zhou, et al.,2008) but the mechanism of action is distinct from statins (Holy, et al., 2009; Kong, Wei, Abidi. et al., 2009; Kim, Lee, Cha. et al., 2009). Berberine reduces LDL cholesterol by upregulating LDLR mRNA expression posttranscriptionally while down regulating the transcription of proprotein convertase subtilisin/kexin type 9 (PCSK9), a natural inhibitor of LDL receptor (Li, Dong, Park. et al., 2009) and increasing in the liver the expression of LDL receptors through extra cellular signal-regulated kinase (ERK) signaling pathway (Abidi, et al., 2005) while statins inhibit cholesterol synthesis in the liver by blocking HMG-CoA-reduktase. This explains why berberine does not cause side effects typical to statins.

Berberine activates AMP-activated protein kinase (Turner, et al., 2008) specifically extrascellular signal-regualted kinases (Lamontagne, et al., 2009), which plays a central role in

glucose and lipid metabolism (Lee, et al., 2006) suppresses proinflammatory cystokines (Jeong, et al., 2009), and reduces MMP-9 and EMMPRIN expression (Huang, et al., 2009), which are all beneficial changes for heart health. Moreover, berberine reduces hepatic fat content in the rats of non-alcoholic fatty liver disease (Chang, et al., 2009). Berberine also prevents proliferation of hepatic stellate cells, which are central for the development of fibrosis during liver injury (Sun, et al., 2009).

5. Central nervous system activity

Anti-inflammatory activity: In the present study, the anti-inflammatory properties of total ethanol extract, three alkaloid fractions, a major alkaloid berberine and oxyacanthine (fig.5) isolated from *B. vulgaris* roots were compared. All these were applied in acute inflammation (carrageenan- and zymosan-induced paw oedema), as the total ethanol extract showed the highest reducing effect. Their ability to alter *in vivo* and *in vitro* complement activity was determined. Also, the total ethanol extract was most effective in a chronic inflammatory model of adjuvant arthritis. The protoberberine fractions Bv2, Bv3 and berberine suppressed a delayed type hypersensitivity (DTH) reaction. Fraction Bv1 and berberine diminished antibody response against SRBC *in vivo*. The *in vitro* treatment of splenocytes with berberine showed that the anti-SRBC antibody synthesis was influenced in a different manner depending on the time course of its application. Oxycanthine was less effective than berberine in the tests used (Ivanovska and Philipov, 1996).

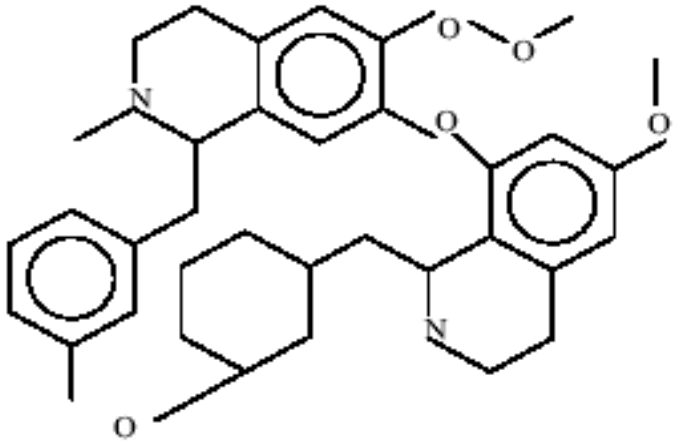

Fig-5: Structure of Oxycanthine

AntidePressant activity: 1**.** The central depressant actions of methanol extract of coptis root, its active ingredients such as non-alkaloids fraction, tertiary base fraction, quarternary base fraction, magnoflorine fraction, berberine hydrochloride, coptisine hydrochloride and the extract from SAN O SHA SHIN TO (reparations which contain coptis root) were investigated in mice. The antigastric ulcer action of these substances was also examined in rats. All substances were given orally. Spontaneous movement and coordinative motor activity were not depressed by methanol extract, non-alkaloid fraction quarternary base fraction, magnoflorine fraction, berberine hydrochloride, coptisine hhdrochloride and the extract from SAN O SHA SHIN TO. There was no inhibition of chemical- and electro-shock-induced convulsion, morphine induced Straub's tail reaction, apomorphine-induced masticating motion and aggressive behavior induced by electrical stimulation. A loss of righting reflex due to hypnotics was not potentiated by the substances. The quarternary base fraction did not elicit central depression, while the tertiary base fraction slightly depressed the function of the central nervous system. Quarternary base alkaloids such as berberine exerted a slight antiulcer effect (Yamahara, 1976).

2. Berberine seems to act as an herbal antidepressant. Berberine inhibits prolyl oligopeptidase in a dose-dependent manner. Berberine is also known to bind sigma like many synthetic

antidepressant drugs. As berberine is a natural compound that has been safely administered to humans, preliminary results suggest the initiation of clinical trials in patients with depression, bipolar affective disorder, schizophrenia, or related diseases in which cognitive capabilities are affected, with either the extract or pure berberine (Kulkarni and Dhir, 2009).

6. Genitourinary system

Reno Protective: A study, investigated the beneficial effects of berberine on renal function and its possible mechanisms in rats with diabetic nephropathy. Male Wistar rats were divided into three groups: normal, diabetic model, and berberine treatment groups. Rats in the diabetic model and berberine treatment groups were induced to diabetes by intraperitonal injection with streptozotocin. Glomerular area, glomerular volume, fasting blood glucose, blood urea nitrogen, serum creatinine and urine protein for 24 hours were measured using commercially available kits. Meanwhile, the activity of superoxide dismutase content of malondialdehyde in serum, activity of aldose reductase and the expression of aldose reductase mRNA and protein in kidney were detected by different methods.

The results showed that oral administration of berberine (200 mg/kg/d) significantly ameliorated the ratio of kidney weight to body weight. Glomerular area, glomerular volume, fasting blood glucose, blood urea nitrogen, serum creatinine and urine protein for 24 hours were significantly decreased in the berberine treatment group compared with the diabetic model group ($P<0.05$). Berberine treatment significantly increased serum SOD activity and decreased the content of MDA compared with diabetic model group ($P <0.05$). Aldose reductase activity as well as the expression of aldose reductase mRNA and protein in the kidney was markedly decreased in the berberine treatment group compared with diabetic model group ($P <0.05$) (Liu, et al., 2008).

7. Antioxidant activity: In study effects of berberine on cultured rabbit corpus cavenosum smooth muscle cells damaged by hydrogen peroxide was studied through examining cell viability by methyl thiazolyl tetrazolium assay and assessing the level of malondialdehyde, superoxide dismutase activity, nitric oxide products, and lactate dehydrogenase release in cells after stimulation with hydrogen peroxide. Treatment with 1 mmol/L hydrogen peroxide significantly decreased the cell viability, nitric oxide products, and superoxide dismutase activity of cultured rabbit corpus cavenosum smooth muscle cells from 100% to 48.57%±4.1% ($P<0.01$), 66.8±16.3 to 6.7±2.1 μ mol/L ($P<0.01$), and 49.5±1.8 to 30.1±2.6 μ mol/mL ($P<0.01$), respectively, and increased lactate dehydrogenase release and malondialdehyde content from 497.6±69.5 to 1100.5±56.3μ mol /L ($P<0.01$) and 3.7±1.3 to 78.4±2.9 n mol/mg protein ($P<0.01$), respectively. However, treatment with different concentrations of Ber (10-1000 μ mol/L) inhibited the damaging effects of hydrogen peroxide, with increased cell viability ($P<0.05$ or $P<0.01$), nitric oxide production ($P<0.01$), and superoxide dismutase activity ($P<0.01$) and decreased lactate dehydrogenase release and malondialdehyde content (both $P<0.01$) (Tan, et al., 2007).

8. AbsorPtion of berberine: The aim of present study was to use the P-glycoprotein inhibitors cyclosporin A, verapamil and the monoclonal antibody C219 in *in vivo* and *in vitro* models of intestinal absorption to determine the role of P-glycoprotein in berberine absorption. In the rat recirculating perfusion model, berberine absorption was improved 6-times by P-glycoprotein inhibitors. In the rat everted intestinal sac model, berberine serosal-to-mucosal transport was significantly decreased by cyclosporin A. In Ussing-type chambers, the rate of serosal-to-mucosal transport across rat ileum was 3-times greater than in the reverse direction and was significantly decreased by cyclosporin A. In Caco-2 cells, berberine uptake was significantly increased by P-glycoprotein inhibitors and by monoclonal antibody C219. P-glycoprotein appears to contribute to the poor intestinal absorption of berberine which suggests P-glycoprotein inhibitors could be of therapeutic value by improving its bioavailability (Pan, et al., 2008).

Clinical studies:

***Oriental sore*:** Clinical studies have established the efficacy of hydrochloride of berberine in the treatment of oriental sore (Dhar, 1980).

***Trachoma*:** Berberine has a long history of use for eye infections. In one study that looked at effectiveness in treating trachoma, berberine was more effective than sulfacetamide in eradicating *Chlamydia trachomatis* from the eye and preventing relapse of symptoms (Babbar, 1982; Mohan, 1982).

***Congestive heart failure*:** To determine the acute cardiovascular effects of berberine in humans, 12 patients with refractory congestive heart failure were studied before and during berberine intravenous infusion at rates of 0.02 and 0.2 mg/kg per min for 30 minutes. The lower infusion dose produced no significant circulatory changes, apart from a reduction in heart rate (14%).

The 0.2 mg/kg per min dose elicited several significant changes: (a) Decreases in systemic (48%, $P<0.01$) and pulmonary vascular resistance (41%, $P<0.01$), and in right atrium (28%, $P<0.05$) and left ventricular end-diastolic pressures (32%, $P<0.01$). (b) Increases in cardiac index (45%, $P<0.01$), stroke index (45%, $P<0.01$), and LV ejection fraction measured by contrast angiography (56%, $P<0.01$). (c) Increases in hemodynamic and echocardiographic indices of LV performance: peak measured velocity of shortening (45%, $P<0.01$), peak shortening velocity at zero load (41%, $P<0.01$), rate of development of pressure at developed isovolumic pressure of 40 mmHg (20%, $P<0.01$), percent fractional shortening (50%, $P<0.01$), and the mean velocity of circumferential fiber shortening (54%, $P<0.01$). (d) Decrease of arteriovenous oxygen difference (28%, $P<0.05$) with no changes in total body oxygen uptake, arterial oxygen tension, or hemoglobin dissociation properties (Marin-Neto, et al., 1988).

***HyPercholesterolemia*:** It was reported recently that berberine lowers cholesterol through a mechanism different than that of the statin drugs, suggesting potential use both as an alternative to the statins and as a complementary therapy that might be used with statins in an attempt to gain better control over cholesterol. In a controlled Chinese study (4), it was shown that berberine, administered 500 mg twice per day for 3 months, and reduced serum cholesterol by 29%, triglycerides by 35% and LDL-cholesterol by 25%. The apparent mechanism is increasing the production of a receptor protein in the liver that binds the LDL-cholesterol, preparing it for elimination (Weijia, et al., 2004).

***TyPe 2 diabetes mellitus*:** 1. In a study, evaluating efficacy of berberine in the treatment of diabetes mellitus, dietary therapy was first introduced to the patients for one month. For those who still had high fasting blood sugar, berberine was administered orally at a dose of 300, 400, or 500 mg each time, three times daily, adjusting the dosage according to the blood glucose levels; this treatment was followed for 1–3 months. A control group without diabetes was similarly treated, with no effect on blood sugar. For the diabetic patients, it was reported that patients had less thirst, consumed less water and urinated less, had improved strength, and had lower blood pressure; the symptoms declined in correspondence with declining blood glucose levels. Laboratory studies suggest that berberine may have at least two functions in relation to reducing blood sugar: inhibiting absorption of sugars from the intestine and enhancing production of insulin (Yanxia, et al., 1995).

2. Berberine has been shown to regulate glucose and lipid metabolism *in vitro* and *in vivo*. In a pilot study efficacy and safety of berberine in the treatment of type 2 diabetes mellitus patients was studied. In study A, 36 adults with newly diagnosed type 2 diabetes mellitus were randomly assigned to treatment with berberine or metformin (0.5 g 3 times a day) in a 3-month trial. The hypoglycemic effect of berberine was similar to that of metformin. Significant decreases in hemoglobin A (1c) was observed (Yin, Xing, and Ye, 2008).

CONCLUSIONS

Berberine has definite potential as drug, since it possesses diverse pharmacological properties. Previous studies established utility of berberine as antibacterial agent. As per recent studies, the striking effect of berberine is on the cardiovascular system. Clinical trials are need of the hour for unearthing therapeutic potential of berberine.

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