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Choleretic and cholagogic effects of anti-cholelithiatic plants

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Abstract

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. The aim of this review is to gather the information of the plants utilized in various parts and societies of the world against gallstones. The information provided is not only useful for common people but also for the scientific community for further phytochemical, toxicological and pharmacological studies which may lead to discovery of new, more effective and safer medicines for gallstones.

Keywords: Gall stone, anticholelithiatic, choleretic, cholagogue, ethnomedicine

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].

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 result 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. Gall- bladder 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 cholergics (increasing bile production) and cholagogues (promoting the flow of bile from the liver and gall bladder into the intestines) [7].

Table 1: Anticholelithiatic plants with cholergic 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>Artemisia absinthium</i> L.	Leaves [16]
<i>Artemisia capillaris</i> Thunberg.	Aerial parts [17-19]
<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, 20-22]
<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>Bupleurum 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.	Whole plant infusion [12]
<i>Fumaria officinalis</i> L.	
<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]
<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 ^[18]
<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]
<i>Viburnum opulus</i> L.	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: Anticholelithiatic plants with cholagogic effects

Medicinal plants	Part/Mode of preparation
<i>Aframomum melegueta</i> K.Schum.	Seeds ^[14]
<i>Anemone hepatica</i> L.	Leaves ^[17]
<i>Chelidonium majus</i> L.	Leaves ^[18]
<i>Chelone glabra</i> L.	Whole plant decoction ^[47]
<i>Chionanthus virginicus</i> L.	Root bark ^[30]
<i>Cichorium intybus</i> L.	Whole plant ^[17] , Leaves and roots ^[48]
<i>Citrus limon</i> L.	Peel oil ^[49]
<i>Combretum micranthum</i> G. Don.	Whole plant ^[17]
<i>Convallaria majalis</i> L.	
<i>Garcinia indica</i> (Thouars) Choisy.	Fruits ^[9]
<i>Gardenia florida</i> (L.) Baill.	Fruits ^[7, 17]
<i>Gentianopsis crinita</i> (Froelich) Ma.	Whole plant ^[7, 50]
<i>Helichrysum arenarium</i> (L.) Moench.	Whole plant ^[17]
<i>Ipomoea digitata</i> L.	Roots and rhizome ^[9]
<i>Iris versicolor</i> L.	Roots ^[9, 51]
<i>Juglans cineraria</i> L.	Bark ^[18]
<i>Laurus nobilis</i> L.	Leaves ^[9]
<i>Lavandula angustifolia</i> Mill.	Flowers ^[9]
<i>Macrotyloma uniflorum</i> (Lam.) Verdc.	Seeds ^[52]
<i>Marrubium vulgare</i> L.	Leaves ^[9]
<i>Mentha arvensis</i> var. <i>piperascens</i> Malinv. ex Holmes	
<i>Menyanthes trifoliata</i> L.	

<i>Meyna laxiflora</i> Robyns	Fruits decoction ^[9]
<i>Moringa oleifera</i> Lam.	Leaves, seeds and roots ^[53] , Flowers ^[54]
<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 ^[55]
<i>Persea americana</i> Mill.	Fruits ^[14]
<i>Phyllanthus amarus</i> Schumach. & Thonn. / <i>Phyllanthus niruri</i> L.	Leaves ^[56]
<i>Pimpinella saxifraga</i> L.	Leaves, roots ^[9]
<i>Piper longum</i> L.	Fruits ^[57]
<i>Piper nigrum</i> L.	Fruits ^[14]
<i>Platycodon grandiflorum</i> (Jacq.) A.DC.	Roots ^[58]
<i>Polypodium vulgare</i> L.	Rhizome ^[9]
<i>Pongamia pinnata</i> (L.) Pierre.	Seed oil ^[59]
<i>Ricinus communis</i> L.	Leaves ^[60]
<i>Rubia tinctorium</i> L.	Roots ^[61]
<i>Rumex crispus</i> L.	Roots ^[18]
<i>Salvia officinalis</i> L.	Leaves and flowers ^[9]
<i>Sanguinaria canadensis</i> L.	Roots ^[62]
<i>Saponaria officinalis</i> L.	Roots ^[9]
<i>Silybum marianum</i> (L.) Gaertn.	Fruits ^[63]
<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]

Table 3: Anticholelithiatic plants with both choloretic and cholagogic effects

Medicinal plants	Part/Mode of preparation
<i>Aloe vera</i> (L.) Burm.f.	Leaves juice ^[64]
<i>Artemisia absinthium</i> L.	Essential oil obtained from leaves and flowers ^[65]
<i>Berberis aquifolium</i> Pursh.	Roots decoction ^[66]
<i>Berberis aristata</i> DC.	Roots decoction ^[51]
<i>Berberis vulgaris</i> L.	Roots decoction ^[67]
<i>Capsicum annuum</i> L.	Fruits ^[68]
<i>Carum carvi</i> L.	Fruits ^[14]
<i>Ceratonia siliqua</i> L.	Pods ^[14]
<i>Cichorium intybus</i> L.	Flowers decoction ^[26]
<i>Citrus × aurantium</i> L.	Essential oil from fruit peel ^[65]
<i>Costus speciosus</i> (J.Koenig) Sm.	Whole plant ^[9, 14]
<i>Curcuma xanthorrhiza</i> Roxb.	Rhizome ^[14]
<i>Cynara scolymus</i> L.	Leaves decoction ^[26]
<i>Dioscorea alata</i> L.	Tuber ^[9]
<i>Elettaria cardamomum</i> (L.) Maton.	Fruits ^[14]
<i>Euonymus atropurpureus</i> Jacq.	Bark decoction ^[66]
<i>Euonymus tingens</i> Wall.	Root bark ^[9]
<i>Eupatorium perfoliatum</i> L.	Flowers ^[64]
<i>Eutrochium purpureum</i> (L.) E.E. Lamont.	Roots decoction ^[9]
<i>Ferula assa-foetida</i> L.	Gum resin ^[14]
<i>Glycyrrhiza glabra</i> L.	Roots ^[69, 70]
<i>Helichrysum arenarium</i> (L.) Moench.	Flowers ^[8]
<i>Hibiscus sabdariffa</i> L.	Leaves infusion ^[14, 71]
<i>Hypericum perforatum</i> L.	Whole plant ^[72]
<i>Juniperus communis</i> L.	Berries ^[14]
<i>Lysimachia christinae</i> Hance.	Whole grass ^[73, 74]
<i>Marrubium vulgare</i> L.	Whole plant ^[75]
<i>Origanum compactum</i> Benth.	Leaves infusion ^[13]
<i>Peumus boldus</i> Molina.	Leaves infusion ^[76]
<i>Picrorhiza kurroa</i> L.	Roots ^[9, 77]
<i>Pinus sylvestris</i> L.	Needles (Leaves) pine oil ^[78]
<i>Podophyllum peltatum</i> L.	Roots - resin ^[18]
<i>Raphanus raphanistrum</i> L.	Roots ^[75]
<i>Rhamnus purshiana</i> DC.	Bark decoction ^[79]

<i>Rosmarinus officinalis</i> L.	Leaves infusion ^[12, 61]
	Flowers infusion ^[26]
<i>Sonchus oleraceus</i> (L.) L.	Leaves ^[75]
<i>Taraxacum officinale</i> (L.) Weber ex F.H.Wigg.	Roots ^[9]
<i>Vanilla planifolia</i> Jacks. ex Andrews.	Pods ^[14, 17]
<i>Veronicastrum virginicum</i> (L.) Farw.	Roots ^[66]

Table 4: Anticholelithiatic plants used in different countries for their choleric and cholagogic effects

Medicinal plants	Country
1. <i>Acorus calamus</i> L.	Russia ^[8]
<i>Ajuga iva</i> (L.) Schreb.	Morocco ^[12]
<i>Allium cepa</i> L.	Morocco ^[13]
<i>Artemisia absinthium</i> L.	Morocco ^[12] , Russia ^[8]
<i>Artemisia arborescens</i> (Vaill.) L.	Morocco ^[12]
<i>Cichorium intybus</i> L.	Italy ^[26]
<i>Cichorium endivia</i> L.	Lebanon ^[25]
<i>Cirsium arvense</i> (L.) Scop.	Italy ^[26]
<i>Curcuma longa</i> L.	Saudi Arabia ^[14, 28]
<i>Curcuma xanthorrhiza</i> Roxb.	Holland ^[14]
<i>Cynara scolymus</i> L.	Italy ^[26]
<i>Fumaria capreolata</i> L.	
<i>Fumaria officinalis</i> L.	Morocco ^[12]
<i>Gnaphalium uliginosum</i> L.	
<i>Helichrysum arenarium</i> (L.) Moench.	Russia ^[8]
<i>Hypericum perforatum</i> L.	Saudi Arabia ^[28]
<i>Inula helenium</i> L.	
<i>Lapsana communis</i> L.	Italy ^[26]
<i>Marrubium vulgare</i> L.	Italy and Tunisia ^[75]
<i>Mentha × piperita</i> L.	Azerbaijan ^[37, 38]
<i>Mentha piperita</i> L.	
<i>Menyanthes trifoliata</i> L.	Russia ^[8]
<i>Momordica subangulata</i> Blume	
<i>Naregamia alata</i> Wight & Arn.	India ^[39]
<i>Origanum compactum</i> Benth.	Morocco ^[13]
<i>Peumus boldus</i> Molina.	Brazil ^[76]
<i>Phyllanthus rheedei</i> Wight.	India ^[40]
<i>Pinellia ternata</i> (Thunb.) Makino.	Japan ^[41]
<i>Raphanus raphanistrum</i> L.	Italy and Tunisia ^[75]
<i>Rosmarinus officinalis</i> L.	Italy ^[26] , Morocco ^[12, 61]
<i>Rubia peregrina</i> L.	Morocco ^[12]
<i>Sonchus oleraceus</i> (L.) L.	Italy and Tunisia ^[75]
<i>Tanacetum vulgare</i> L.	
<i>Taraxacum officinale</i> (L.) Weber ex F.H.Wigg.	Russia ^[8]
<i>Viburnum opulus</i> L.	
<i>Zea mays</i> L.	Azerbaijan ^[37] , Russia ^[8]
<i>Zygophyllum gaetulum</i> Emb. & Maire.	Morocco ^[12]

Conclusion

This review gives a brief look at herbal remedies against gallstone with significant data with respect to their strategy of preparation. However, for testing the scientific validity of these herbal preparations clinical studies are required, to establish their safe therapeutic use. The present review is not only be helpful for the overall population yet in addition pull in the scientific world for anticholelithiatic drug discovery. This significant ethno pharmacological data may lead towards disclosure of new anticholelithiatic compounds.

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