

Boerhavia erecta: A Phytopharmacological Potential in Gall Stone Prevention- A Review on Hepatoprotective, Choleric and Lipid Modulating Mechanism

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ABSTRACT

Gallstone disease affects ten to twenty percent of the global population and is characterized by oxidative stress, inflammation, bile stagnation, and cholesterol saturation. Amongst the hepatoprotective *Opuntia* relatives, the same phytochemicals (betalains, flavonoids, phenolics, and mucilage) are shared with *Boerhavia erecta*, a member of the Cactaceae family that has been traditionally used for gallbladder conditions and jaundice. This review summarizes the evidence from related Cactaceae: In CCl₄ models, extracts from *Opuntia ficus-indica* decrease liver enzymes (ALT/AST), trap ROS by Nrf2/HO-1 activation, block COX-2/TNF- α inflammation, reduce serum cholesterol (15-61%) through phytosterol/fiber binding, enhance bile flow (20-50% increase), and regulate blood glucose (20-46% glucose drop). In toxicity models with choleric effects, the roots of *Boerhavia erecta* normalize bilirubin and proteins. *Boerhavia erecta* is a potential herbal supplement for gallstone prevention as integrated processes target enterohepatic dysregulation. Clinical validation is needed.

Keywords: Gall stone, *Boerhavia erecta*, oxidative stress, cholesterol saturation..

INTRODUCTION

Gallstone disease is one of the most prevalent digestive disorders that result from the disruption of the bile mixture. The key factors of this disease are gallbladder dysfunction, oxidative damage, inflammatory processes, lack of bile salts, and the excess of cholesterol^[1-2]. Excess cholesterol in the bile leads to the process of crystallization and ultimately the formation of gallstones that may block the ducts carrying bile. Due to the invasiveness of the traditional treatments, the surgical removal of the gallbladder (cholecystectomy) being the most common one, there is consequently a rising interest in the search for herbal or plant-based alternatives that can provide a therapeutic effect without the need for such procedures.

Boerhavia erecta, which belongs to the Cactaceae family, is said to possess one of the plant species with the ability to alleviate gallstone disease due to its liver-protecting and bile-modifying properties. This

species of cactus is considered by herbal medicine to be one of the most effective plants for treating gallbladder stones and jaundice and may have similar therapeutic potential as other cactus species known for their liver-protecting property^[3]. Of great interest, some Cactaceae species, like *Opuntia ficus-indica*, *Nopalea cochenillifera*, and *Hylocereus polyrhizus*, have been the source of promising biological pretreatment with regard to gallstone prevention through liver protection, antioxidation, and choleric effects^[4-7-9].

Plant Profile:

Kingdom	Plantae
Clade	Angiosperms
Clade	Eudicots
Order	Caryophyllales
Family	Nyctaginaceae
Genus	<i>Boerhavia</i>
Species	<i>Boerhavia erecta</i> L

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Figure 1: *Boerhavia erecta*

Phytochemical Profile of *Boerhavia erecta*

Flavonoids	quercetin, kaempferol, isorhamnetin ^[7-8]
Betalains	betanin, indicaxanthin ^[8-9]
Phenolic acids	ferulic, p-coumaric, Gallic ^[9]
Polysaccharides & mucilage	improve digestion and bile flow ^[16]

Key Phytochemicals Present in *Boerhavia erecta*:

- **Flavonoids:** The mentioned class includes substances such as isorhamnetin, kaempferol, and quercetin. The anti-inflammatory and antioxidant properties of these substances are well acknowledged^[7-12]. They play a role in the detoxification of free radicals which in turn prevents the liver and gallbladder from oxidative damage.
- **Betalains:** Betanin and indicaxanthin are the two most notable betalains found in *Boerhavia erecta*. These pigments are also contributors to the plant's overall anti-inflammatory properties and they are also very potent antioxidants^[12-3]. Due to their property of stabilizing cell membranes, especially the hepatocyte membranes, the liver might benefit from the protection against oxidative stress-induced damage that comes with the presence of betalains.
- **Phenolic Acids:** These are made up of gallic acid, ferulic acid, and p-coumaric acid-like substances. According to Tenore et al. (2012), the phenolic acids are really strong

antioxidants that let oxidative stress and inflammation go. Besides, they have the power to affect lipid metabolism life-style and even pull the plug on cholesterol.

- **Mucilage and polysaccharides:** It is said that these substances can lead to an increase of bile flow and digestion, potentially avoiding bile stasis and stirring up bile secretion, the two processes that are very important for the prevention of gallstones^[16]. Mucilage from the cactus species also improves the digestive by providing less acid reflux and supporting gut health.

3. Hypothesis

Opuntia ficus-indica has flavonoids and betalains that have been proved to be able to inhibit liver oxidative stress, inflammatory mediators such as COX-2 and TNF- α , and improve lipid metabolism that lowers bile cholesterol saturation and formation of gallstones^[7-4-12]. Other mechanisms that enhance bile production and inhibit intestinal absorption of cholesterol add to the hypolipidemic and choleretic properties of phenolic acids and cactus polysaccharides^[8-16]. It is not so irrational to hypothesize that perhaps *Boerhavia erecta* can offer the same preventive advantages in gallstone disease considering that it has identical phytochemical composition to the previous plant mentioned above.

4. Pharmacological Operations Pertinent to Gallstones

The numerous factors that contribute to gallstone disease include the various factors of bile composition, oxidative stress, inflammation, and the malfunctioning of the gallbladder along with the metabolic abnormalities. Medicinal plants that are capable of influencing these pathogenic pathways might offer non-invasive options for managing and preventing gallstones effectively. *Boerhavia erecta* is believed to possess several pharmacological activities that are associated with gallstones, such as hepatoprotective, antioxidant, anti-inflammatory, hypolipidemic, choleretic, and metabolic regulatory effects, owing to its phytochemical similarities with other members of the Cactaceae family. The effectiveness of these actions is supported by

considerable evidence from the closely related cactus species [1-2].

4.1 Hepatoprotective Action

The liver has several important roles, one of which is the production of bile acids and the regulation of cholesterol levels in the body. One of the major factors leading to the formation of gallstones is the hepatic dysfunction which results in the bile being supersaturated with cholesterol. The various cactus species have been extensively studied and proved to have hepatoprotective effects through their antioxidant actions and stabilizing the cell membranes. In the case of feeding liver toxins to experimental animals, the administration of *Opuntia ficus-indica* extracts significantly lowered the blood levels of hepatic enzymes ALT, AST, and ALP, which points to the preservation of liver cell integrity^[4]. The flavonoids and betalains acting as antioxidants and the liver cell membrane protectors are being credited with these protective effects, which also include the prevention of oxidative damage^[6]. In addition, the scientific evidence indicates that the use of plant-derived antioxidants can mitigate the damage done to the liver by free radicals and also help restore the normal process of bile synthesis and secretion^[12]. *Boerhavia erecta* might very well possess similar hepatoprotective benefits when one considers its phytochemical similarities to other cactus species which might have an indirect effect on altering bile composition abnormalities related to gallstone disease^[3-1].

4.2 Activity of Antioxidants

Oxidative stress, by promoting lipid peroxidation, gallbladder epithelium damage, and cholesterol crystal nucleation, has an important role in the development of the pathophysiology process of gallstones. There is an indication that oxidative markers have increased in patients suffering from gallstone disease^[10].

- Antioxidant substances, and among them the most important are betalains, flavonoids, and phenolic acids, are very common in cactus species. Betalains, such as betanin and

indicaxanthin, in biological membranes have very high ability to be free radical scavengers and prevent lipid peroxidation^[7].

- Because of the activity of phenolic substances like ferulic acid and gallic acid in the antioxidant protection area, the defense against ROS is further enhanced^[9].
- *Boerhavia erecta* may impede the early cholesterol nucleation events and protect the gallbladder epithelium from oxidative injury by reducing oxidative stress in the liver and biliary tissues, thus leading to a lower incidence of gallstone formation^[5].

4.3 Anti-inflammatory Effects

The chronic inflammation of the gallbladder wall is a contributing factor to gallstone formation as it increases mucin secretion and supports the holding of cholesterol crystals. Among the pro-inflammatory mediators that are involved in this process are TNF- α , IL-6, nitric oxide, and cyclooxygenase. Cactus extracts have been reported to significantly counteract inflammation via cessation of COX-2 function and downregulation of pro-inflammatory cytokine production^[11-12]. Polysaccharides from cactus diminish chronic inflammatory reactions by blocking inflammatory signals and nitric oxide production^[1]. These findings indicate that *Boerhavia erecta* might offer relief from gallbladder inflammation, intervene in the pathological remodeling of the biliary epithelium, and block the inflammatory cascade that accelerates the formation of gallstones^[11-13-22].

4.4 Activity that Lowers Cholesterol and Hypolipidemia

One of the main factors contributing to the formation of cholesterol gallstones is the presence of high cholesterol in the blood. The rise in blood cholesterol levels results in the liver transferring more cholesterol into the bile, thus leading to bile supersaturation. The consumption of cacti has been indicated in various research studies as one of the most effective ways to lower blood triglycerides, LDL cholesterol, and total cholesterol. Dietary fibers and mucilage from cacti work by decreasing the absorption of cholesterol in the intestines and increasing the excretion of bile acids



in feces^[14]." Phenolic compounds do the same by lowering fat deposition in the liver and modulating lipid metabolism^[16]. *Boerhavia erecta* may not only lower cholesterol but also influence metabolic pathways in the liver, hence, reducing biliary cholesterol saturation and the risk for cholesterol gallstone formation^[14-17].

4.5 Digestive and Choleric Activity

Bile stasis due to reduced bile flow or ineffective gallbladder contractions is one of the major factors contributing to the formation of gallstones. Choleric medications enhance biliary drainage and boost bile flow. As per the findings of studies performed on animals, cactus extracts have a positive effect on the bile formation and the acids in the bile have been altered so that less sludge is formed^[18-19]. The mucilage of cactus species assists in the emptying of the gallbladder thus, improving digestion which leads to a shorter period of bile retention^[16-23]. These properties indicate that *Boerhavia erecta* might be able to provide the right composition of bile for the prevention of gallstones, to avoid biliary stasis and to promote healthy bile flow^[16-18-19].

4.6 Modulating Effects on Metabolic Syndrome and Antidiabetes

The connection between gallstone disease and metabolic syndrome, which is characterized by obesity, insulin resistance, and diabetes mellitus, is very strong^[20]. Insulin resistance is responsible for the reduction of gallbladder activity as well as the increase of cholesterol production in the liver. Cactus species have shown remarkable antidiabetic activity by lowering postprandial blood glucose levels and increasing insulin sensitivity^[15-17-21]. Metabolic regulation takes away the hepatic lipogenesis and cholesterol release into bile. Thus, it can be said that the ever-increasing glucose metabolism and the decrease of metabolic risk factors by the plant can offer indirect support against the gallstone formation^[15-17-20-21].

5. Combined Mechanism of Action for Preventing Gallstones

Boerhavia erecta, through its synergistic phytochemical effects that tackle oxidative stress,

inflammation, bile stasis, and cholesterol supersaturation in the enterohepatic circulation, lowers the production of gallstones. Flavonoids and betalains protect hepatocyte integrity and bile acid production via upregulating CYP7A1, besides activating the Nrf2/HO-1/NQO1 pathways and upregulating GSH, GPx, and GR to reduce ROS and lipid peroxidation.

Molecular Routes

- Taxifolin and betalains (betanin) neutralize biliary nucleation promoters by DPPH/ABTS radical trapping (TEAC > vitamin E), iron chelation, GSH pool restoration, and Nrf2-mediated detoxification enzyme (HO-1, NQO1, GST) induction^[7-10].
- Hepatic/gallbladder inflammation: Through the control of PPAR γ , polysaccharides not only rescind mucin hypersecretion and crystallization in the inflammatory mucosa but also inhibit the production of NF- κ B, COX-2, TNF- α , IL-6, and NO, thus suppressing the inflammation in the affected area^[11-13].
- Hepatocyte protection/bile acid synthesis: extracts are actively preventing the liver cell damage in CCl₄ model by maintaining the balance of glycogen and GSH, as well as increasing the size of the bile acid pool through the FXR/CYP7A1 pathway. As a result, a range of abnormalities reflected in the levels of ALT/AST/ALP, bilirubin, and proteins are corrected^[4-6].

Physiological Impacts

- Bile secretion/flow: One of the key physiological impacts of mucilage (Mw $\sim 3 \times 10^6$ Da) is the increase in intestinal transit, gallbladder contractility and bile volume coupled with acid production up to 50%. The shear-thinning gels and cholagogue activity further assist in reducing stasis/sludge^[16-18].
- Fiber and phytosterols are hip and get active by blocking HMG-CoA/NPC1L1 as well as increasing the pool of bile acids which



consequently leads to the lowering of the saturation index. The mechanism includes intestinal cholesterol binding, PPAR γ -LXR α -ABCA1/G1 activation (15-61% LDL decrease), and HMG-CoA/NPC1L1 blocking [14-17].

- **Metabolic/glycemic regulation :** The combination of insulin sensitization and α -glucosidase inhibition (IC₅₀ 67 μ g/mL) results in the reduction of hyperglycemia (20–46%) which in turn lowers the prevalence of obesity-related BA deficiency and lithogenicity. The processes mentioned above are highly interdependent: on the one hand, lipid regulation is leading to the production of less lithogenic bile; on the other hand, choleretic/mucilage actions are efficiently removing the sludge; while Nrf2/antioxidants are protecting the BA synthesis thus reducing the entry of cholesterol [15-20-21].

6. Discussion

Gallstone disease is one of the diseases that affects the digestive system the most, with a pathophysiological process that is very complicated, consisting of bile supersaturation, gallbladder dysmotility, oxidative stress, inflammation, and metabolic abnormalities. The surgery is still considered the last resort in treatment, but the interest in non-invasive and preventive methods has led to the research of medicinal plants with hepatobiliary protective potential. A cactus species, in particular, *Boerhavia erecta*, which has a common phytochemical profile with well-known ones, is featured as an option in this context, although it is the least studied among the Cactaceae family.

A variety of research has proven that oxidative stress plays a major role in gallstones' formation by promoting the peroxidation of lipids and the precipitation of cholesterol in bile. It has been found that gallstone patients have higher levels of oxidation markers, thus emphasizing the need for antioxidant management. The compounds derived from cacti namely betalains, flavonoids and phenolic acids, possess strong antioxidant properties by quenching reactive oxygen species and protecting cell

membranes. Since its phytochemical profile is similar to that of related species like *Opuntia ficus-indica*, the effects attributed to these antioxidants are likely to be seen in *Boerhavia erecta* as well. The inflammation of gallbladder epithelium that leads to increased mucin production and cholesterol crystal trapping is one more factor that contributes to gallstone formation. According to the studies, cactus polysaccharides and betalains are effective in preventing the production of pro-inflammatory cytokines, nitric oxide, and cyclooxygenase activity.

Dysregulated lipid metabolism is another major characteristic of the gallbladder disease. The excess bile is due to the hypercholesterolemia's marked increase in biliary cholesterol production. As per several studies, Cactus species decrease blood cholesterol and triglyceride levels by dietary fiber-mediated reduction of cholesterol absorption and hepatic lipid metabolism modification. *Boerhavia erecta* may decrease the frequency of cholesterol gallstone production by the reduction of the cholesterol saturation index of bile through the improvement of lipid profiles. Preventing bile stasis, a precursor to gallstones, needs both increased bile flow and choleretic activity. In the case of cactus extract, experimental research has resulted in increased bile output and a change in the bile acid composition. The polysaccharides in cactus species are mucilaginous, and they are responsible for gallbladder emptying facilitation, thus reducing the duration of bile retention. These measures might reduce the harm done to the gallbladder wall and prevent the subsequent chronic inflammation that promotes the development of gallstones. The proppant status of *Boerhavia erecta* as a gallstone disease prevention facilitator is additionally supported by these digestive and choleretic impacts.

Nowadays, diabetes mellitus and metabolic syndrome are recognized as major contributors to the development of gallstones. Insulin resistance leads to sluggishness of the gallbladder and increased cholesterol secretion from the liver. On the other hand, the antidiabetic effects of cactus species like *Boerhavia erecta*, including enhancement of insulin sensitivity and reduction of blood glucose, may point to its indirect protective role against gallstone disease caused by metabolic factors. However, the limits of



the available data must be acknowledged despite these promising signals. The antidiabetic ability of cactus species that prevent gallstones mostly comes from researches on related species or experimental animals rather than direct research on *Boerhavia erecta*. In order to establish its therapeutic efficacy, standardization of extracts, identification of bioactive markers, and validation through in vivo gallstone models and clinical trials are still essential.

7. Conclusion

The review brings to light the multifunctionality of *Boerhavia erecta* as a medicinal herb to be considered for gallstone disease management and prevention. According to the information from the closely related Cactaceae family, *Boerhavia erecta* is expected to exert various actions such as hepatoprotective, antioxidant, anti-inflammatory, hypolipidemic, choleretic, and metabolic regulation all at once, thus covering the major steps of gallstone creation. *Boerhavia erecta* can be the non-intrusive, safe, and cost-effective option in addition to the gallstone treatments that are based on bile homeostasis restoration, oxidative stress and inflammation reduction, lipid metabolism improvement and bile flow increase. Although the outcomes are promising, further experimental and clinical studies are required for the validation of its efficiency, formulation standardization and dosage method identification.

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