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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 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. 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 chologogic 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.

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 Oddi A Review. *International Scholarly Research Notices* 2013, P837-630.
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;14:66-70.
7. Spiridonov N. Mechanisms of action of herbal Chologogues. *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.* Choleric 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):46-54.
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 choleric 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. Choleric 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, P890-842.
29. Saéñz Rodriguez T, García Giménez D, De la Puerta Vázquez R. Choleric 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 choleric 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. Gorzalczy S *et al.* Choleric 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;4:80-88.
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 choleric 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 choleric 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.* Choleric 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. Hoffmann D. *Medical Herbalism: The Science and Practice of Herbal Medicine*. Healing Arts Press 2003.
48. Katiyar P *et al.* Kasni (*Cichorium intybus* L.) A propitious traditional medicinal herb. *International Journal of Pharmacognosy* 2015;2(8):368-380.

49. Bell G. Cholelitholytic agents. *Pharmacology & Therapeutics* 1983;23(1):79-108.
50. Nikolaev S *et al.* Comparative choleric properties of natural xanthone compounds from *Gentianopsis barbata*. *Eksperimental'naia i Klinicheskaia Farmakologija* 2003;66(4):29-31.
51. Bone K. *A Clinical Guide to Blending Liquid Herbs E-Book: Herbal Formulations for the Individual Patient*. Elsevier Health Sciences 2003.
52. Bigoniya P, Bais S, Sirohi B. The effect of *Macrotyloma uniflorum* seed on bile lithogenicity against diet induced cholelithiasis on mice. *Ancient Science of Life* 2014;33(4):242-251.
53. 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.
54. Anwar F *et al.* *Moringa oleifera*: a food plant with multiple medicinal uses. *Phytotherapy Research* 2007;21(1):17-25.
55. Valan M, Venkataraman R. Phytoconstituents with hepatoprotective activity. *International Journal of Chemical Sciences* 2010;8(3):1421-1432.
56. Paithankar V *et al.* *Phyllanthus Niruri*: A magic herb. *Research in Pharmacy* 2011;1(4):1-9.
57. Manoj PP *et al.* Recent studies on well-known spice, *Piper longum* Linn. *Natural Product Radiance* 2004;3(4):222-227.
58. Arai I *et al.* Stimulative effects of saponin from kikyoto, a Japanese herbal medicine, on pancreatic exocrine secretion of conscious rats. *Planta Medica* 1997;63(5):419-424.
59. 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.
60. 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.
61. 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.
62. Pengelly A *et al.* *Appalachian plant monographs: Sanguinaria canadensis L., Bloodroot*. *Appalachian Center for Ethnobotanical Studies* 2011. <http://www.frostburg.edu/aces/appalachian-plants/>.
63. Morazzoni P, Bombardelli E. *Silybum marianum* (*Carduus marianus*). *Fitoterapia* 1995;66(1):3-42.
64. Zora N, DeGrandpre M, DeGrandpre Z. *Botanical Therapeutics: Actions, Interactions and Indications* 2010. Lulu.com.
65. Schiller C, Schiller D, Schiller J. *The Aromatherapy Encyclopedia: A Concise Guide to Over 385 Plant Oils*. Basic Health Publications, Inc 2008.
66. Bone K, Mills S. Herbal approaches to system dysfunctions, in *Principles and Practice of Phytotherapy (Second Edition)*. Churchill Livingstone: Saint Louis 2013, P183-350.
67. Rahimi-Madiseh M *et al.* *Berberis vulgaris*: specifications and traditional uses. *Iranian Journal of Basic Medical Sciences* 2017;20(5):569-587.
68. Srinivasan K. Spices as influencers of body metabolism: an overview of three decades of research. *Food Research International* 2005;38(1):77-86.
69. Ross IA. *Medicinal Plants of the World: Chemical Constituents, Traditional and Modern Medicinal Uses*. Springer Science & Business Media 2001;2.
70. Nasyrov K, Chepurina L, Kireeva R. The hepatoprotective and cholagogic action of glycyrrhizic acid derivatives. *Eksperimental'naia i Klinicheskaia Farmakologija* 1994;58(6):60-63.
71. Mariod AA, Saeed Mirghani ME, Hussein I. Chapter 11 - *Hibiscus sabdariffa* L. Roselle, in *Unconventional Oilseeds and Oil Sources*, A.A. Mariod, M.E. Saeed Mirghani, and I. Hussein, Editors. Academic Press 2017, P59-65.
72. Luminita ID, Daniela N, Capraru G. *Hypericum perforatum* L. in modern phytotherapy. *Analele Științifice ale Universității. Alexandru Ioan Cuza*, Secțiunea Genetică și Biologie Moleculară 2007;8(1):253-256.
73. Deng J *et al.* *Lysimachia christinae* Hance regresses preestablished cholesterol gallstone in mice. *Journal of Ethnopharmacology* 2015;166:102-108.
74. Yang X *et al.* Evaluation of *Lysimachia christinae* Hance extracts as anticholecystitis and cholagogic agents in animals. *Journal of Ethnopharmacology* 2011;137(1):57-63.
75. Loporatti ML, Ghedira K. Comparative analysis of medicinal plants used in traditional medicine in Italy and Tunisia. *Journal of Ethnobiology and Ethnomedicine* 2009;5(1):31.
76. Silva PS, Francisconi LS, Gonçalves RD. Evaluation of major and trace elements in medicinal plants. *Journal of the Brazilian Chemical Society* 2016;27(12):2273-2289.
77. Basu K *et al.* Chemistry and pharmacology of apocynin, isolated from *Picrorhiza kurroa* Royle ex Benth. *Current Science* 1971;40(22):603-604.
78. Tadtong S *et al.* Chemical components of four essential oils in aromatherapy recipe. *Natural product communications* 2015;10(6):1091-1092.
79. Page L. *How to be Your Own Herbal Pharmacist: Herbal Traditions - Expert Formulations*. Healthy Healing, Inc 1998.