Ethnopharmacological survey of herbal remedies used in the treatment of hepatitis

Wahid Hussain, Saima Batool, Sabiha Bahar, Bibi Shahida, Bushra Bangash, Amjad Ali, Hidayat Hussain, Iftikhar Ali, Maroof Ali, Rainer W. Bussmann

Databases and Inventories

Abstract

Background: Hepatitis is a serious illness and can be fatal, which has caused a dangerous ratio round the globe especially in the developed and under-developing countries. About 1.4 million deaths are reported each year from the different types of hepatitis especially hepatitis B virus (HBV) and hepatitis C virus (HCV) which cause 90% mortality and the other 10% deaths are caused due to all other hepatitis types.

Methods: By using different online database such as Google scholar, Science Direct Navigator, ISI Web of Knowledge, Elsevier, springer link, Test databases, research gate and PubMed, date were retrieved by giving different keywords. Various keywords were used on plants used traditionally to treat hepatitis.

Results: A total of 128 medicinal plant species were identified, belonging to 108 genera and 61 botanical families by reviewing 220 research articles. From the study, it showed that the medicinal plants are used from the very ancient time to cure hepatitis worldwide. These medicinal plants are used in different parts of the world as a traditional herbal medicine for the control of hepatitis.

Conclusion: Our literature review will help the scientific communities to identify anti-hepatitis plant in order to isolate novel anti-hepatitis natural products.

Keywords: Hepatitis, medicinal plants, treatment, ethnopharmacological, survey

Correspondence

Wahid Hussain[1]*, Saima Batool[1], Sabiha Bahar[1], Bibi Shahida[1], Bushra Bangash[1], Amjad Ali[2], Hidayat Hussain[3], Iftikhar Ali[4], Maroof Ali[5], Rainer W. Bussmann[6]

[1]Department of Botany, GPGC Parachinar Kurram Pakistan
[2]Department of Sustainable Crop Production, Università Cattolica del Sacro Cuore, Via Emilia Parmense, 84 29122 Piacenza Italy
[3]Department of Bioorganic Chemistry, Leibniz Institute of Plant Biochemistry Weinberg 3, D-06120 Halle (Saale), Germany
[4]Shandong Analysis and Test Center, Shandong Provience,(250014), China
[5]College of Life Science, Anhui Normal University, Wuhu 241000, China
[6]Institute of Botany, Department of Ethnobotany, Ilia State University, Georgia

Corresponding Author:
wahidhussainwahid@gmail.com

Ethnobotany Research & Applications
20:24 (2020)

خلاصہ:

پس منظر: ہیپاٹائٹس ایک سنگین بیماری ہے اور یہ مہلک بھی ہوسکتا ہے ، جس کی وجہ سے خاص طور پر ترقی یافتہ اور ترقی پذیر ممالک میں دنیا بھر میں ایک خطرناک تناسب پیدا ہوا ہے۔ ہیپاٹائٹس بی وائرس (HBV)اور ہیپاٹائٹس سی وائرس (HCV) کی مختلف اقسام سے ہر سال تقریبا 1.4 ملین اموات کی اطلاع دی جاتی ہے جو 90% اموات کا سبب بنتی ہے اور دیگر 10%اموات ہیپاٹائٹس کی دوسری تمام اقسام کی وجہ سے ہوتی ہیں۔ اس کے علاوہ ، دواؤں کے پودوں کے فوائد کی وضاحت کرنے کے لئے جو ہیپاٹائٹس کے علاج کے لئے استعمال ہوتے ہیں۔

*طریقے:*گوگل اسکالر ، سائنس ڈائرکٹ نیویگیٹر ، آئی ایس آئی ویب آف نالج ، ایلسیویئر ، اسپرنگر لنک ، ٹیسٹ ڈیٹا بیس ، ریسرچ گیٹ اور پب

Manuscript received: 24/06/2020 – Revised manuscript received: 12/09/2020 - Published: 18/09/2020

http://dx.doi.org/10.32859/era.20.24.1-29

میڈ کے جیسے مختلف آن لائن ڈیٹا بیس کا استعمال کرکے ، تاریخ کو مختلف اہم الفاظ دے کر تلاش کیا گیا۔ دنیا کے کچھ حصوں میں پودوں اور ان کی نسلی دواسازی کی تعلیم کے بارے میں تفصیلی معلومات حاصل کرنے کے لئے تلاش کے عمل کے دوران مختلف اہم الفاظ استعمال کیے گئے۔
نتائج:کل 128 دواؤں کے پودوں کی انواع کی نشاندہی کی گئی ، جن کا تعلق 108 نسلوں اور 61 نباتاتی خاندانوں سے ہے۔ مطالعے سے ، یہ ظاہر ہوا ہے کہ دواؤں کے پودوں کو دنیا بھر میں ہیپاٹائٹس کے علاج کے لئے بہت قدیم زمانے سے ہی استعمال کیا جاتا ہے۔ یہ دواؤں کے پودوں کو ہیپاٹائٹس کے کنٹرول کے لئے روایتی جڑی بوٹیوں کی دوائی کے طور پر دنیا کے مختلف حصوں میں استعمال کیا جاتا ہے۔
نتیجہ اخذ کرنا: ہمارے لٹریچر کا جائزہ سائنسی برادریوں کو اینٹی ہیپاٹائٹس پلانٹ کی شناخت کرنے میں مدد دے گا تاکہ ناول اینٹی ہیپاٹائٹس قدرتی مصنوعات کو الگ تھلگ کیا جاسکے۔
اہم الفاظ: ہیپاٹائٹس ، دواؤں کے پودوں ، علاج ، ایتھنوفرماکولوجیکل ، سروے ۔

Background

The liver is an organ and paramount importance. It aids in the metabolism of ingested substances like food, alcohol, dietary substances and most medications (Govind and Pandey 2011, Thomas *et al.* 2011). There are many causes of liver disorders, but the major causes are various toxic chemicals, some antibiotics, alcohol, and food. In addition, liver disorders are also caused due to the infections of various kinds of parasites, viruses, fungi or bacteria. Different liver disorders like hepatitis, jaundice, inflammation of liver, cirrhosis (a digestive disorder that is the result of liver fibrosis), and liver cancer also be caused by autoimmune distractions (Govind & Pandey 2011). The word hepatitis originates from two Greek words, hepta that refers to liver and it is meaning inflammation. Hepatitis is present in many forms such as including virus hepatitis, autoimmune hepatitis, fatty liver hepatitis, alcoholic hepatitis and toxin induced hepatitis these all types of hepatitis is identified as a hepatitis virus that attack and harm liver cells (Khan *et al.* 2010).

The Hepatitis B virus was first studied in 1963 (Cusheri 2002) and it is estimated that more than two billion people have ate some point been infected with HBV on global level (World Health Organization 2000. About, 520000 patients annually from hepatitis type B and C (International consensus conference 2002). Hepatitis C was first cloned (Choo *et al.* 1989, Alamo *et al.* 2013). About 170 million people are affected by hepatitis C virus, according to World Health Organization (WHO), which causes liver cirrhosis or hepatocellular carcinoma (Chen & Morgan 2006). The percentage of prevailing HBV and HCV infections among the people of Pakistan is 35–38% and 4-14% respectively (Hakim *et al.* 2008). Pakistan is confronting a huge burden of these diseases. Almost 30 genotypes of HCV have been describing until now (Kato 2000). HCV causes a chronic liver disease responsible 8000-10000 deaths in Pakistan per year (Moyer *et al.* 1999).

All hepatitis viruses have different ways of transmission. For instance, the hepatitis A virus is easily transmitted under unhygienic condition and in poor sanitation. Hepatitis B virus (HBV) is transmitted via blood and also in some case it transmitted from the blood-derived products (Seeger *et al.* 2020).

There is a complex biological and cultural relationship between plants and human beings (Balick 1996) and herbal medicines have a great role in the discovery of different drugs, and they are used for the cure of different disorders all over the world. Usually these sources are available in abundance and traditional medicines benefits 80 percent of population on earth (Gewali & Awake 2008, Wangchuk *et al.* 2011). In modern pharmacopoeia, almost 25 percent of all drugs were derived from plants (Phytomedicines) and other are synthetic analogous of natural products (Pseudo natural products) built on prototype compounds derived from plants (Bandaranayake 2006). Several medicinal plants and their formulations have been used around the world for the treatment of liver diseases and this has encouraged the scientific community to research the effect of these medicinal plants which can treat HCV in a comprehensive manner (Ashfaq & Idress 2014). Many drugs have been reported against HCV until date and many of them are found successful in clinical trials, but viral resistance and the negative effects of these drugs have made their therapeutical application against HCV limited (Kitazato *et al.* 2007). The effect of *Acacia nilotica* (AN) in inhibition of HCV and of other plants e.g. against herpes simplex virus (HSV), poliovirus type 1, coxsackievirus B5 and Echovirus have been confirmed (Konowalchuk and Spears 1976). Our study aims to elicit plant species used against liver disorders especially hepatitis.

Materials and Methods

By using different online database such as Google scholar, Science Direct Navigator, ISI Web of Knowledge, Elsevier, springer link, Test databases, research gate and PubMed, date were retrieved by using different keywords in order to derive detailed information of plants and their ethno-pharmacological studies of various regions of the world (Adnan *at el.* 2014). With the help of taxonomic literature, botanical names of plants and their families were verified (Ullah *et al.* 2018).

Data analysis

Data were compared using Venn diagrams and calculating the Jaccard (similarity) Index (JI) of each

couple of datasets (Jaccard 1902, Kayani *et al.* 2015).
To determine the similarity between two sets the following formula was used:
Jaccard Index = (the number in both sets) / (the number in either set) * 100

The formula in notation is as follows:

$$J(X, Y) = |X \cap Y| / |X \cup Y| * 100$$

Moreover, the recorded data were also compared with the wild food ethnobotanical literature of Pakistan in order to assess their possible novelty (Abbas *et al.* 2020, Ahmad and Pieroni 2016, Ahmad *et al.* 2019).

Family Importance Value
FIV represents the comparative position of families. It provides the regional prominence of the species. The intention was to compel the percentage that came from informants who mentioned the family as follows;

$$FIV = \frac{FC}{N} \times 100,$$

Where FC is the sum of informers revealing the family, while N is the sum of informants who participated in the research.

Results and Discussion

Diversity of the medicinal flora
During the current review, a total of 128 taxa belonged to 108 genera, from 66 plant families were documented to be consumed as medication for hepatitis diseases all over the world (Fig. 1).

There was only one family of fungi, pteridophytes, and gymnosperms with one species each, and 125 species belonging to 63 angiosperm families. Plant species were laterally registered with the corresponding family, botanical names, local names, part used, preparation of different remedies, route of administration, and medicinal uses as mentioned in Table 1.

Plant Parts Used
Based on a total of 191 citation reports, the part of the plants most frequently used for curing hepatitis were leaves (27%), followed by aerial parts (18%), fruit (16%), fruit (15.7%), flower (11%), root (10%), seed (7%), stem (5%),bulb, bark, rhizome each (1%), fruiting body and flower top (1%) as shown in Figure 2. The least reported plant part used bulb, bark, rhizome each (1%), fruiting body and flower top each with 1 percent.

Family Importance Value
The importance of a plant family increases with the increase in the frequency of citations of its all species. Table 1 represents 66 plant families with maximum FIV, amongst which Asteraceae was the dominant family (13.8%), followed by Fabaceae (7.8%), Euphorbiaceae (2.7)%, Cucurbitaceae (2.5%) and Gentianaceae (2.0%). Acanthaceae, Amaryllidaceae, Apiaceae, Brassicaeae and Poaceae had (1.5 %) family importance values. Rest of the families had less than (1.5%) family importance values as shown in Figure 3.

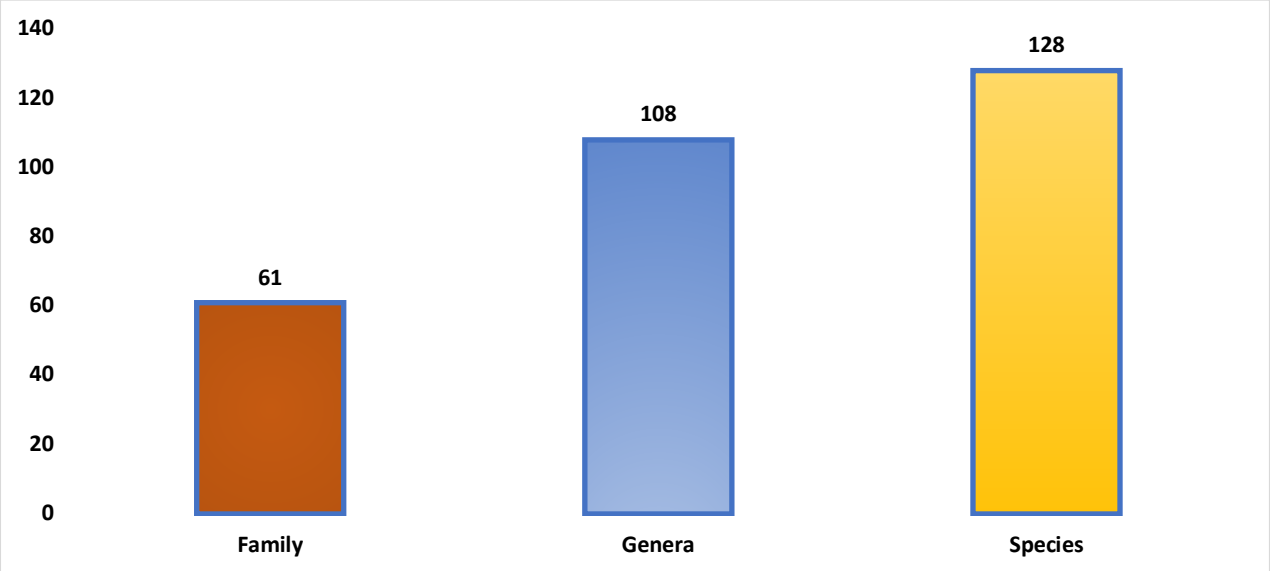

Figure 1. Diversity of medicinal flora used for the treatment of hepatitis

Table 1. List of the plants used for the treatment of various types of hepatitis all over the world

Family	Plant Name	Part used	Chemical constituents	Uses	Citation
Acanthaceae	*Acanthus ilicifolius* L.	Leaves	Aceteoside, isoaceteoside, acanthaminoside	Used for hepatitis, and also for anti-ulcer activities	Samani & Kopaei, 2018, Kumar & Choyal, 2012
	Justicia adhatoda L.	Roots	Alkaloids, polyphenolics, glycosides.	Decotion of its roots is taken by the patients for one month in the treatment of jaundice.	Kumar & Choyal, 2012, Medeiros et al., 2012
	Justicia schimperiana (Hochst. ex A. Nees) T. Anderson	Leaves, Stem	Alkaloids, lignans, flavonoids, and terpenoids	Chopped and used to take a smoke bath; boiled and used as a body wash; leaves and stems are crushed and pounded and then taken orally	Kpodar *et al*. 2015, Corrêa & Alcântara, 2012
Adiantaceae	*Adiantum capillus-veneris* L.	Leaves	Flavonoids, terpenoids,tannins, muciliage, volatile oils, gallic acid	Used for hepatitis and also for inflammatory diseases	Jan *et al.* 2017, Prajapati *et al*. 2006
Aizoaceae	*Trianthema portulacastrum* L.	Aerial parts	Trianthenol, 3-acetylaleuritolic acid, leptorumol,3,4-dimethoxy cinnamic acid, 5-hydroxy-2-methoxybenzaldehyde, p-methoxybenzoic acid	Liver infections	Zaman *et al.* 2018, Mahmood *et al.* 2013, Shivhare *et al.* 2012
Amaryllidaceae	*Allium cepa* L.	Bulb	Guercetin, fructose, quercetin-3-glucoside, isorhamnetin-4-glucoside, xylose, galactose, glucose, mannose, organosulfur compounds, allylsulfides,	Bulb is dried and ground powder is used for cure of jaundice problem	Ullah *et al.* 2020, Marrelli *et al.* 2019, Medeiros *et al.* 2012
	Allium satium L.	Bulb	Flavonoids, flavenols, S-alk(en)yl cysteine sulfoxides, cycloalliin, selenium, thiosulfinates, and sulfu	Bulb is dried and ground powder is used as hepatodepurative	Ceuterick *et al.* 2008
	Ruscus aculeatus L.	Leaves	*P*-coumaric and caffeic acids and rutin	Liver depurative	Pieroni *et al.* 2014, Hadžifejzović *et al.* 2013
Amaranthaceae	*Achyranthes aspera* L	Root	Triterpenoid, saponins, alcohol and 17-penta triacontanol,	Used for treatment of jaundice	Barkatullah, *et al.* 2015, Srivastav, 2011
	Amaranthus graecizans subsp. *thellungianus* (Nevski) Gusev	Aerial parts	Brenan, trolox and gallic acid	Liver tonic	Yaseen *et al.* 2015, Ishtiaq *et al.* 2014, Pieroni *et al.* 2005
Anacardiaceae	*Pistacia integerrima* L.	Aerial parts	Alkaloids, flavonoids, tannins, saponins and sterols	Used for treatment of jaundice	Jan *et al.* 2017, Bibi *et al.* 2015

	Pistacia chinensis Bunge ssp. *integerrima*	Leaves, bark	Sitosterol, alnusidiol, gallic acid, naringenin and amentoflavone	Leaves and bark decoction to cure jaundice	Ali *et al.* 2018a, Uddin *et al.* 2011
Apiaceae	*Coriandrum sativum* L.	Leaf, seed, fruit	Aromatic acid containing 2-decenoic acid (30.8%), capric acid (12.7%), undecanoic acid (7.1%), linalool (37.7%), grenyl acetate (17.5%), gama-terpinene (14.4%)	Liver disorders	Al-Snafi Ali Esmail 2016
	Pleurospermum candollei (DC.) Benth. ex C.B. Clarke	Aerial parts	------	A decoction of the whole plant is made and taken twice a day	Abbas *et al.* 2016, Agelet *et al.* 2003
	Oenanthe japonica (Blume) DC.	Leaves	Longiborneol, geranyl linalool and T-cadinol	Powder of leaves is used for cure of hepatitis b	Samani & Kopaei, 2018, Pattram *et al.* 2011
	Trachyspermum ammi (L.) Sprague	Leaves	V-terpinene, ρ-cymene, and thymol	Used for treatment of hepatitis B	Samani & Kopaei 2018, Gandomi *et al.* 2014
Apocynaceae	*Carissa spinarum* L	Leaves	Triterpenes, cardiac glycosides, sesquiterpenes, monoterpenes, flavonoids,lignans, fatty acids and esters	Used for treatment of jaundice	Rashid *et al.* 2018, Wangteeraprasert *et al.* 2012
Aracea	*Colocasia esculenta* (L.) Schott	Bulb	Active phytoconstituents such as flavonoids, sterols, glycosides, and other micronutrients	The bulb of this plant cooked as vegetable And dried bulb is cut in to pieces and then crushed to make powder which is used for the treatment of jaundice	Kidane *et al.* 2018, Kumar & Choyal 2012,
Asparagaceae	*Asparagus adscendens* Roxb.	Root	Essential oils, asparagine, arginine, tyrosine, flavonoids (kaempferol, quercetin, and rutin), resin, and tannin.	Extract of root is used for treatment of jaundice	Fawad 2016, Yaseen *et al.* 2015, Negi *et al.* 2010
Asteraceae	*Artemisia campestris* L.	Flowers	B-pinene, spathulenol, α-pinene, limonene and o-cymene	Hepatic protector	Al-Jahid *et al.* 2017, Asadi *et al.* 2015
	Artemisia genipi Stechm.	Whole plant	Sesquiterpene lactones	For the treatment of inflammation of jaundice	Vitalini *et al.* 2013, Appendino *et al.* 1982
	Ageratum conyzoides	Leaves	Alkaloids, flavonoids, tannins, saponins, and cyanic acid	Lease paste is used for treatment of Jaundice	Zaman *et al.* 2018, Okunade 2002
	Carthamus oxyacantha M.Bieb	Flowers	Linoleic oil, palmitic acid, stearic acid, oleic acid, linoleic acid	Flowers are used for the cure of Jaundice	Zaman *et al.* 2018, Ahmad *et al.* 2009, Ahmad *et al.* 2007

	Calendula officinalis L.	Flowers	Flavonoids, particularly patulitrin and patuletin	Infusion is used to cure liver diseases	Pieroni *et al.* 2012, Mulley *et al.* 2009
	Cynara scolymus L.	Leaves, flowers	Cynarin, cynaroside, scolymoside, ferulic and caffeoylquinic	Leaves and flowers hepatitis	Samani & Kopaei 2018, Ceuterick *et al.* 2011, Pieroni *et al.* 2004, Lutz *et al.* 2011
	Eclipta prostrata (L.) L	Aerial parts	Glycosides eclalbasaponin I and eclalbasaponin II	Decoction of boiled whole parts is used for the treatment of Jaundice, hepatitis and other liver disorders	Zaman *et al.* 2018,Shinwar *et al.* 2016, Mahmood *et al*. 2012
	Matricaria chamomilla L.	Aerial parts	Essential oils, glycoside, flavonoids,	Aerial paets powder is uaes for the treatment of hepatitis	Samani & Kopaei, 2018, Egea *et al.* 2015, Singh *et al*. 2011
	Tanacetum artemisioides L.	Aerial parts	Flavonoids, tanacetamide,5-demethylnobiletin	To cure hepatitis B	Hussain *et al.* 2018, Hussain *et al.* 2013
	Taraxicum officinale L.	Leaves	Proteins, fatty acid, potassium, calcium	For the treatment of inflammation of jaundice	Samani & Kopaei 2018, Jan *et al.* 2017, Pieroni *et al.* 2014, Hussain *et al.* 2012, Ikram & Hussain1978, Escudero *et al*. 2003
	Taraxacum campylodes G. E. Haglund	Rhizome	Taraxin, taraxacerine, inuin, vitamin C	Decoction of boiled rhizome is used for the treatment of Jaundice, hepatitis and other liver disorders	Samani & Kopaei 2018, Prajapati *et al.* 2006
	Silybum marianum L.	Leaf,fruit, seed	Flavoligrans, silybin, isosiybin and silymarin (6%), Flavolagnans, silybin, silydianin, silychristine	To cure jaundice and hepatitis	Samani & Kopaei, 2018,Khan *et al*. 2016, Foster 1991
	Sonchus asper (L.) Hill	Aerial parts	N-Hexane, alkaloids, saponins, flavonoids, phenols and tannins	To cure hepatitis B	Ali *et al*. 2020, Hussain *et al.* 2018
Berberidaceae	*Berberis lycium* Royle.	Fruit, root	Alkaloids, cardioactive glycosides, saponins, tannins, anthocyanins, vitamins,carbohydrates, proteins, lipids, fiber content, β carotein, cellulose, phytic acid and phytate phosphorous.	For the treatment of jaundice	Ali *et al.* 2018b, Rashid *et al.* 2018, Ahmad *et al.* 2017 Shabir *et al.* 2012, Tyler *et al*. 1981

	Berberis pseudumbellata R. Parker	Seeds,flower , fruits,	Alkaloids, steroids, glycosides, flavonoids, saponins, terpenoids and reducing sugar	Seeds and fresh fruits are eaten while a flower decoction is recommended three times a day	Yasil & Inal 2019, Khan *et al.* 2016
Boraginaceae	*Onosma hispida* Wall. & G. Don.	Aerial parts	Naphthaquinones, alkaloids and phenolic compounds	The whole plant is cooked in water as a vegetable and taken twice a day as needed	Yeşil & İnal 2019, Kumar *et al*. 2012
Brassicaceae	*Brassica rapa* L.	Flowers	β-sitosteryl-3β-glucopyranoside-6′-O-fatty acid esters, β-sitosterol, chlorophyll and phytyl fatty acid esters	Used for treatment of hepatitis	Ragasa *et al.* 2016, Barkatullah, *et al.* 2015
	Lepidium sativum L.	Leaves	Hexadecadienoic acid, heneicosanoic acid,10-octadecenoic acid,15-tetracosenoic acid, hexadecanoic acid and steric acid	Leaves powder is used to treat hepatitis	Samani & Kopaei, 2018, Gokavi *et al.* 2004
	Rhaphanus sativus L.	Root	Raphanin, glycosinolates, enzymes, trace elements, anthocyanin, pectin, protein, and Vitamin C	Decoctions of its roots are recommended for the treatment of jaundice. Fleshy part and its juice is used for treatment of jaundice	Ong & Kim 2014, Prajapati *et al.* 2006,
Burseraceae	*Boswellia carterii Birdw.*	Stem (resin)	Essential oils, pyrolysates ***boswellic*** acids	Resin is used for cure of hepatitis C	Samani & Kopaei 2018, Moussaieff *et al.* 2008
Caryophyllaceae	*Herniaria glabra* L.	Leaves	Triterpene,saponins:herniaria saponins, gypsogen, flavonoids and hydroxycoumarins	For jaundice (anti-icterus)	Alsanfi 2018, Rigat *et al.* 2007
Chenopodiaceae	*Chenopodium album* L.	Aerial parts	Phenols, tannins, phytic acid phytate phosphorus, alkaloids	For the cure of hepatic disorders	Zaman *et al.* 2018, Jan *et al.* 2017, Alsanif 2015, Ceuterick *et al.* 2008
	Chenopodium ambrosioides L.	Leaves, flowers	Cymene, alpha-terpinene and limonene	Hepatodepurative	Ceuterick *et al.* 2011, Barros *et al*. 2013
Convolvulaceae	*Ipomoea paniculata* Burm. f	Aerial parts	Tetracosane, myristic acid, beta-sitosterol, beta-carotene, daucosterol and quercetin	Liver cirrhosis	Ahmad *et al.* 2018, Heiurich *et al.* 1998
Crassulaceae	*Rhodiola kirilowii (Regel) Maxim.*	Root	Arbutin, epigallocatechin gallate, rhodiocaynocide, lotaustralin	Root powder is used to cure hepatitis C	Samani & Kopaei 2018, Wiedenfeld *et al.* 2007

Cucurbitacae	*Citrullus colocynthis* (L.) Schrad.	Stem, flowers	Arbohydrate, protein, separated amino acid, tannins, saponins, phenolics, flavanoids, flavone glucosides, terpenoids, alkaloids, anthranol, steroids, cucurbitacins, saponarin, cardic glycoloids	For the cure of hepatitis	Zaman *et al.* 2018, Gurudeeban *et al.* 2010, Gewali *et al.* 2008
	Cucumis sativus L.	Fruit	Methyl-phytosterol, amyrin, adenosine trialcohol	Fresh fruit slices used for the treatment of jaundice and hepatitis and also for skin diseases	Prajapati *et al*. 2006, Chen *et al*. 1992
	Cucumis melo subsp. agrestis Naudin	Fruit	Lipids, arginine, aspartic and glutamic acids while limiting amino acids were methionine and lysine	For the cure of hepatitis disease	Yasil *et al.* 2019, De melo *et al.* 2000
	Momordica charantia L.	Fruit	Proteins, polysaccharides, flavonoids, saponins	For hepatitis	Ahmad *et al.* 2017, Kumar & choyal 2012
	Ecballium elaterium (L.) A. Rich	Fruit	Flavonoids such as rutin, narcissin and kaempferol	For the cure of hepatitis disease	Touihri *et al.* 2019, G¨unes *et al*. 2017
Cuscutaceae	*Cuscuta reflexa* Roxb.	Aerial parts	Scoparone, melanetin, quercitin, caffeoylquinic.	Paste from whole plant of is taken orally to cure jaundice	Ahmad *et al.* 2017, Prajapati *et al.* 2006
Cupressaceae	*Juniperus phoenicea* L.	Leaves	Lipids, sugars, flavonoids, gallic acid and minerals like Na, K	Hepatic anti-inflammatory	Nasri *et al.* 2011, Agellete & Valles 2003
Dioscoreaceae	*Dioscorea deltoidea* Wall.	Leaves	glycosides, flavonoids, phenols, resin and tannins	For the treatment of jaundice	Hussain *et al.* 2013, Haq *et al.* 2011
Euphorbiaceae	*Euphorbia hirta* L.	Leaves, Stem	Alkanes, triterpenes, phytosterols, tannins, polyphenols, and flavanoids	Stem and leaf extracts are used in jaundice.	Ali *et al.* 2018, Kumar & Choyal 2012
	Euphorbia prostrata Ait	Aerial parts	2-phenylethanol, tannins, allic acid, corilagin, 1,2,3-tri-O-galloyl-D-glucose,geraniin,tellimagradin I, II, and rugosin	Decoction is used for the treatment of jaundice	Rasid *et al.* 2018, Shah *et al.* 2016, Yaseen *et al*. 2015, Chen *et al.* 1992
	Jatropha curcas L.	Seeds	Essential oil, α-epi-cadinol , pulegone, chrysanthenyl acetate	Powdered dry seed is mixed with sugar and water for the treatment of hapititis	Samani & Kopaei, 2018, Adebowale *et al.* 2006
	Phyllanthus embilica L.	Fruit	Alanine, aspartic acid, glutamic acid, proline, fats and Fe	Powdered dry fruit is mixed with sugar and water for the treatment of jaundice	Ashfaq *et al.* 2014, Prajapati *et al.* 2006

	Phyllanthus niruri L.	Root	Phyllanthine, flavonoids, quercetin, isoquercetin,	Liver diseases	Farooq *et al.* 2019, Prajapati *et al.* 2006
Equisetaceae	*Hippochaete debilis* (Roxb. ex Vaucher)	Aerial parts	Ash, Lipid, protein, Ca, Ascorbic acid, and niacin	For hepatitis	Tareen *et al*. 2010, Hakim *et a*l. 2008, Mangario *et al.* 1995
Fabaceae	*Acacia nilotica* L.	Flowers, bark	Amines and alkaloids, cyanogenic glycosides, cyclitols, fatty acids and seed oils, fluoroacetate, gums, nonprotein amino acids, terpenes	Used for jaundice	Samani & Kopaei 2018, Zaman *et al.* 2018, Banso 2009, Haq *et al.* 2011
	Acacia jacquemontii Benth	Leaves	Ester-cetyl triacontanoate along with n-triacontanol, n-octacosanol, ß-sitosterol and stigmasterol	Extract of leaves is used for jaundice	Yaseen *et al.* 2015, Singh *et al.* 2010
	Argyrolobium roseum (Cambess.) Jaub. & Spach	Aerial parts	Favonoids, glycoside, and vitexin, D-pinitol	Used for liver diseases	Ram *et al.* 2007, Gupta *et al.* 2005,
	Cassia fistula L.	Leaaves, flower	Gum containing arabin, tannic and galic acid	Hepatitis	Iqbal *et al.* 2016, Adnan *et al.* 2014
	Glycyrrhiza glabra L.	Root	Glycyrrhitic acid,multiple flavonoids, isoflavonoids, sterols	Hepatitis	Mahmood *et al*. 2013, Dhiman *et al.* 2005
	Mimosa pudica L.	Aerial parts	Alkaloids, flavonoid C-glycosides,sterols, terenoids, tannins, saponin and fatty acids	The crude powder of prevents liver cell necrosis and lysosomal latency	Qadir *et al.* 2017, Umair *et al.* 2017
	Prosopis cineraria (L.) Druce	Flowers	Methyl heptacosanoate, heneicosanoic acid,hydroxybenzoic acid, methyl 4-hydroxycinnamate and methyl 2-methoxy-5-hydroxycinnamate	The crude powder of flowers prevents liver disorders	Zaman *et al*. 2018, Khan *et al*. 2006
	Tamarindus indica L.	Root, fruit	β-amyrin, compesterol, β-sitosterol and seven hydrocarbons.The aerial parts of this plant have demonstrated the presence of tartaric acid, acetic acid, and succinic acid, gum, pectin, sugar, tannins, alkaloid, flavonoids, sesquiterpenes, and glycosides.	A decoction of its roots is used in the treatment of Jaundice, hepatitis and other liver disorders. Fruit also act as a remedy for the treatment of jaundice	Kidane *et al.* 2018, Kumar & Choyal, 2012

	Trigonella foenum graecum (Nevski) Afan. & Gontsch.	Seeds	N,N'-dicarbazyl, glycerol monopalmitate, stearic acid, beta-sitosteryl glucopyranoside, ethyl-alpha-D-glucopyranoside, D-3-O-methyl-chiroinsitol and sucrose	Seeds are used to cure hepatitis	Samani & Kopaei 2018, Shang *et al.* 2002
	Sophora flavescens Aiton	Root	Maackiain; trifolirhizin 6'-monoacetate, formononetin,2,4-dihydroxy benzoic acid and #beta#-sitosterol	Root decoction is used for the cure of hepatitis C	Samani & Kopaei 2018, Li *et al.* 2004
Fagaceae	*Quercus infectoria G. Olivier*	Seeds	Syringic, gallic and ellagic acids	Seeds are rusted in hot ash used for the control of hepatitis C	Samani & Kopaei 2018, Ikram & Nowshad, 1977
Fumaraceae	*Fumaria indica (*Hausskn.) Pugsley	Leaves, flowers	Alkaloids, oxyhydrastinine, noroxyhydrastinine, fumaramiine, stylopine, bisnorargemonine and fumaritine	Mixture powder of leaves and flowers used for cure of hepatitis	Shah *et al*. 2016; P Gupta *et al.* 2012 Asia
	Fumaria officinalis L	Aerial parts	Allocryptopine, chelidonine, protopine, bicuculline, sanguinarine, cheleritrine, stylopine and hydrastine	For the treatment of jaundice	Ahmad *et al.* 2017, Paltinean *et al.* 2016, Bhatia *et al.* 2014
Ganodermataceae	*Ganoderma lucidum (Curtis) P. Karst*	Fruiting body	Triterpenoids and polysaccharides	Fruiting body cooked and useful for hepatitis B	Samani & Kopaei, 2018, Boh *et al.* 2007
Gentianaceae	*Centaurium erythraea* Rafin.	Leaves	Loganin, copaene, selinene, and alpha-cadinol	For the treatment of jaundice	Mustafa *et al.* 2012, Yöney *et al*. 2010
	Swertia petiolata D. Don	Aerial parts	Flavonoids, steroids, triterpenoids, alkaloids, glycosides, carbohydrates, tannins, phenolic compounds e	For the treatment of jaundice	Samani & Kopaei, 2018, Ahmad *et al.* 2017, Bader *et al*. 2017
	Swertia chirayita (Roxb.) Buch.-Ham. ex C.B. Clarke	Leaves	Stigmasterol 4 and 1,5-dihydroxy-3-methoxyxanthone-8-O-β-D-glucopyranoside	For the treatment of hepatitis B	Samani & Kopaei 2018, Negi *et al.* 2011
	Swertia patens Burkill	Aerial parts	Elucidated, angelone, gentiogena, erythricin, erythrocentaurin, gentianine, swertiakoside, swertiamarin, actylswertiamarin, and amarogentin	For the cure of hepatitis B	Samani & Kopaei 2018, He et al., 2015

Hippocastinaceae	*Aesculus indica* (Wall. ex. Cambl.) Hook.f.	Seeds	Flavonols, phenols ree α-amino acids and carbohydrates	Used for the treatment of jaundice	Paterska *et al.* 2017, Haq *et al.* 2011
Hypericaceae	*Hypericum perforatum* L.	Aerial parts	Flavonoids, rutin, hyperoside, isoquercetin, quercitrin, quercetin, amentoflavone, biapigenin, astilbin, myricetin, miquelianin, kaempferol, luteolin, phenolic acids	Infusion is used for liver diseases	Pieroni *et al.* 2012,m Egea *et al.* 2015, Nahrstedt *et al.* 1997
Lamiaceae	*Ajuga bracteosa* Wall. ex Benth	Leaves	Exacosanol, B-sitosterol, tetracosanoic acid and B-sitosterol-B-D-glucoside	Used for liver jaundice	Ali *et al.* 2018, Haq *et al.* 2011, Riaz *et al*. 2007
	Mentha longifolia (L.) L	Leaves	Pulegone, isomenthone, 1,8-cineole, borneol and menthol	Used for the treatment of hepatitis A	Samani & Kopaei 2018, Mkaddem *et al*. 2009
	Ocimum basilicum L.	Leaves, flowers tops	Eugenol and linalool		Samani & Kopaei 2018, Govindarajan *et al.* 2013
	Salvia bucharica M. Pop	Flowers	Terpenoids, bucharioside and buchariol	Infusion of flowers are useful in jaundice	Bibi *et al.* 2014, Ahmad *et al.* 1999
	Rosmarinus officinalis L	Leaves	Phenolic compounds, di- and triterpenes and essential oils	Leaves pase is used for the treatment of jaundice	Idm'hand *et al.* 2020, Andrade *et al.* 2018
Lythraceae	*Lagerstroemia speciosa* (L.) Pers	Leaves, flowers	Corosoli acid [6], lageracetal, amyl alcohol, ellagic acid, gallic acid, 4-hydroxyl benzoic acid, beta sitosterol, Asiatic acid, alphitolic acid	For the treatment of jaundice	Ong & Kim 2014, Bai *et al.* 2008
Malvaceae	*Abutilon indicum* L.	Leaves, flowers	Carbohydrates, steroids, glycosides, flavonoids, tannins and Phenolic compounds	For cure of liver diseases	Yaseen *et al.* 2015, Kuo *et al.* 2008
	Alcea rosea L	Whole plant	Flavonoid , salicylic, vanillic, ferulic, syringic, caffeic, p-hydroxybenzoic, p-coumaric, and p-hydroxyphenylacetic acid	Whole plant is powder and decoction is used for jaundice	Ullah *et al.* 2020, Ammar *et al.* 2013
	Corchorus depressus (L.) Stock	Aerial parts	Flavonol glycosides, flavonoids, steroids	Liver tonic	Yaseen *et al*. 2015, Zahid *et al.* 2002

Meliaceae	*Melia azedarach* L.	Leaves	Quercetin, astragalin and 2-methoxy-4-(2-propenyl)phenyl β-D-glucoside	Used for the treatment of jaundice	Bibi *et al.* 2014, Kumar & Choyal 2012, Hadjiakhoondi *et al.* 2006
Menispermaceae	*Stephania abyssinica* Dillon and A. Rich	Leaves, flowers	Oxoxylopine, liriodenine, atherospermidine,	The leaf part is boiled, and about 1 cup is drunk for liver disease	Tuasha *et al.* 2018, Omole *et al.* 2014
	Tinospora cordifolia (Willd) Miers.	Stem	Terpenoid, alkaloid, lignans, steroids.	Fresh stem decotion is considered good for the treatment of jaundice and seminal weakness.	Kumar & Choyal 2012
	Peumus boldus Molina	Leaves	Trans-sabinene, pinocarveol, pinocarvone, 4-terpineol, ascaridole, piperitone oxide, and limonene dioxide	Hepatodepurative, liver ailments, combined with lemon juice, to balance the harmful properties should not be taken during more than one week, 3 leaves/cup, 3 times/day	Ceuterick *et al.* 2011, Ceuterick *et al.* 2008, Mazutti *et al.* 2008
Moraceae	*Morus alba* L.	Fruit	Ascorbic acid, carotene, vitamin D, glutathione, Ca, Cu, Zn, Volatile oil, nicotinic acid	Crushed fruits are used to cure jaundice and hepatitis	Zaman *et al*. 2018, Bhatia *et al.* 2014, Pieroni 2008a, Haq & Hussain *et al.* 2007, Ercisli & Orhan 2007
	Morus nigra L.	Fruit	Olcanolic acid, apigenin, cyclocommunol., morusin and cyclomorusin	To cure jaundice	Wang *et al.* 2007, Kassoye *et al.* 2006
Myrsinaceae	*Embelia schimperi Vatke*	Fruit	Alkaloid benzoate, oxacillin, embelin and tetracycline	Fruit is used to cure hepatitis C	Samani & Kopaei 2018, Van Damme & Kokoska 2015
Nyctaginaceae	*Boerhavia diffusa L.*	Aerial parts	B-Sitosterol, a-2-sitosterol, palmitic acid, ester of b-sitosterol, tetracosanoic, hexacosonoic, stearic, arachidic acid, urosilic acid, Hentriacontane, b-ecdysone, triacontanol	Used to treat of jaundice	Malede *et al.* 2020, Maity *et al.* 2015,
Myrtaceae	*Syzygium aromaticum (L.) Merr. & L.M. Perry*	Flower bud	Kaempferol, myricetin, rhamnocitrin, gallic acid, oleanolic acid, ellagic acid, and flavonoids	Used to treat of hepatitis C	Batiha *et al.* 2020, Samani & Kopaei 2018
Oleaceae	*Olea europaea* L	Aerial parts	Caffeic acid, verbascoside, oleuropein, luteolin 7-*O*-glucoside, rutin and apigenin	Hepatoprotective	Pieroni *et al*. 2014, Periera *et al.* 2007

Oxalidaceae	*Oxalis corniculata* L.	Leaves	Flavonoids, vitamin C and β-carotene, minerals like calcium, potassium	For the cure of hepatic disorders	Jan *et al*. 2017,Srikanth *et al*. 2012
Papaveraceae	Papaver somniferum L.	Fruit	Codeine, morphine, noscapine, papaverine, and thebaine	Used for liver diseases	Ullah *et al*. 2020, Da Cheng *et al.* 2015
Phyllanthaceae	*Phyllanthus emblica* L.	Fruit	Flavonoids	For cure of jaundice	Habib-ur-Rehman 2007, Kadir *et al*. 2007
Piperaceae	*Piper cubeba* Bojer	Root	Terpinen-4-ol (42.41%), α-copaene (20.04%), and γ-elemene	For the cure of hepatitis B	Rigat *et a*l. 2007, Blick 1996
Poaceae	*Desmostachya bipinnata* (L.) Stap	Root	Camphene, isobornyl acetate, caryophyllene diepoxide, β-eudesmol, eseroline and calarene	Juice of the root about 4 teaspoons three times a day is given in case of jaundice.	Malla *et al*. 2015, Kumar *et al*. 2010
	Hordeum vulgare L.	Seed	Arginine, Histidine, lysine, tyrosine, methionine	Dried seeds are used for hepatitis	Prajapati *et al*. 2006
	Saccharum officinarum L.	Stem	Flavonoids:naringenin, tricin, apigenin and luteolin derivatives	Juice extracted from stem considered good remedy for jaundice	Kumar & Choyal 2012
Portulacaceae	*Portulaca quadrifida* L.	Leaves	Gallotannins, omega-3 fatty acids, ascorbic acid, α-tocopherols, kaempferol, quercetin, and apigenin	For cure of hepatic	Zaman *et al*. 2018, Zhou *et al.* 2015
Podocarpaceae	*Podocarpus falcatus* (Thunb.) Mirb	Stem, leaves	Nagilactones, dilactones and derivates	The shoot is boiled, and 1 cup is drunk; Oozing liquid from the stem is mixed with cold water and is drunk for cure of liver disease	Tuasha et al., 2018, Addo et al., 2015
Polygonaceae	*Rumex hastatus* D. Don	Aerial parts	Triterpenoids, stilbene glycosides, tannic acid, saponins, resveratrol, sterols, amino acids, alkaloids, phenolic compunds and vitamin	For treatment of jaundice	Haq *et al*. 2011, Liang *et al.* 2010, Pieroni *et al.* 2008
	Rumex nepalensis Spreng.	Aerial parts	Torachrysone, rumexoside, orientaloside ,orcinol glucoside , aloesin and lyoniresinol	For the treatment of liver disease	Liang *et al.* 2010, Giday *et al*. 2009,
Punicaeae	*Punica granatum* L.	Fruit,seed	Citric acid, sorbitol, mannitol, pelletierine, isoquercetin, glucose, sucrose, maltose, and oxalic acid	Seeds of P. granatum are grounded together along with sugar dissolved in water can be used for hepatitis	Ouelbani 2016, Ikram & Hussain 1978
Ranunculaceae	*Anemone hepatica* L.	Leaves	Triterpenoids, saponins, steroids, lactones, fats and oils, saccharides, and alkaloids	Infusion is used for protection of liver	Hao & Xio,2017, Bonet *et al.* 1999

	Nigella sativa L:	Seeds	*Thymoquinone* (TQ), thymohydroquinone (THQ), dithymoquinone, *thymol*, *carvacrol*, α and *β-pinene*, d-*limonene*, d-citronellol, *p-cymene* volatile oil	Decoction is used for jaundice	Kidane *et al.* 2018, Forouzanfar *et al*. 2014
Rhamnaceae	*Ziziphus jujuba* Mill.	Fruit	Sterols, flavonoids, cerebrosides	Used for treatment of jaundice, hepatitis, and other liver disorders	Kumar & Choyal 2012
	Ziziphus mauritiana Lam.	Leaves	Betulinic aldehyde, betulinic acid, ceanothic acid, frangufoline, spinosin and stearic acid	For cure of hepatic disorders	Zaman *et al.* 2018, Guo *et al.* 2014
Rosaceae	*Prunus domestica* L.	Fruit	D-galactose, D-mannose, L-arabinose, D-xylose, glucoronic acid, prudumestin	Extract of dried fruit of P. domestica soaked are used for hepatitis.	Prajapati *et al*. 2006, Pieroni *et al.* 2014
	Rubus ellipticus Smith	Fruit	Gallic acid, catechin, chlorogenic acid and caffeic acid	Charbohydrates, Alkaloids, Saponins, Tannins, Flavonoids, Tritorpinoids	Ahmad *et al.* 2017, Badhni *et al.* 2015, Sharma & Kumar 2011
	Prunus jacquemontii Hook. f.	Fruit	Proanthocyanidin, epicatechin	For the cure of hepatitis C	Hussain *et al.* 2018, Pant *et al.* 1992
	Prunus spinosa L.	Fruit	Anthocyanin, hydroxycinnamic acids	Hepatoprotector'	Sabatani *et al.* 2020, Pieroni *et al.* 2004
Rubiaceae	*Aegle marmdos* (L.) Correa	Leaves, roots	Tannin, flavonoids, and steriods	Decoction of leaves and unripe fruit is used for treatment of jaundice and other liver disorder.	Kumar & Choyal 2012
	Morinda citrifolia L.	Fruit	Scopoletin, octanoic acid, potassium, vitamin C, terpenoids, alkaloids, anthraquinones,nordamnacanthal, morindone, rubiadin	For the cure of hepatitis	Samani & Kopaei, 2018, Su *et al.* 2005
	Rubia cordifolia L.	Roots	Anthraquinone, lucidin primeveroside, ruberythric acid and three new anthraquinones,	Decoction is used for liver problems	Ahmad *et al*. 2017, Itokawa 1983
Rutaceae	*Citrus sinensis (L.) Osbeck*	Fruit	Atripliside B, β-sitosterol, and β-sitosterol-3-*O*-β-D-glucopyranoside	For the cure of hepatitis C	Samani & Kopaei, 2018, Ceuterick *et al.* 2008, Saleem *et al*. 2010
	Citrus limon (L.) Osbeck	Fruit	β-Pinene, Limonene, Linalool and α-Terpineol	Dink the juice with honey for liver infections	Hsouna *et al.* 2017, Ellena *et al*. 2012

Saxifragaceae	*Saxifraga melanocentra Franch*	Aerial parts	Kaermpferol (1), quercetin, kaempferol, beta glucoside, quercetin, -D-glucoside	For the cure of hepatitis C	Samani & Kopaei, 2018, Zuo *et al.* 2005
Scrophulariaceae	*Picrohiza kurooa* Royle ex.Benth	Rhizome	Kutkin, a bitter glycoside which contains two C-9 iridoid glycosides-Picroside I and Kutakoside.	Rhizome powder is used in the treatment of liver troubles and jaundice	Kumar & Choyal 2011
Solanaceae	*Solanum nigrum* L.	Leaves	Gentisic acid, luteolin, apigenin, kaempferol, m-coumaric acid. anthocyanidin	To cure hepatitis, A,B,C	Hussain *et al.* 2016
Urticaceae	*Arietaria judaica* L.	Leaves	Piperitone, camphor and ethyl cinnamate	Used as antiviral	Maxia *et al.* 2008
Zingiberaceae	*Curcuma longa* L.	Root	Ar-turmerone, β-sesquiphellandrene and curcumenol, c*urcumin*	Decoction is used for hepatitis C	Abduel-Lateef *et al.* 2016, Sandhu *et al.* 2005
	Zingiber officinale Roscoe	Root	6-gingerol**,** 6 shogaol**,** and 6-paradol, zingiberene and bisabolene, gingerols and shogaols	Decoction is used for jaundice	Feng *et al.* 2011, Heinrich *et al.* 1998

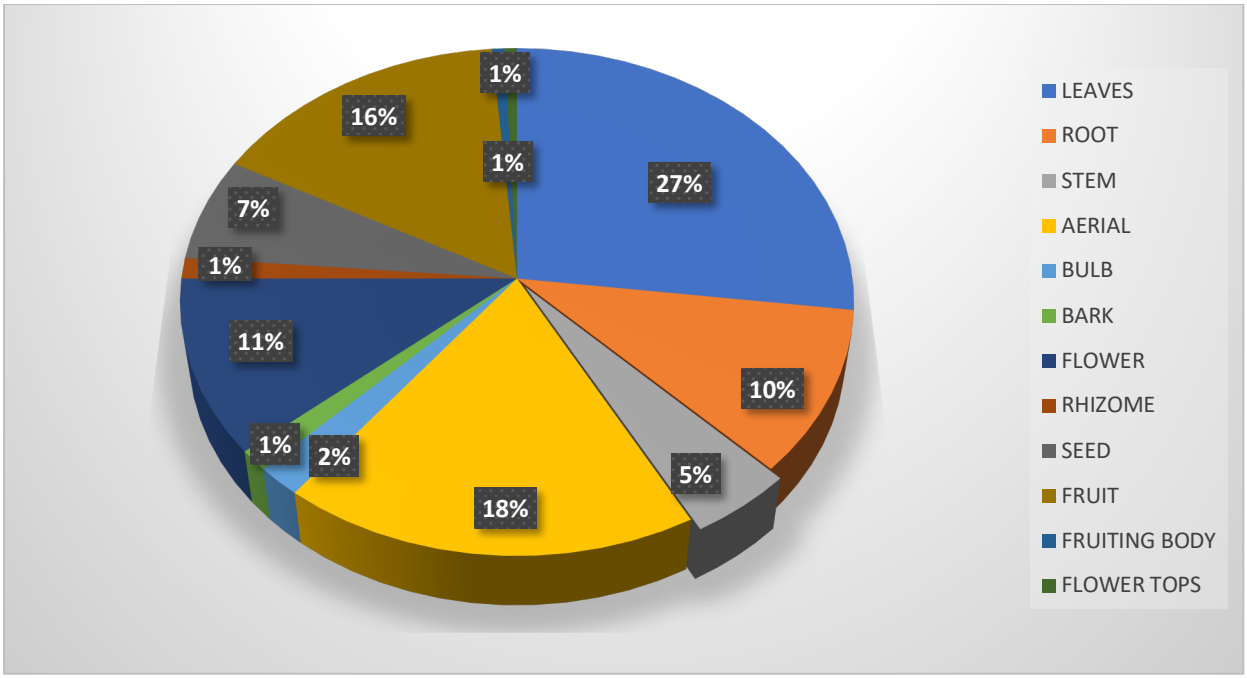

Figure 2. Medicinal Plants Part used for the treatment of hepatitis

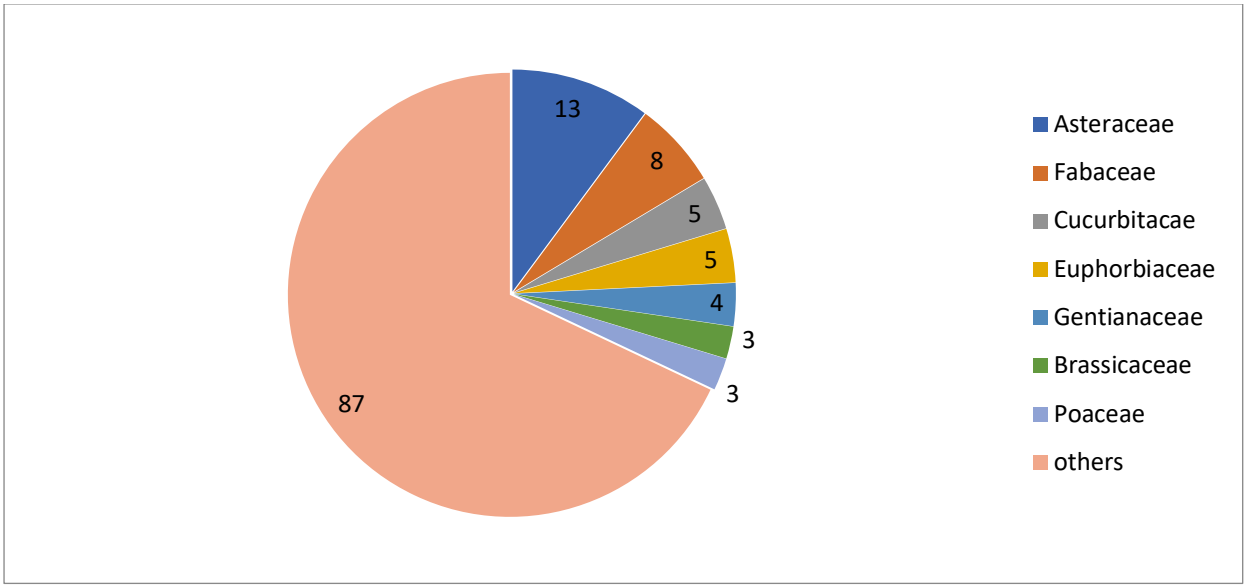

Figure 3. Frequency of the most represented botanical families (Number species)

In order to assess how geographical and ecological factors may have affected indigenous practices, the recorded data were subjected to regional comparison. The medicinal plants were divided into four groups (a) Pakistan (b) Asia (c) Europe (d) Rest of the world. Jaccard's similarity index was applied to determine similarities on the medicinal flora used for the cure of different types of hepatitis in different cultural communities all over the world. According to the Jaccard's index of similarity, the Pakistani communities used sum total of 58 species, Asia 56 species, Europe 24 species and rest of the world 18 species for the cure of hepatitis. Between Pakistani and Asia community's 14 species (12%) were found to be the same while between Asia and Europe 5 species (6.2 %) were found in common. The similarity between Pakistan and Europe communities was 7 species (11%). The current study documented 6 species (7.8 %) similarity between Pakistan and rest of the world and 5 species (6.2%) were shared between Asia and Europe. The similarity between Asia and Rest of the world were recorded as 4 (5.4%) Figure 4. The maximum similarities were observed between Pakistan and Asia (12 %).

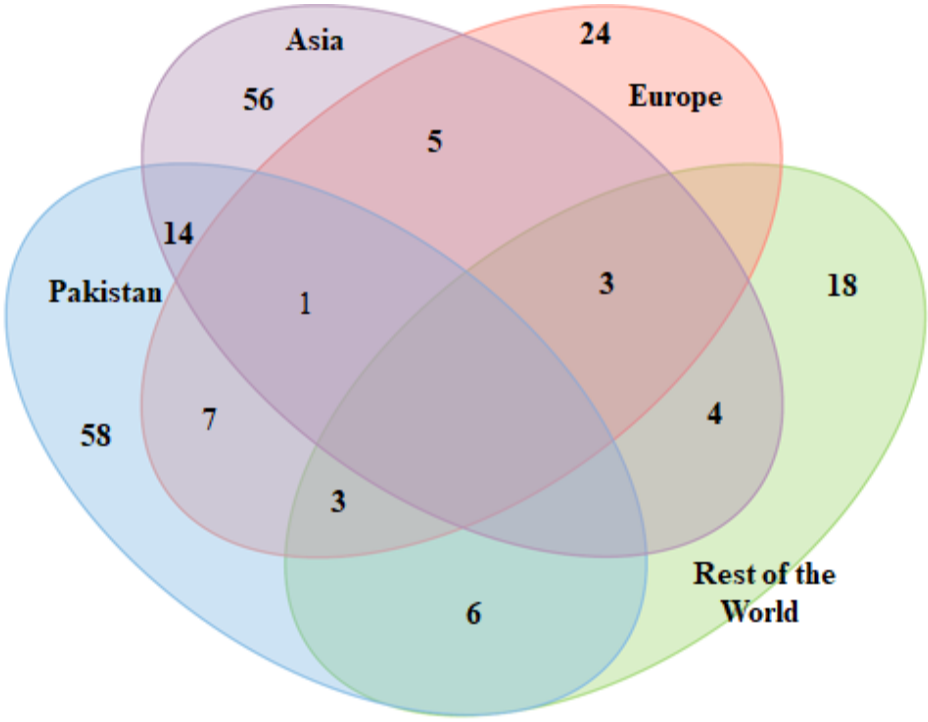

Figure 4. Venn diagram showing the comparison among the four studied regions (number of recorded plant species).

Silybum marianum (Milk thistle) has been used to treat liver diseases since the 16th century. Its major constituents are the flavonoids silibinin, silidianin, silichristin, and isosilibinin of which silibinin is the biologically most active compound and used for standardization of pharmaceutical products (Wagner *et al.* 1976).The pharmacological profile of Silymarin has been well defined and hepatoprotective properties of Silymarin were investigated both in vitro and in vivo. Glycyrrhizin is an extract of the *Glycyrrhiza glabra*, used in medicine traditionally to relieve bronchitis, gastritis and jaundice. The compounds present in glycyrrhizin are glycyrrhetic acid, flavonoids, hydroxycoumarins, and beta-sitosterol. For treatment of chronic hepatitis, a standardized extract containing glycyrrhizin, cysteine and glycine is organized as Stronger Neo-Minophagen C (Stickel & Schuppan 2007). The plants of the genus *Phyllanthus* are found in most tropical and sub-tropical countries and have long been used to treat chronic liver diseases. Phyllantins, hypophyllantins and several polyphenoles are major constituents of which chemical and pharmacological properties are well described (Calixto *et al.* 1998). The active compounds within Phyllanthus showed anti-viral activities against hepatitis B virus infection through mRNA transcription and replication (Venateswaran *et al.* 1987). Recently, a number of trials were evaluated regarding *Phyllanthus* extract preparations in a systematic review which led to clinical evidences for the treatment of chronic hepatitis B (Liu *et al.* 2001). To cure liver disorders numerous herbal mixtures are identified through search in traditional Oriental Medicine Database (Chen *et al.* 1998). Among these, extracts from *Plantago asiatica* appear to exert hepatoprotective activity without significant toxicity. In United States, for both acute and chronic hepatitis with focal necrosis and portal fibrosis *Lycopodium serratum* has been considerably used based on duration of intake. It has sleep-inducing properties (Woolf *et al.* 1994, Picciotto *et al.* 1998). In U.S. ephedrine in Ma Hung (Ephedra sp.) used to lose weight. A person with acute hepatitis used Ma-Hung for only 3 weeks, he developed anti-nuclear antibodies and muscle anti-bodies (Nadir *et al.* 1996).

Many plant species have been examined for a broad-spectrum activity to cure liver disorders (Asadi-Samani *et al.* 2015). *Panax ginseng* belongs to family Araliaceae. Roots of ginseng inhibit toxin hepatic damage by decreasing vital genes expression, which is essential for normal liver functions (Hafez *et al.* 2017). *Cynara scolymus* (artichoke) of the Asteraceae family, a species, is traditionally used for the treatment of digestive disorders, moderate hyperlipidemia and liver and biliary diseases. *C. scolymus* leaf extract has been used for its hepatoprotective effects (Gebhardt 1997). By studying literature it has been confirmed that *C. scolymus* was important in maintaining normal liver function parameters, maintaining liver redox status, as manifested by a significant increase in the activities of antioxidant enzymes and a

reduction in glutathione accompanied by inhibition of lipid peroxidation (LPO) and protein oxidation, decreased nitric oxide and tumor necrosis factor alpha, and stabilized membrane in untested paracetamol-intoxicated rats (Ali *et al.* 2012). *Hedyotis diffusa* and some of its active constituents have a wide variety of reported pharmacological activities, including anticancer, chemo preventive, hepatoprotective, antiviral, antibacterial, antidiabetic, antioxidant, and gastroprotective properties (Qi *et al.* 2015). *Nigella sativa* belongs to family Ranunculaceae is used traditionally for the different disorders such as asthma, cough, bronchitis, headache, rheumatism, fever, influenza, and eczema. Antioxidant activity and resolution of hepato-renal toxicity have been reported for N. sativa seeds (Al-Ghamadi 2001). Juice of *Ananas comosus* (L.) Merr (Bromeliaceae) commonly known as pineapple, has liver protective action (Mohamad *et al.* 2015) by controlling different protein expression, antioxidant levels and liver marker enzymes against paracetamol-induced toxicity. Fruit seeds of *Cassia fistula* (golden shower tree of family (Fabaceae) have protective potential against hepatotoxins-induced liver damage and have non-significant effect on hematological parameters (Iqbal *et al.* 2016). Fruiting bodies of *Oudemansiella radicata* Relhan ex Fr an edible mushroom and belong to the family Physalacriaseae has hepatoprotective activity by antioxidant mechanisms attributed to heteropolysaccharides (mannose, glucose and galactose) prepared from the mushroom (Liu *et al.* 2017). Heteropolysaccharides (arabinose and galactose) from *Ziziphus jujube Mill* commonly known as red date family Rhamnaceae has been involved in liver protective activity via alleviating liver marker enzymes (Liu *et al.* 2015). *Phyllanthus amarus* Schum et Thonn (Bhuia amla in Hindi) is a medicinal herb belonging to the family Euphorbiacae. The whole plant is used commonly in central and southern India. It is an ayurvedic herb and has a wide range of traditional uses including jaundice (Bhragwal *et al.* 2010). *Monochoria hastata* is used for the treatment of hepatitis in tehsil Shakargarh, Punjab, Pakistan (Ali *et al.* 2020). Ullah *et al.* (2010) showed that the root of *Gynosporia royleana* is used to cure of hepatitis C. The leaves of *Pegonia cretica* are used to treat hepatitis. The ethnobotanical survey in Taiwan showed that there are (69) different types of raw drugs and (107 species) of therapeutic taxa, which are highly applied for the cure of hepatitis by increasing the liver safety and to increase the ability of the liver to resist hepatitis (Lin & Kan 1990). For the treatment of viral hepatitis people in Dembia district in Ethiopia used the medicinal plants viz., *Adhatoda schimperiana, Phytolacca dodecandra* and *Calpurnia aurea* for the treatment of hepatitis by taking their juice directly (Tadele *et al.* 2015; Asmamaw and Achamyeleh 2018;). Similarly, the trace elements present in the leaves of plants and in other tissues of herbal taxa used in control of hepatitis as reported by some authors (Malede *et al.* 2020). Yao *et al.* (2020) reported that the one of the most famous tradition Chinese medicinal herb *Abrus cantoniensis* Hance (AC) is used to cure hepatitis B virus (HBV) by inhibiting the production of HBV DNA as well as Hepatitis Be Antigen (HBsAg), and Hepatitis B surface antigen (HBsAg). From India (Monika *et al.* 2020) also showed that some medicinal plants i.e. the leaf and flower part of the *Pandanus fascicularis* Lam, the root of the *Berberis aristata* DC and the whole plant of *Oxalis corniculata L* is used for the treatment of hepatitis. Farzaei *et al.* (2020) showed that the *Glycyrrhiza glabra* (Licorice) used for the treatment of hepatitis, besides from the treatment this plant also famous for the treatment of cough and sore throat.

Many other medicinal plant species are traditionally used to treat hepatitis. Plants derived natural products such as flavonoids, terpenes, protein, lignans and alkaloids to inhibit the replication cycle of DNA and RNA viruses (Prajapati *et al.* 2006). *Argyrolobium roseum* (Fabaceae) produces vitex (flavonoid) and D-pinitol (monosaccharide) and these two compounds are reported to control hepatitis C (Gupta *et al.* 2005, Ram *et al.* 2007). Medicinal plants such as *Adiantum capillus-veneris, Argyrolobium roseum, Equisetum debile, Carissa opaca, Phyllanthus emblica, Segeretia brandrethiana, Viola serpens, Plantago ovate, Woodfordia fruticosa, Saccharum officinarium* and *Prunus domestica* have more recently been reported for the treatment of hepatitis. The medicinal plant *Adiantum capillus-veneris* (Adiantaceae) comprising chemical constituents, which are used for the treatment of hepatitis. It is important to confirm that which plant parts are used in liver diseases because in most of the phytochemical investigations, the secondary metabolites are different in plants parts. Different types of plants used by the local communities of Kalat and Huzdar region of Baluchistan, Pakistan traditionally to cure various types of hepatitis (Table 1). In addition, it has also been reported that, mostly plants used as a treatment of Hepatitis in the Soan Valley Salt Range Pakistan (Tareen *et al.* 2010, Bibi *et al.* 2014). The main natural products report from these plants are flavonoids, terpenoids, tannins, volatile oil, gallic acid (Khanum *et al.* 2013). The main secondary metabolites reported from *Berberis lycium* (Berberidaceae) have been shown active in curing hepatitis, as has *Equisetum debile* (Equisetaceae), *Cucumis sativus* (Cucurbitaceae), *Cuscuta reflexa* (Convolvulaceae) showed anti hepatitis activity

((Abbasi *et al.* 2010, Khan *et al.* 2010). The seeds of *Hordeum vulgare* contain chemical constituents for the cure of hepatitis e.g. arginine, histidine, lysine, tyrosine, methionine (Abassi *et al.* 2009). Some compounds reported from *Morus alba* (Moraceae) fruit treat jaundice and hepatitis. *Morus nigra* (Moraceae) produce olcanolic acid, apigenin, cyclocommunol, morusin and cyclomorusin which are used to cure jaundice (Wang *et al.* 2007). *Oxalis corniculata* (Oxalidaceae) leaves contain, glyxylic acid, oxalic acid, vitexin, isovitexin, vitamin C and tocopherols that are useful to treat hepatitis A and B types. The main constituents of the fruits of *Phyllanthus emblica* (Euphorbiaceae) anti-hepatitis compounds such as alanine, aspartic acid, glutamic acid, proline, fats, and iron (Abassi *et al.* 2009). The root extracts of *P. niruri* (Euphorbiaceae) are used to treat liver diseases; the extracts of this plant are reported to contain phyllanthine, flavonoids such as quercetin and isoquercetin. *Prunus domestica* (Rosaceae) fruit contains D-galactose, D-mannose, L-arabinose, D-xylose, glucoronic acid, flavonoid, and prudomestin. *Punica granatum* L. (Punicaceae) contain citric acid, sorbitol, mannitol, pelletierine, isoquercetrin, glucose, sucrose, maltose and oxalic acid in their fruits and seeds (Ikram 1978) and both plants show anti-hepatitis activity. *Silybum marianum* (Asteraceae) is most important for the treatment of hepatitis. Extracts of *Silybum marianum* (milk thistle) have been recognized as “Liver tonic” for centuries. Milk thistle has been reported to have protective effects on liver and to greatly improve its function (Hackett *et al.* 2013). *Silybum marianum* leaves are reported to contain flavoligrans, silybin, isosilybin and silymarin and these compounds have application to cure jaundice. The main compounds reported from *Silybum marianum* are the flavolagnans silybin, silydianin, and silychristine collectively called as silymarin. Silybin is the most important compound with range of biological activities. Moreover, Silymarin found in the whole plant but its more concentrated in fruits (6% in ripe fruit) and seeds. In addition, extracts of milk thistle have been recognized as liver tonic (Dhiman *et al.* 2005). Another plant, *Ziziphus mauritiana* (Rhamnaceae) contains twenty-one compounds, including ten triterpenoids, two sterols, six flavonoid and three cerebrosides, these were isolated from the fruit of *Zizyphus mauritiana* for the disorder of liver diseases. *Melia azedarach* is found to be useful to treat hepatitis. Many of these plants show antioxidant activity, possibly explaining their hepatoprotective activity (Moradi *et al.* 2016). The crude powder of *Mimosa pudica* prevents liver cell necrosis and lysosomal latency by normalizing serum biochemical parameters against carbon tetrachloride induced hepatotoxicity (Qadir *et al.* 2017). The roots of *Boerhavia diffusa,* commonly known as 'Punarnava', are used by a large number of tribes in India for the treatment of various hepatic disorders. The hepatoprotective activity of different parts of Boerhavia diffusa L. (Nyctaginaceae) such as root and aerial parts was evaluated against Ibuprofen persuade hepatotoxicity in Wistar albino rats (Maity *et al.* 2015).

Conclusions

Our study showed that many medicinal plants have been used since ancient time to cure hepatitis worldwide. Our literature review will help the scientific community to identify anti-hepatitis plants in order to isolate novel anti-hepatitis compounds.

Declarations

List of abbreviations: HAV:Hepatitis A Virus, HBV:Hepatitis B Virus, HCV:Hepatitis C Virus, WHO:World Health Organization, LPO:lipid peroxidation, DNA:Deoxy-ribo Nucleic Acid, RNA:Ribo-Nucleic Acid, HIV:Human Immune Virus

Ethics statement: Thius study ia pure literature reveiw, and no ethics approval was required.

Conflict of Interest: The authors declare no conflicts of interest.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors’ contributions: Wahid Hussain designed the project wrote initial draft, Saima Batool, Sabeha Bahar, Bibi Shahida, Bushra Bangash helped in data collection. Amjad Ali, Hidayat Hussain, Iftikhar Ali, Maroof Ali and Rainer W. Bussmann helped in the revision of the manuscript. All the authors approved the final manuscript after revision.

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