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THE PHARMACOLOGICAL POTENTIAL OF BERBERINE: A REVIEW

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ABSTRACT :

In Chinese and Ayurvedic medicine, berberine is a naturally occurring yellow plant extract with a long history of therapeutic applications. It is an alkaloid found in the rhizomes, leaves, bark, stem, and roots of numerous plants, including Tinospora cordifolia and Berberis vulgaris. Berberine stimulates the AMPK enzyme, which controls biological processes that restore energy, lipid, and glucose balances. Research has indicated that berberine possesses a multitude of pharmacological properties, including anti-inflammatory, anti-viral, anti-bacterial, anti-diabetic, and anti-viral properties. For short-term usage, berberine may be safe for most humans, but it is harmful to newborns, babies, pregnant and lactating women, and people with diabetes.

Keywords: Berberine, Cardiovascular disease, Central Nervous System, Gastro intestinal tract, Anti-inflammatory

1. Introduction :

The isoquinoline alkaloid berberine (BBR), which is a member of the protoberberine alkaloids class, is produced by plants in the families Papaveraceae, Ranunculaceae, and Berberidaceae.

It can be found in the stem bark, rhizomes, and roots of many different plant species, such as Phellodendron amurense, Goldenseal (Hydrastis canadensis L.), celandine (Chelidonium), barberry (Berberis vulgaris), and meadow rue (Thalictrum). It appears as a bright yellow solid with a distinct bitter flavor that is odorless. Berberine dissolves very slightly in water, scarcely in methanol, and somewhat in ethanol. Its IUPAC name is 9,10-Dimethoxy-5,6-dihydro[1,3]dioxolo[4,5-g] isoquinolino[3,2-a]isoquinolin-7-ium. Its chemical formula is C20H18NO4 +. Its molecular weight is 336.367g/mole. The usual technique for isolating berberine involves extracting it with alcohol in neutral or acidic.

Berberine has not been employed as a stand-alone herb but rather only in polyherbal preparations in conventional and complementary medicine. Because it is not very bioavailable and has a low permeability, it has little therapeutic impact. Remarkably, the isoquinoline skeleton that makes up berberine's chemical structure provides a scaffold that makes it easier to rationally build and functionalize a variety of derivatives. Researchers have been able to obtain derivatives of berberine that have valuable pharmacological qualities using a variety of chemical transformation processes. It is vital to summarize the findings of pertinent research investigations on synthetic berberine derivatives in order to support the effective development of berberine-based pharmaceutical products. In addition to the medicinal uses of berberine in many traditional medical systems, studies in the scientific community have verified its pharmacological actions and characteristics (pharmacokinetic and toxic).

2. PHARMACOLOGICAL ACTIONS OF BERBERINE :

2.1 CARDIOVASCULAR EFFECTS

2.1.1 Heart failure

Congestive heart failure, another name for heart failure, is the result of the heart muscle failing to pump blood. The heart can become weak due to high blood pressure and heart artery narrowing (1). According to one study, berberine may have enhanced heart function by raising the amount of calcium in heart muscle cells. Because of its impact on potassium channels, berberine raises the high energy phosphate in heart failure patients. Berberine decreased the delay in depolarization caused in part by sodium influx and prevented ventricular fibrillation. Additionally, berberine improved cardiac contractility in rats used in experiments by lowering plasma noradrenaline, adrenaline, and adrenaline levels in ventricular tissue. Nitric oxide, which relaxes the arteries, boosts blood flow, reduces blood pressure, and guards against atherosclerosis, is released when berberine is stimulated (2).

2.1.2 Atherosclerosis

This illness disrupts blood flow throughout the body, which increases the possibility of life-threatening consequences. The first step is monocyte attachment to the endothelium leading to the development of atherosclerosis. Berberine lowers pro-inflammatory cytokines caused by hyperglycemia and involved in the development of atherosclerotic plaques. It also decreases the amount of adhering monocytes on endothelial cells (3).
Berberine inhibits the activation of the unfolded protein response and the inflammatory response in macrophages, thereby preventing HIV protease inhibitor-induced atherosclerosis (1).

2.2 CENTRAL NERVOUS SYSTEM

2.2.1 Alzheimer's

Alzheimer's is a degenerative illness that progressively impairs memory and other critical mental abilities. Its symptoms gradually appear, impacting the brain and degenerative, resulting in a gradual deterioration. Alzheimer's disease is influenced by a number of risk factors, including diabetes, hypertension, and dyslipidemia. By addressing these risk factors, the severity of Alzheimer's will be reduced. By reducing the impact of these risk factors and enhancing the metabolic syndrome linked to Alzheimer's disease, berberine is thought to be a viable treatment strategy to prevent and delay the onset of the disease (4).

2.2.2 Depression

Millions of people worldwide suffer from common, persistent, recurrent mental illnesses known as mood disorders. Bipolar disorder and major depressive disorder are the two main types of mood disorders. The majority of patients with mood disorders benefit in some way from the therapies that are offered. However, because of the complicated pathophysiology, complete remission of clinical symptoms is uncommon. It has recently been demonstrated that the herbal medication berberine, which is used in traditional Chinese medicine, can help with a variety of mood disorders. Thus, berberine may eventually find widespread use as a medication to treat mood disorders. Berberine is beneficial for a number of neuropsychiatric and neurodegenerative conditions. Recent research indicates that berberine has a protective effect on disorders of the central nervous system and that it can easily cross the blood-brain barrier when administered systemically (5). Inhibitors of monoamine oxidase are a significant class of antidepressants. Depression is caused by a deficiency in this particular enzyme, which breaks down neurotransmitters like dopamine, noradrenaline, and serotonin in the neural tissue. Berberine can reduce the symptoms of depression by blocking the activity of monoamine oxidase. (1)

2.2.3 Diabetes mellitus

An endocrine system metabolic disorder is diabetes mellitus (DM) (6). Diabetes mellitus (DM) is a metabolic disease characterized by elevated blood sugar levels in patients (also referred to as hyperglycemia) brought on by abnormalities in the body's metabolism of proteins, fats, and carbohydrates (7) A balanced diet, sensible exercise, the use of oral hypoglycemic medications, and/or subcutaneous insulin injections are all part of the standard treatment for type 2 diabetes (6). According to one study, berberine can reduce diabetes and its complications by acting on multiple targets and signaling pathways. This makes it a useful therapeutic antidiabetic agent. According to a molecular docking study, berberine exhibits a lower binding affinity value than standard vildagliptin to dipeptidyl peptidase-IV (DPP-IV). However, compared to acarbose, the standard inhibitor of amylase, berberine has a lower binding affinity value. Based on these research findings, it can be inferred that berberine is not as effective as its standard medication when used in enzymatic antidiabetic therapy. (7)

2.3 GASTROINTESTINAL TRACT

2.3.1 Liver Fibrosis

Liver fibrosis is the excessive accumulation of extracellular matrix proteins including collagen that occur most types of chronic liver diseases (1). By triggering ferrous-ion redox reactions to trigger reactive oxygen species (ROS)-mediated ferroptosis in hepatic stellate cells, BBR reduces liver fibrosis and raises the possibility of a liver fibrosis treatment plan. Effects of BBR were also shown in liver fibrosis models generated by carbon tetrachloride (CCl_4).The multi-targeted mode of action of BBR may be responsible for its efficacy against several chronic illnesses. Liver fibrosis is primarily caused by oxidative stress and inflammation, and BBR has been shown to have anti-oxidative and anti-inflammatory properties (12)

2.3.2 Non-Alcoholic Fatty Liver Disease (NAFLD)

abnormal accumulation of lipids in nonadipose tissues (steatosis), known as nonalcoholic fatty liver disease (NAFLD), a chronic condition that is currently the leading cause of referrals to hepatology clinics (13). Clinical research and experimental models both suggest that berberine may be a useful treatment for NAFLD. In hyperlipidemic hamsters, berberine significantly lowers liver fat accumulation. In mice fed a high-fat diet (HFT), berberine lowers hepatic steatosis and reduces liver lipid content by 14%. Additionally, it has been demonstrated to lessen liver necrosis in steatosis caused by hepatitis C infection as well as non-alcoholic steatosis (1).

2.4 ANTI INFLAMMATIOR EFFECT

2.4.1 Bacterial Infection

Berberine has antidiabetic, antidiarrhoeal, antimicrobial, immuno-stimulating, hypotensive and anti-inflammatory properties (14). The majority of research on berberine's antibacterial action has been on its bacteriostatic and/or bactericidal effects on various bacterial species. According to reports, berberine is more active against Gram-positive bacteria and less effective against Gram-negative ones. The blocking of various bacterial resistance mechanisms, such as the bacterial efflux pump inhibitory effect of berberine compounds, may be the cause of the interaction of berberine with various antimicrobial drugs (15)

2.4.2 Parasitic Infection

BBR targets various stages of the viral life cycle, making it an ideal target for novel antiviral drug and therapy development. BBR has been demonstrated to inhibit viral replication and target specific interactions between virus and host. It intercalates with DNA, inhibiting DNA synthesis and reversing the activity of reverse transcriptase. BBR inhibits viral replication of HSSV, HCMV, HPV, and HIV. This alkaloid has been shown to regulate the metabolic enzyme MEK-ERC, the metabolic enzyme AMPK/MTOR, and the metabolic enzyme NF-κB, which are essential for virus replication (16).

3. SIDE EFFECTS OF BERBERINE :

Due to the low toxicity rating of berberine, there are not many side effects to be aware of. In animal studies, berberine has been found to be very low in toxicity and side effects. However, due to the risk of brain damage caused by bilirubin, it is important that jaundice infants, pregnant women and nursing women do not consume berberine or berberine-containing plants. Allergic reactions after intravenous administration have been reported.
The side effects associated with the use of berberine are:

- Digestion
- Cramping
- Diarrhea
- Flatulence
- Constipation
- Stomach pain

4. CONCLUSION :

From the protoberberine group of benzylisoquinoline alkaloid, berberine is a quaternary ammonium salt found in many medicinal plants that have been utilized extensively for hundreds of years in traditional Chinese medicine. Numerous studies have shown that species are abundant in alkaloids, the main and perhaps most potent of which is berberine, which is biologically active. Current studies have demonstrated that berberine exhibits a number of pharmacological actions via diverse routes. It is a natural medication used clinically for a variety of illnesses and pathological situations, including diabetes, PCOS, cancer, atherosclerosis, Alzheimer's disease, and bacterial and viral infections. In standard dosages, it has very low toxicity and provides therapeutic advantages without significant adverse effects. It might provide information for upcoming drug development and discovery efforts.

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