

Choleretic and Cholagogic Effects of Anticholelithiatic Plants

Subjects: **Gastroenterology & Hepatology**

Contributor: Salman Ahmed

A large number of people suffer from gall stone worldwide and this problem is now being increased significantly due to the malnutrition, changes in living style, lack of exercise and conditions *i.e.* industrialization. Medicinal plants are used from centuries due to their cultural acceptability, efficacy, safety and fewer side effects as compared to modern synthetic medicines.

Gall stone

anticholelithiatic

choleretic

cholagogue

ethnomedicine

1. Introduction

Gallstone is a worldwide problem. Its pervasiveness gives off an impression of being higher in Western world (>10%) than in Asian countries (3–10%). Female sex, older age, hyperlipidemia, higher body mass index (BMI), diabetes mellitus and alcohol consumption have been accounted for as danger factors for gallstone problem. Cholelithiasis (gallstone formation) is generally found in adults as compared to children. The frequency of gall stones among children is 1.9%. About 10 - 20% adult population of Western countries suffers from gall stones ^[1].

The gallbladder is a sac situated under the liver. It stores and concentrates the bile, produced in the liver. Bile acids play an important role in the assimilation of fats and is delivered from the gallbladder into the upper small digestive tract (duodenum) in response to food, especially fats. Development of stones inside the gall bladder is known as cholelithiasis. In this condition, hard stones of cholesterol or bile pigments are formed in the gallbladder. If these stones are found in the common bile duct, the condition is known as choledocholithiasis. Most of the stones are composed of cholesterol ^[2].

Bile is composed of bile salts, cholesterol and lecithin. It is present in a solution form by a delicate harmony. The proportion between bile salts and cholesterol is very important. In bile, cholesterol is in equilibrium with bile salts and with phosphatidylcholine. When the cholesterol becomes too concentrated in the bile then it saturates the bile acids and start to form crystals. As a result, a sludge is formed which contains cholesterol, calcium salts, mucin, and bilirubin and ultimately stones are developed ^[3].

2. Choleretic and Cholagogic Effects of Anticholelithiatic Plants

It is reported that the gallbladder smooth muscle (GBSM) bundles and their associated contractions are responsible to form gallbladder tone. The gallbladder performed a motor function, with 20-30% emptying at 1-2 hrs. intervals during the fasting state while 70–80% emptying after stimulation by cholecystokinin (CCK) when a diet is taken. The gallbladder contraction and relaxation is very important in driving the flow of bile salts in enterohepatic circulation and facilitate the absorption of lipids and fat-soluble vitamins. It is observed that changes occur in gallbladder smooth muscles in the gallbladder harboring lithogenic bile prior to inflammation and stone formation. Many factors are responsible in the pathogenesis of gallstone disease in which, gallbladder hypomotility and the resultant prolonged stasis of lithogenic bile are the most important. This malfunction is a very early event in the development of Gallstone disease, which occurs only in a few days after the onset of the lithogenic diet and becomes worse as the ailment progresses from microlithiasis to gallstones. Muscle contractility is diminished in gallbladders from patients with cholesterol stones. Impaired emptying of gallbladder may results in prolonged stasis of lithogenic bile in the gallbladder, which allows more time and a permissive environment for cholesterol crystallization and aggregation of that cholesterol into macroscopic gallstones.

A longer stay of bile in the gallbladder may lead to its hyperconcentration by gallbladder epithelial cells (GBECs). Increase in secretion of pro-nucleating mucins by GBECs is considered as an important factor responsible for gallstone formation. The gel-forming mucins made favorable environment for gallstone formation as it accelerate the nucleation of cholesterol monohydrate crystals from supersaturated bile ^[4]. There are three important factors responsible for cholesterol gallstone formation, bile composition (in particular cholesterol supersaturation and hydrophobic bile salts), factors promoting cholesterol crystallization (e.g. certain biliary proteins) and impaired gall bladder motility. In cholesterol gallstone disease, elevated biliary concentrations of cholesterol and hydrophobic bile salts are associated with biliary stasis. The main features of gallstone problems are biliary cholesterol elevation, cholesterol stones, decreased gallbladder contractility and cholecystitis ^[5]. Improving gallbladder motility with a prokinetic agent leads to a significant reduction in cholesterol crystallization. Gallbladder motility is promoted or increase or stimulated by CCK (Cholecystokinin) release, CCK receptor stimulation and decrease inflammation ^[6]. Medicinal plants having hepatobiliary effect are important therapeutic agents for cholestasis. These are called as choleretics (increasing bile production) and cholagogues (promoting the flow of bile from the liver and gall bladder into the intestines) ^[7].

Table 1 shows the anticholelithiatic plants with choleretic effects.

Table 1. Anticholelithiatic plants with choleretic effects.

Medicinal plants	Part/Mode of preparation
<i>Acorus calamus</i> L.	Rhizomes ^[8]

<i>Achillea millefolium</i> L.	Aerial parts [9] [10]
<i>Agrimonia eupatoria</i> L.	Leaves infusion and decoction [11]
<i>Ajuga iva</i> (L.) Schreb.	Leaves infusion [12]
<i>Allium cepa</i> L.	Bulb extract [13]
<i>Alpinia officinarum</i> Hance.	Roots [14]
<i>Amomum compactum</i> Sol. ex Maton.	Roots and rhizome [14]
<i>Andrographis paniculata</i> (Burm.f.) Nees.	Whole plant [9] [15]
<i>Apium graveolens</i> L.	Fruits and seeds [14]
<i>Armoracia rusticana</i> P.Gaertn., B.Mey. & Scherb.	Leaves [14]
<i>Artemesia absinthium</i> L.	Leaves [16]
<i>Artemesia capillaris</i> Thunberg.	Aerial parts [17] [18] [19]
<i>Artemisia abrotanum</i> L.	Aerial parts [17]
<i>Artemisia absinthium</i> L.	Whole plant [8] , Leaves decoction [12]
<i>Artemisia arborescens</i> (Vaill.) L.	Leaves decoction [12]
<i>Artemisia scoparia</i> Waldst. & Kitam.	Aerial parts [17] [20] [21] [22]

<i>Artemisia vulgaris</i> L.	Leaves [9] [16]
<i>Azadirachta indica</i> A. Juss.	Leaves [23]
<i>Boerhaavia diffusa</i> L.	Whole plant [24]
<i>Buplureum rotundifolium</i> Griffithii.	Aerial parts [17]
<i>Camellia sinensis</i> Kuntze.	Leaves [18]
<i>Canscora decussata</i> (Roxb.) Roem. & Schult.	Roots and rhizomes [17]
<i>Cercis siliquastrum</i> L.	Seeds [17]
<i>Cichorium endivia</i> L.	Flowers [25]
<i>Cinnamomum verum</i> J. Presl.	Bark [14]
<i>Cirsium arvense</i> (L.) Scop.	Leaves and roots decoction [26]
<i>Cnicus benedictus</i> L.	Whole plant [27]
<i>Coptis chinensis</i> Franchet.	Rhizome [18]
<i>Crocus sativus</i> L.	Flower petal [14]
<i>Curcuma longa</i> L.	Roots [14] [28]
<i>Cynara scolymus</i> L.	Leaves and roots [29]

<i>Dioscorea villosa</i> L.	Roots ^[30]
<i>Dipteryx odorata</i> (Aubl.) Willd.	Seeds ^[14]
<i>Eclipta alba</i> (L.) Hassk.	Whole plant ^[31]
<i>Elaeocarpus ganitrus</i> Roxb. ex G.Don.	Leaves ^[9]
<i>Euonymus europaeus</i> L.	Root bark ^[16]
<i>Euphorbia palustris</i> L.	Aerial parts ^[17]
<i>Euphorbia stepposa</i> Zoz ex Prokh.	
<i>Fumaria capreolata</i> L.	
<i>Fumaria officinalis</i> L.	Whole plant infusion ^[12]
<i>Galium aparine</i> L.	Aerial parts ^[9]
<i>Gardenia jasminoides</i> J.Ellis. & <i>Gardenia fructus</i>	Fruits ^[32]
<i>Gentiana lutea</i> L.	Roots ^[33]
<i>Gentiana manshurica</i> Kitag.	Roots and rhizome ^[34]
<i>Gentiana scabra</i> Bunge.	Roots ^[18]
<i>Gnaphalium uliginosum</i> L.	Whole plant ^[8]

<i>Hibiscus sabdariffa</i> L.	Flowers [9]
<i>Hypericum perforatum</i> L.	Aerial parts [28]
<i>Inula helenium</i> L.	Roots decoction [26]
<i>Kaempferia galanga</i> L.	Rhizome [14]
<i>Lapsana communis</i> L.	Whole plant extract [26]
<i>Lindera benzoin</i> (L.) Blume	Leaves [14]
<i>Linum usitatissimum</i> L.	Seed decoction [35]
<i>Lippia integrifolia</i> (Griseb.) HIERON	Aerial parts [36]
<i>Mentha × piperita</i> L.	Leaves decoction [37] [38]
<i>Mentha piperita</i> L.	Leaves [8]
<i>Mentha pulegium</i> L.	Whole plant [18]
<i>Menyanthes trifoliata</i> L.	Leaves [8]
<i>Momordica subangulata</i> Blume	Leaves [39]
<i>Moringa oleifera</i> Lam.	Seeds [14]
<i>Naregamia alata</i> Wight & Arn.	Whole plant [39]

<i>Nasturtium officinale</i> R.Br.	Fresh plant as salad [27] [14]
<i>Nigella sativa</i> L.	Seeds [14]
<i>Persea americana</i> Mill.	Fruits, Leaves [14]
<i>Phellodendron amurense</i> Rupr.	Bark [18]
<i>Phyllanthus rheedei</i> Wight.	Whole plant [40]
<i>Pinellia ternata</i> (Thunb.) Makino.	Rhizomes [41]
<i>Plantago major</i> L. / <i>Plantago asiatica</i> L.	Seeds [17]
<i>Polygonum bistorta</i> (L.) Samp.	Whole plant [42]
<i>Prunus dulcis</i> (Mill.) D.A.Webb.	Seeds oil [14]
<i>Raphanus sativus</i> var. <i>niger</i> (Mill.) J.Kern.	Root juice [43]
<i>Reseda luteola</i> L.	Flowers [17]
<i>Rheum palmatum</i> L.	Roots [27]
<i>Rheum paltatum</i> L.	Roots [18] [21]
<i>Rhus coriaria</i> L.	Leaves [14]
<i>Rubia peregrina</i> L.	Roots infusion [12]

<i>Saussurea amara</i> (L.) Candolle.	Aerial parts [44]
<i>Schisandra chinensis</i> (Turcz.) Baill.	Berries [45]
<i>Scutellaria baicalensis</i> Georgi.	Roots [18] [19] [21]
<i>Silybum marianum</i> (L.) Gaertn.	Leaves [16]
<i>Solanum melongena</i> L.	Fruits [46]
<i>Sophora flavescens</i> Aiton.	Roots [19]
<i>Syringa oblata</i> Lindley, Gard. Chron.-	Leaves [17]
<i>Tanacetum vulgare</i> L.	Flowers [8]
<i>Taraxacum mongolicum</i> Handel-Mazetti.	Whole plant [18]
<i>Taraxacum officinale</i> (L.) Weber ex F.H.Wigg.	Leaves [8]
<i>Tecomella undulata</i> (Sm.) Seem.	Bark [9]
<i>Theobroma cacao</i> L.	Beans [14]
<i>Tilia platyphyllos</i> Scop.	Bark [17]
<i>Trigonella foenum-graecum</i> L.	Seeds [14]
<i>Uncaria gambir</i> (W.Hunter) Roxb.	Leaves [17]

	Berries [8]
<i>Zea mays</i> L.	Cobs and corn silk [8]
<i>Zygophyllum coccineum</i> L.	Leaves [17]
<i>Zygophyllum gaetulum</i> Emb. & Maire	Leaves decoction [12]

Table 2 shows the anticholelithiatic plants with cholagogic effects.

Table 2. Anticholelithiatic plants with cholagogic effects.

<i>Meyna laxiflora</i> Robyns	Fruits decoction [9]
<i>Moringa oleifera</i> Lam.	Leaves, seeds and roots [47] , Flowers [48]
<i>Moringa pterygosperma</i> Gaertn.	Flowers [9]
<i>Naregamia alata</i> Wight & Arn.	Roots [9]
<i>Nyctanthes arbor-tristis</i> L.	Leaves [9]
<i>Ononis arvensis</i> L.	Aerial parts [17]
<i>Patrinia villosa</i> (Thunb.) Juss.	Roots [49]
<i>Persea americana</i> Mill.	Fruits [14]
<i>Phyllanthus amarus</i> Schumach. & Thonn. / <i>Phyllanthus niruri</i> L.	Leaves [50]

<i>Pimpinella saxifraga</i> L.	Leaves, roots [9]
<i>Piper longum</i> L.	Fruits [51]
<i>Piper nigrum</i> L.	Fruits [14]
<i>Platycodon grandiflorum</i> (Jacq.) A.DC.	Roots [52]
<i>Polypodium vulgare</i> L.	Rhizome [9]
<i>Pongamia pinnata</i> (L.) Pierre.	Seed oil [53]
<i>Ricinus communis</i> L.	Leaves [54]
<i>Rubia tinctorium</i> L.	Roots [55]
<i>Rumex crispus</i> L.	Roots [18]
<i>Salvia officinalis</i> L.	Leaves and flowers [9]
<i>Sanguinaria canadensis</i> L.	Roots [56]
<i>Saponaria officinalis</i> L.	Roots [9]
<i>Silybum marianum</i> (L.) Gaertn.	Fruits [57]
<i>Solanum melongena</i> L.	Whole plant [17]
<i>Syzygium aromaticum</i> (L.) Merr. & L.M. Perry.	Flowering buds [9] [17]

<i>Terminalia belerica</i> Roxb.	Fruits ^[17]
<i>Terminalia tomentosa</i> Wight & Arn.	Leaves ^[9]
<i>Vangueria spinosa</i> (Roxb. ex Link) Roxb.	Fruits ^[9]
<i>Veronicastrum virginicum</i> (L.) Farw.	Bark ^[18]
<i>Yucca gloriosa</i> L.	Fruits ^[9]
<i>Zea mays</i> L.	Cobs and corn silk ^[37]
<i>Zingiber officinale</i> Roscoe.	Rhizome ^[14]

References

1. Stinton LM, Shaffer EA. Epidemiology of gallbladder disease: cholelithiasis and cancer. Gut and liver 2012;6(2):172-187.
2. Behar J. Physiology and Pathophysiology of the Biliary Tract: The Gallbladder and Sphincter of OddiA Review. International Scholarly Research Notices 2013, P837630.
3. Wang DQH, Cohen DE, Carey MC. Biliary lipids and cholesterol gallstone disease. Journal of lipid research 2009;50S:S406-S411.
4. Chen Y, Kong J, Wu S. Cholesterol gallstone disease: focusing on the role of gallbladder. Laboratory Investigation 2015;95(2):124-131.
5. Lavoie B et al. Disruption of gallbladder smooth muscle function is an early feature in the development of cholesterol gallstone disease. Neurogastroenterology and Motility 2012;24(7):e313-e324.
6. Van Erpecum K et al. Agents affecting gall bladder motility–role in treatment and prevention of gallstones. Alimentary Pharmacology and Therapeutics 2000;14:6670.
7. Spiridonov N. Mechanisms of action of herbal Cholagogues. Medicinal and Aromatic Plants 2012;1:107.

8. Shikov AN et al. Medicinal Plants of the Russian Pharmacopoeia; their history and applications. *Journal of Ethnopharmacology* 2014;154(3):481-536.
9. Khare CP. Indian medicinal plants: an illustrated dictionary. Springer Science & Business Media 2007.
10. Benedek B et al. Choleretic effects of yarrow (*Achillea millefolium*) in the isolated perfused rat liver. *Phytomedicine* 2006;13(9):702-706.
11. Mehdiyeva N et al. *Agrimonia eupatoria* L. Rosaceae, in *Ethnobotany of the Caucasus*, R.W. Bussmann, Editor, Springer International Publishing: Cham 2017, P1-5.
12. El Abbouyi PA et al. Inventory of medicinal plants prescribed by traditional healers in El Jadida city and suburbs (Morocco). *International Journal of Green Pharmacy (IJGP)* 2014;8(4):242-251.
13. Briguiche H, Rochdi A, Zidane L. The catalogue of medicinal plants used in the region of El Jadida. *International Journal of Herbal Medicine* 2015;2(5):4654.
14. Duke JA. CRC handbook of medicinal spices. CRC press 2002.
15. Chellappann DK. Hepatoprotective effects of aqueous extract of *Andrographis paniculata* against ccl4 induced hepatotoxicity in albino Wistar rats. *Asian Journal of Pharmaceutical and Clinical Research* 2011;4(3):93-94.
16. Hobbs C. *Natural Therapy for Your Liver: Herbs and Other Natural Remedies for a Healthy Liver*. Avery 2002.
17. Handa S, Sharma A, Chakraborti K. Natural Products and plants as liver protecting drugs. *Fitoterapia* 1986;57(5):307-351.
18. Evans W. Trease and Evans' Pharmacognosy, WB. Saunders Company: UK 1997, P475-508.
19. Shenghong Z. Thirty cases of chronic cholecystitis treated by acupuncture and oral administration of Da Chai Hu Tang. *Journal of Traditional Chinese Medicine* 2008;28(3):173-174.
20. Zhang Q, Zhang Y. Determination of choleretic constituents in *Artemisia scoparia* Waldst. et Kit. by TLC densitometry. *Yao Xue Xue Bao=Acta pharmaceutica Sinica* 1989;24(1):43-47.
21. Qi YZ, Zhang LZ, Ying L. Eighty cases of chronic cholecystitis treated by oral administration of Dan An Tang. *Journal of Traditional Chinese Medicine* 2009;29(4):288-290.
22. Liu CX, Ye GZ. Choleretic activity of p hydroxyacetophenone isolated from *Artemisia scoparia* Waldst. et Kit. in the rat. *Phytotherapy Research* 1991;5(4):182-184.
23. Ofem O, Ikpi D, Essien N. Increased bile flow rate and altered composition of bile induced by ethanolic leaf extract of *Azadirachta indica* (neem) in rats. *Nigerian Journal of Experimental and Clinical Biosciences* 2013;1(1):18-22.

24. Chandan B, Sharma A, Anand K. Boerhaavia diffusa: A study of its hepatoprotective activity. *Journal of Ethnopharmacology* 1991;31(3):299-307.
25. Duke JA. *Duke's Handbook of Medicinal Plants of the Bible*. CRC Press 2007.
26. Guarino C, De Simone L, Santoro S. Ethnobotanical study of the Sannio area, Campania, southern Italy. *Ethnobotany Research & Applications* 2008;6:255-317.
27. Tamayo C et al. The chemistry and biological activity of herbs used in Flor Essence™ herbal tonic and Essiac. *Phytotherapy Research* 2000;14(1):1-14.
28. Al-Asmari AK et al. A review of hepatoprotective plants used in Saudi traditional medicine. *Evidence-Based Complementary and Alternative Medicine* 2014, P890842.
29. Saénz Rodríguez T, García Giménez D, De la Puerta Vázquez R. Choleretic activity and biliary elimination of lipids and bile acids induced by an artichoke leaf extract in rats. *Phytomedicine* 2002;9(8):687-693.
30. Hechtman L. *Clinical Naturopathic Medicine - E-Book*. Elsevier Health Sciences 2012.
31. Satheesh Naik K et al. Hepatoprotective Role of Eclipta alba against High Fatty Diet Treated Experimental Models - A Histopathological Study. *Maedica* 2018;13(3):217-222.
32. Aburada M et al. Pharmacological studies of gardenia fruit. III. Relationship between in vivo hydrolysis of geniposide and its choleretic effect in rats. *Journal of Pharmacobio-dynamics* 1978;1(2):81-88.
33. Bone K, Mills S. *Principles and Practice of Phytotherapy - E-Book: Modern Herbal Medicine*. Elsevier Health Sciences 2013.
34. Huang KC. *The Pharmacology of Chinese Herbs, Second Edition*. CRC Press 1998.
35. Johnson T. *CRC Ethnobotany Desk Reference*. Taylor & Francis 1998.
36. Gorzalczany S et al. Choleretic and antispasmodic effects of Lippia integrifolia aqueous extract. *Revista Brasileira de Farmacognosia* 2008;18(1):16-20.
37. Ibadullayeva S et al. Medico-ethnobotanical inventory (liver and gallbladder ducts illnesses) of Nakhchivan AR, Azerbaijan. *International Journal of Sciences* 2015;4:8088.
38. Grigoleit HG, Grigoleit P. Pharmacology and preclinical pharmacokinetics of peppermint oil. *Phytomedicine* 2005;12(8):612-616.
39. Asha V. Preliminary studies on the hepatoprotective activity of Mamordica subangulata and Naragamia alata. *Indian Journal of Pharmacology* 2001;33(4):276-279.
40. Suresh V, Asha V. Preventive effect of ethanol extract of Phyllanthus rheedii Wight. on D-galactosamine induced hepatic damage in Wistar rats. *Journal of Ethnopharmacology* 2008;116(3):447-453.

41. NI. M.A.O.S. The Natural Health Dictionary: Your comprehensive A-to Z guide for healing with herbs, nutrition, supplements, and secret remedies. Ask Dr. Mao 2011.
42. Kumar MD, Deepmala J, Sangeeta S. Antioxidant, antipyretic and choleretic activities of crude extract and active compound of *Polygonum Bistorta* (Linn.) in albino rats. *International Journal of Pharmacy and Biological Sciences* 2012;2(1):25-31.
43. Barillari J et al. Antioxidant and choleretic properties of *Raphanus sativus* L. sprout (Kaiware Daikon) extract. *Journal of Agricultural and Food Chemistry* 2006;54(26):9773-9778.
44. Glasl S et al. Choleretic effects of the Mongolian medicinal plant *Saussurea amara* in the isolated perfused rat liver. *Planta Medica* 2007;73(01):59-66.
45. Balch PA. Prescription for Herbal Healing. Penguin 2002.
46. Choubey A et al. Potential of medicinal plants in kidney, gall and urinary stones. *International Journal of Drug Development and Research* 2010;2(2):431-447.
47. Rajanandh M. et al. *Moringa oleifera* Lam. A herbal medicine for hyperlipidemia: A pre-clinical report. *Asian Pacific Journal of Tropical Disease* 2012;2:S790-S795.
48. Anwar F et al. *Moringa oleifera*: a food plant with multiple medicinal uses. *Phytotherapy Research* 2007;21(1):17-25.
49. Valan M, Venkataraman R. Phytoconstituents with hepatoprotective activity. *International Journal of Chemical Sciences* 2010;8(3):1421-1432.
50. Paithankar V et al. *Phyllanthus Niruri*: A magic herb. *Research in Pharmacy* 2011;1(4):1-9.
51. Manoj PP et al. Recent studies on well-known spice, *Piper longum* Linn. *Natural Product Radiance* 2004;3(4):222-227.
52. Arai I et al. Stimulative effects of saponin from kikyo-to, a Japanese herbal medicine, on pancreatic exocrine secretion of conscious rats. *Planta Medica* 1997;63(5):419-424.
53. Pulipati S et al. A phyto pharmacological review on a versatile medicinal plant: *Pongamia pinnata* (L.) pierre. *Journal of Pharmacognosy and Phytochemistry* 2018;7(4):459-463.
54. Shukla B et al. Hepatoprotective effect of an active constituent isolated from the leaves of *Ricinus communis* Linn. *Drug Development Research* 1992;26(2):183-193.
55. Younis H. Herbal medicine in Egypt, in Identification of wild food and non-food plants of the Mediterranean region, V. Heywood, Editor. Centre International de Hautes Etudes Agronomiques Méditerranéennes (CIHEAM): Chania P 1997, P45-55.
56. Pengelly A et al. Appalachian plant monographs: *Sanguinaria canadensis* L., Bloodroot. Appalachian Center for Ethnobotanical Studies 2011. <http://www.frostburg.edu/aces/appalachian-plants/>.

57. Morazzoni P, Bombardelli E. *Silybum marianum* (*Carduus marianus*). *Fitoterapia* 1995;66(1):3-42.

Retrieved from <https://encyclopedia.pub/entry/history/show/63325>