



# **A Comparative Review on Medicinal Plants Used for the Treatment of Liver Disorders as in Ayurved, Siddha and Unani [ASU] Systems of Medicine- Part I- Contextual and Clinical Aspects**

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## **ABSTRACT**

In recent times the liver dysfunction has gained significant importance as a precursor and for a broad range of metabolic disorders. Both, chronic and acute liver diseases irrespective of age, sex, region or race are the major cause of morbidity and mortality across the world. Natural products are used and examined for various types of liver disorders. Large number of compound formulations and single drugs from *Ayurved*, *Siddha* and *Unani* systems are commonly used without much adverse effects to manage a variety of liver disorders.

Various liver diseases are described in in Ayurveda, Unani and Siddha systems that are explained in the light of presently available biomedical information. This review is outcome of a systematic effort and analyses of hepatoprotective formulations and ingredients particularly in the context of contextual and clinical information and research undertaken. An attempt has been made to short list twenty-five (25) potential medicinal plants out of 106. The enlistment of these 25 plants with relevant updated information as compiled and categorised will provide insights to choose possible treatment approaches and to examine further potentials. This review can help enhance translational research by connecting fundamentals of traditional systems with the modern scientific parameters and thereby reducing the screening time, efforts and costs.

**KEY WORDS:** Liver disorders, Ayurved, Siddha, Unani, Medicinal plants

## **BACKGROUND**

Liver diseases are a major cause of morbidity and mortality across the world. As per WHO estimates, about 500 million people are living with chronic hepatitis infections resulting in the death of over one million people annually. Chronic liver disease occurs throughout the world irrespective of age, sex, region, or race<sup>[1-2]</sup>. Liver diseases are the tenth most common cause of death in India and may affect one in five Indians. Around 10 lakh patients of liver cirrhosis are newly diagnosed every year. Liver cirrhosis is the 14<sup>th</sup> leading cause of death in the world and could be the 12<sup>th</sup> leading cause of death in the world by 2020<sup>[3-4]</sup>.

The liver is a vital glandular organ of digestive system having multifold functions including glycogen synthesis, making of proteins and blood clotting factors, manufacturing tri glycerides and cholesterol, and bile production<sup>[5]</sup> and involved in the maintenance of metabolic functions and detoxification of the exogenous and endogenous challenges.

*Ayurved*, *Siddha* and *Unani* [ASU] are indigenous systems of medicine of India that provide descriptions of different types of liver diseases and offer therapeutic approaches, products, and ingredients of natural origin to treat them. Hundreds of liver tonics based on these systems are prescribed and used by physicians. Several of these compound formulations and ingredients are clinically studied for a variety of therapeutic benefits in liver dysfunctions.

## METHODOLOGY

Many scientific articles and papers including review articles and research on liver diseases and ASU are published from time to time. A series of review papers have been published by *Bhatt et al* pertaining to liver disorders, therapeutics and medicinal plants used in the treatment of liver diseases with elaborate compilation of classical, proprietary and patented Ayurvedic products providing extensive information and explaining the liver diseases. These give common drugs used for various preparations along with pharmacological actions<sup>[6-10]</sup>.

The therapeutic potentials offered by the ASU in the treatment of liver diseases in a combined manner have not been explored. In this comprehensive review an effort has been made, probably for the first time, to provide all-inclusive information on liver disorders and pooled data on medicinal plants used for liver diseases in all the three - ASU classical texts, pharmacopoeias and national formularies. Further, these formulations and ingredients are assessed for their contextual and clinical information in a summarised manner to help examine their potentials<sup>[11]</sup>.

## LIVER IN ASU SYSTEMS

### Ayurvedic Perspective<sup>[12-16]</sup>

In Ayurveda liver – *yakrita*, jointly with spleen - *pleeha* is considered root of the *Raktvahasrotas* –the biological channels associated with the formation, transportation, and transformation of blood (the *raktadhatu*). The disorders of liver are explained in terms of *dosa*, the functional (or humoral) systems, particularly *pitta*- the bile, the *dhatu*s namely *rakta* and *mamsa*-the metabolic tissue systems of blood and muscle, *hrid*- the heart, and *pranavahasrotas*- the respiration and formation of *ranjak pitta*- through hepatobiliary excretion. Significantly, the liver gets affected in the diseases where above systems are involved.

Liver and spleen are the considered location of *Ranjaka pitta* [subtype of *pitta*- *Ranjaka* means -to induce color] that represent the water and fire components in a fluid form in the body and is responsible for transversion/transformation of all metabolites. It gives color to the blood and to all tissues all over the body (it even influences skin, hair, and eye color). Thus, the function of *Ranjaka pitta* governing the transformation of *rasa dhatu* (plasma) into *raktadhatu* (red blood cells) is closely related to the liver where the disintegration of hemoglobin and production of bile and enzymes occur. This correlates to the regulatory and functional link between liver, spleen, gastrointestinal system, and the bone marrow.

As per *tridosas* [three biological functional systems of the body] concept, *pitta* is responsible for metabolic functions at cellular or molecular levels as well. All liver disorders are due to either aggravated or diverted or obstructed flow of *Pitta* [bile]. Excessive bile production or a blockage in the flow of bile usually indicates excessive *pitta* – inflammatory activity which in turn affects the *agni* or enzymatic activities responsible for absorption, digestion, and metabolism. The diminished state of disturbed metabolism (*dhatwagni* imbalance) results in the progressive growth of the liver tissue and creates metabolic crisis

where anabolic phase exceeds the catabolic phase (aggravation of *vata* forces and suppression of *kapha* forces) leading to its fibrosis, necrosis or proliferation.

The symptoms of hepatic disorders include *pittavridhhi*- increased bile, *yakrutadhatwagnimanya* – decreased hepatic uptake, *saman vikruti* - decreased hepatic conjugation, *yakrutashotha*- hepatocellular inflammation or damage, *sang*- biliary stasis, *yakrut-medojsiragranthi*- steatosis, and *yakrutshosh*- cirrhosis. It is clearly stated that *ekadesavriddh*- liver enlargement is accompanied by *anyasthaniyakshaya* - weight loss as in metastatic liver.

Several liver diseases and their subtypes like *pandu* - anemia of different origins, *kaamala* - Jaundice, *kumbha kamala* and *halimak*- hepatitis and acute inflammatory liver, *udarroga* - abdominal alteration or distortion, *jalodara* - ascites, *yakritdalthadara* (ascites with hepatomegaly), *yakritplihadara* – hepatosplenomegaly, *yakritkshaya* - cirrhosis, *pittasmari*- cholithiasis and such others are described in Ayurvedic classical texts<sup>[17-18]</sup>. An effort is made to compare cirrhosis of liver with the etiopathogenesis, signs and symptoms of *yakrddalyudara* and its management as mentioned in classical Ayurvedic texts<sup>[19]</sup>.

*Saleem et al and Rane et al* have compiled promising phytochemicals from medicinal plants that have been tested in hepatotoxicity models using modern scientific system<sup>[20-21]</sup>.

*Panda et al.* have documented more than 200 cases of liver diseases of which 50% rely on Ayurveda and herbal medicine and 40% of among which were Non-Alcoholic Fatty liver diseases followed by Cirrhosis of liver. They have reported more than three hundred herbo-mineral preparations used in Ayurveda for the treatment of jaundice and chronic liver diseases<sup>[13]</sup>. *Kasar N. V. et al* has revealed the similarities about the genesis of liver diseases between the ancient and modern medicine<sup>[22]</sup>.

*Yan Li et al* have summarized that Ayurvedic herbal compounds are found to be efficacious and safe in single centre limited studies in the treatment and prevention of HCC and cirrhosis, but need to validate with Phase 2 and Phase 3 studies<sup>[23]</sup>.

#### **Siddha perspective<sup>[24]</sup>**

In Siddha system liver is considered an important organ for metabolic functions. Irregular food habits, environmental exposures, lifestyle [*Unavahiseyalmarupadu*] and genetic causes [*Karma vinai*] are considered the primary causes of liver diseases. *KalleeralNoi*, the enlargement of liver is classified in to three types based on the three humoral systems as *ValliKalleraiNoi*, *AzhalKalleraiNoi*, *IyaKalleraiNoi*. The humoral system of *pitham* gets affected and in association with other humors results in different types of liver dysfunctions. The affected *pitham* causes affection in the first two physical constituents, the metabolites [*Udalthathukal*] namely *Saram*- nourishing juice similar to plasma and *Kuruthi* – the blood. This leads to depletion of tissue systems and obstruction in the natural functional pathway of *pitthuneer*, the bile. Along with this *Keezhnakkukal* and *Melnokkukal*, the two types of *Vatham*, movements are deranged, leading to the dysfunction of the liver that develops into different types of liver disorders. These details are available on National Health portal, Government of India.

*Ponniahamsy G et al.* have reviewed the hepatoprotective plants and formulations used in the Siddha medicine to treat liver disorders<sup>[25]</sup>. Some of these formulations have been tested in toxicity model and preliminary studies using modern parameters<sup>[26-27]</sup>. A review by *D. Prakash et al* suggested that Siddha herbals and herbo mineral formulations might provide the right path for the management of the liver diseases<sup>[28]</sup>. *Parthiban P. et al* have reported 15 plant drugs that possessed effective hepato-protector activity<sup>[29]</sup>.

#### **Unani perspective<sup>[30-32]</sup>**

Liver described as the largest and unique organ in Unani system is recognized as the source of *hararat-e-ghariziya*, the innate heat for the body. In human body it is stated to represent sun, as a source of energy to other planets, to other parts of the body. Liver is considered essential for production of *akhlal* - humours and its four vital controls - *quwaa* namely, *quwat-e-jaziba* - control of absorption, *quwat-e-ghaziya* – control of

digestion, *quwat-e-masikah*- control of retention and *quwat-e-dafiya* – control of excretion that relates to all bodily functions. The disturbance in the functioning of any of these four controls leads to disturbance in the temperament of humours, the functional systems. Further, the activities & the characteristics of the functional systems lead to accumulation of *mawad-e-fasida* - morbid matter and ultimately pathological changes take place in the liver. The derangement of temperament of humours may be simple - *saada* which need simple therapeutic measures or it may be complex- *maddi* where organic disturbance and quantitative changes take place in the liver cells.

Simply stated, in Unani system the liver is recognized as the prime regulator of all bodily functions and several papers on these therapeutic principles have been published. *Shabnam Ansari et al* have summarized different diagnostic, pathological, treatment and drugs options useful in treatment of various types of liver ailments<sup>[33-34]</sup>. *Hoosen M* has described various temperaments of liver as an indicator of normal or pathological state<sup>[35]</sup>. Numerous case studies demonstrating significant decrease in fibrosis and improvement in liver functions in conditions of decompensate liver cirrhosis are reported by *Mohammed Akhtar Siddiqui et al*<sup>[36]</sup>.

### **Common approach to liver disorders in ‘ASU’ systems**

The significance of the liver in the context of blood as an important fluid-component of human biology is explicit to ASU systems of medicine. According to Ayurveda and Siddha, liver is actively involved in all metabolic functions primarily across *Ranjak Pitta*, the biliary route. Unani system has emphasized on liver as a source and regulator of *hararat-e-ghariziya*- innate heat, the energy for the body. Siddha system believes that *pitham*, the transformational functional system gets afflicted by the other humors that results in the liver dysfunction. The deviation of the hepato-biliary channels and their functions characterised by heat and inflammation, thus in all the three systems are considered responsible for various types of liver disorders.

Different types of liver disorders as in ASU are given in Table - 1.

**Table – 1: List of Various Liver Disorders in ASU Systems<sup>[8]</sup>**

No.	<i>Modern term</i>	<i>Ayurved terms</i>	<i>Siddha term</i>	<i>Unani term</i>
1.	Abdominal Swelling	<i>Gulma</i>	<i>Vippuruthi</i>	-
2.	Abdominal Distortion	<i>Udarroga</i>	<i>Kunmam</i>	-
3.	Abscess of Liver	<i>Yakridvidradhi</i>	<i>Pitta Vippuruti</i>	<i>Dabila-e-Jigar</i>
4.	Anemia	<i>Pandu</i>	<i>VeluppuNōy</i>	<i>Su-ul-Qinaya</i>
5.	Ascites	<i>Jalodara</i>	<i>Peruvayiru</i>	<i>Istiska</i>
6.	Chronic non obstructive Jaundice with Oedema	<i>Kumbhakamla</i>	<i>KumbaKamalai</i>	--
7.	Cholelithiasis	<i>Pittashamari</i>	<i>Hisat-e-Mararah/ Hisat-e-Kabid</i>	<i>Pithappaikal</i>
8.	Cirrhosis of Liver	<i>Yakrddalyudara, Kumbhakamla</i>	-	<i>Segar-e-Jigar</i>
9.	Dullness of Liver, Hepatosis /Hypocholeretic	-	-	<i>Zauf-e Jigar</i>
10.	Hepatomegaly [Enlargement of Liver]	<i>Yakrita-Vriddhi, Yakritodara</i>	-	-
11.	Hepatalgia, Hypocholeretic	-	-	<i>Dard-e-Jigar/ Waj-ul-kabid</i>
12.	Hepatic obstruction	-	-	<i>Sudda-e-Jigar</i>

13.	Hepatitis	<i>YakrtgataDosa</i>	-	<i>Warm-e-Jigar/ Kabib</i>
14.	Humoral Dysfunction Specific to Liver	-	-	<i>Su-e- Mizaj</i>
15.	Induration of spleen/ Liver	-	-	<i>Salabat-e-Tehal&amp;Salabat-e-Kabid</i>
16.	Jaundice	<i>Kamala</i>	<i>Kaamaalai / Mañcaḷ Nōy</i>	<i>Yarqan</i>
	Hemolytic Jaundice	<i>KoshthashritKamla</i>		
	Hepatic Jaundice	<i>ShakhashritKamla</i>		
	Chronic Obstructive Jaundice	<i>Halimak, Alasak</i>		
17.	Liver disease	<i>Yakurta-vyadhi</i>	<i>KalleeralNoi</i>	-
18.	Liver cancer	<i>Granthi/ Arbuda</i>	<i>Katti</i>	-
19.	Trauma	-	-	<i>Zarba-e-Jigar</i>
20.	Weakness of liver	-	-	<i>Zof-e-kabid</i>

The above diseases vary in nature and are result of one or more of hepatic dysfunction like sluggishness, inflammation, enlargement, obstruction or trauma. While there are many similarities amongst the three indigenous systems, the Unani system offers some distinctive features of the liver dysfunction.

A large number of treatment modalities and medicinal products of many plant, animal and mineral drugs used singly or in proportionate combinations and at times special processes or dosage forms are ascribed for variety of clinically distinguishable pathological liver conditions.

### **TREATMENT MODALITIES**

There does not exist a definitive safe and effective therapeutic solution to several of the well-defined group of liver diseases being of different origins and of variable progression. Medicinal products and agents are mostly aimed at symptomatic relief with limited therapeutic interventions that manage the underlying cause and provide reversal of the disease process, particularly in serious hepatic diseases.

It is most noteworthy that liver is not only recognized in ASU systems of medicine as an important organ in the body but clinically distinguishable hepatic dysfunctions are clearly described in these ancient texts much before the present-day familiarity. An exceptionally large number of classical formulations, herbo-mineral compounds and ingredients in various dosage forms are mentioned in ASU texts for a variety of liver diseases.

### **MEDICINAL PLANTS LISTED IN ASU SYSTEMS<sup>[37-48]</sup>**

Hundreds of formulations and ingredients are described and used in ASU systems for the treatment of liver disorders. After a careful and critical review of material compiled and consolidated from all the three – Ayurveda, Unani and Siddha systems earlier an updated list of 106 medicinal plants that are used either singly or in different formulations for the treatment liver disorders is prepared. (**Table - 2**)

Several formulations in classical dosage forms and natural ingredients other than medicinal plants like minerals or animal products are not included in this list because of poor availability of relevant scientific data and due to challenges related to their standardization.

**Table – 2: Medicinal Plants for Liver Disorders in ASU Systems**

Sr. No.	Botanical name	Common name	Ayurved	Unani	Siddha
1.	<i>Abrus precatorius</i> L.	Rosary pea	√		
2.	<i>Acalypha indica</i> L.	Indian Acalypha			√
3.	<i>Achille millefolium</i> Linn	Common yarrow	√		
4.	<i>Aconitum herterophyllum</i> Wall	Himalayan Monkshood	√		
5.	<i>Aegle marmelos</i> (L) Corrêa	Bael	√		√
6.	<i>Aegiceras corniculatum</i> (L) Blanco	River Mangrove	√		
7.	<i>Allium cepa</i> L.	Onion			√
8.	<i>Allium sativum</i> Linn.	Garlic			√
9.	<i>Aloe vera</i> (L) Burm.f. i/ <i>barbadensis</i> Mill.	Aloe	√	√	√
10.	<i>Alstonia scholaris</i> (L.) R. Br.	Devil tree	√		√
11.	<i>Alternanthera sessilis</i> (L.) R.Br. ex	Sessile Joyweed			√
12.	<i>Amaranthus tricolor</i> L.	Edible amaranth			√
13.	<i>Amomum subulatum</i> Roxb.	Black cardamom		√	
14.	<i>Amoora rohituka</i> (Roxb.) Wight & Arn.// <i>Tecoma undulata</i> (Sm.) G.Don	Rohida	√		√
15.	<i>Andrographis paniculata</i> Nees.	Green chireta	√		√
16.	<i>Apium graveolens</i> Linn.	Celery		√	
17.	<i>Artemisia absinthium</i> L.	Afsantin	√		
18.	<i>Aquilaria agallocha</i> Roxb.	Agarwood	√	√	
19.	<i>Asarum europaeum</i> L.	Wild Ginger		√	
20.	<i>Asparagus racemosus</i> (Wild.)	Shatavari	√		
21.	<i>Asteracantha longifolia</i> Nees.	Kokilaksha	√		√
22.	<i>Azadirachta indica</i> A. Juss	Margosa	√		√
23.	<i>Berberis aristata</i> DC. / <i>Berberis lyceim</i> Royle	Indian Barberry	√	√	√
24.	<i>Boerhaavia diffusa</i> Linn.	Hogweed	√		√
25.	<i>Borage officinalis</i> Linn	Borag		√	
26.	<i>Calotropis gigantea</i> (Linn)R.Br.	Crown flower, Madar	√		
27.	<i>Capparis spinosa</i> L.	Himsra	√		
28.	<i>Cassia fistula</i> L.	Golden tree	√		√
29.	<i>Cassia occidentalis</i> L.	Negro coffee, Senna coffee	√		√
30.	<i>Cedrus deodara</i> (Roxb.) G.Don	Cedar, Deodar	√		
31.	<i>Cichorium intybus</i> L.	Chicory	√	√	
32.	<i>Cinnamomum zeylanicum</i> Blume	Cinnamon	√	√	
33.	<i>Cinnamomum cassia</i> (L.) J.Presl	Tajkalmi		√	
34.	<i>Citrullus colocynthis</i> (L.) Schrad.	Colocynth, bitter apple	√		
35.	<i>Citrus species</i>	Lemon	√	√	
36.	<i>Coccinia grandis</i> (L.) Voigt	Ivy gourd			√

37.	<i>Colchicum luteum</i> Baker	Suranjan	√		√
38.	<i>Commiphora mukul</i> (Hook. ex Stocks) Engl./ <i>Commiphora myrrha</i> (Nees) Engl.	Indian bdellium-tree	√	√	
39.	<i>Coptis teeta</i> Wall.	Gold thread	√		
40.	<i>Crataeva religiosa</i> G.Forst.	sacred garlic pear	√		
41.	<i>Crocus sativus</i> L.	Saffron		√	
42.	<i>Croton oblongifolius</i> Roxb.	Nagdanti	√		
43.	<i>Curcuma longa</i> L.	Turmeric	√	√	
44.	<i>Cuscuta reflexa</i> Roxb.	Giant dodder	√	√	
45.	<i>Cymbopogon jwarnicus</i> (Jones) Schult.	Jwarnicus grass		√	
46.	<i>Cyprus rotundus</i> , L.	Nut grass, purple nut sedge	√		
47.	<i>Eclipta alba f. prostrata</i> (L.) Hassk.	False Daisy	√		√
48.	<i>Elattaria cardamomum</i> (L.) Maton	Cardamom	√		√
49.	<i>Embelia ribes</i> , Burm.f.	False black pepper	√		√
50.	<i>Embllica officinalis</i> Gaertn.	Indian gooseberry	√		√
51.	<i>Euphorbia neriifolia</i> Linn.	Common milk hedge	√		√
52.	<i>Ferula narthex</i> L.	Asafetida	√		√
53.	<i>Ficus asperrima</i> Roxb.	Sandpaper tree	√		
54.	<i>Ficus benjamin</i> , Linn.	Weeping fig,	√		
55.	<i>Fumaria parviflora</i> Lam.	Fine-leaved fumitory	√		√
56.	<i>Garcinia indica</i> (Thouars) Choisy	Gamboge	√	√	
57.	<i>Gentiana kurroo</i> Royld.	Indian gentian	√	√	
58.	<i>Glycyrrhiza glabra</i> L.	Liquorice	√		√
59.	<i>Hemidesmus indicus</i> (L.) R. Br. ex Schult.	Indian sarsaparilla	√		√
60.	<i>Indigofera tinctoria</i> L.	Indigo	√		√
61.	<i>Leptadenia reticulata</i> (Retz.) Wight & Arn.	Jivanti	√		
62.	<i>Luffa echinata</i> Roxb.	Bitter sponge guard	√		√
63.	<i>Mentha longifolia</i> Linn.	Mint		√	√
64.	<i>Momordica charantia</i> L.	Bitter guard	√		√
65.	<i>Moringa oleifera</i> Lam.	Drumstick	√		√
66.	<i>Murraya koenigii</i> (L.) Spreng	MithaNeem	√		
67.	<i>Myristica fragrans</i> Houtt.	Nut meg	√	√	
68.	<i>Nardostachys jatamanasi</i> DC.	Jatamansi, Balchar	√	√	
69.	<i>Nelumbo nucifera</i> Gaertn.	Lotus		√	√
70.	<i>Nigella sativa</i> L.	Black onion seeds	√	√	
71.	<i>Ocimum sanctum</i> L.	Holy basil	√		√
72.	<i>Phyllanthus nirur</i> iLinn. & species	Stonebreaker	√		√
73.	<i>Picrorrhiza kurroa</i> Royle ex Benth DC.	Katuki	√		√

74.	<i>Piper longum L.</i>	Long pepper	√	√	√
75.	<i>Piper nigrum L.</i>	Black pepper	√	√	√
76.	<i>Pistacia integerrima J. L. Stewart ex Brandis</i>	Crabs claw	√	√	
77.	<i>Pistacia lentiscus L</i>	Rumimasatagi		√	
78.	<i>Plumbago zeylanica L.</i>	Chitrak	√	√	
79.	<i>Punica granatum Linn.</i>	Pomegranate		√	
80.	<i>Ricinus communis L.</i>	Castor	√		√
81.	<i>Rheum emodi Wall</i>	Rewandchini	√	√	
82.	<i>Rosa damascene Herrm</i>	Rose		√	
83.	<i>Rubia cordifolia L.</i>	Indian madder	√		√
84.	<i>Salvadora persica Linn</i>	Miswak (Toothbrush plant)	√		
85.	<i>Santalum album L.</i>	Sandal wood			√
86.	<i>Saussurea lappa C.B. Clarke</i>	Indian costus root		√	
87.	<i>Semecarpus anacardium L.f</i>	Marking nut	√		
88.	<i>Sida cordifolia L.</i>	Country mallow			√
89.	<i>Solanum indicum L.</i>	Indian nightshade			√
90.	<i>Solanum nigrumL.</i>	Black night shade	√		√
91.	<i>Sphaeranthus hirtus Willd</i>	Gorakhamundi			√
92.	<i>Swertia chirata Buch Ham.</i>	Chireta	√		
93.	<i>Symplocos racemose Roxb.</i>	Lodh tree	√		√
94.	<i>Tamarix gallica L.</i>	Jhavuka	√		
95.	<i>Tephrosia purpurea (L.) Pers</i>	Wild indigo	√		√
96.	<i>Terminalia arjuna (Roxb. ex DC.) Wight &amp; Arn</i>	Arjuna	√		√
97.	<i>Terminalia bellirica (Gaertn.) Roxb</i>	Bellericmyrobalan	√		√
98.	<i>Terminalia chebulaRetz</i>	Chebolicmyrobalan	√	√	√
99.	<i>Tinospora cordifolia (Willd.) Miers</i>	Guduchi, Giloy	√		√
100.	<i>Trachyspermum ammi (L.) Sprague</i>	Bishop's weed	√	√	
101.	<i>Trichosanthes cordata Roxb</i>	Parwal	√		√
102.	<i>Triticum sativum Lam</i>	Common wheat	√		√
103.	<i>Vitex negundo Linn</i>	Five-leaved chaste tree	√		√
104.	<i>Vitis vinifera L.</i>	Common grapes	√		√
105.	<i>Woodfordia fruticosa (L.) Kurz</i>	Fire Flame Bush			√
106.	<i>Zingiber officinale Roscoe</i>	Dry ginger	√	√	√
<b>Total 106</b>			<b>82</b>	<b>35</b>	<b>57</b>

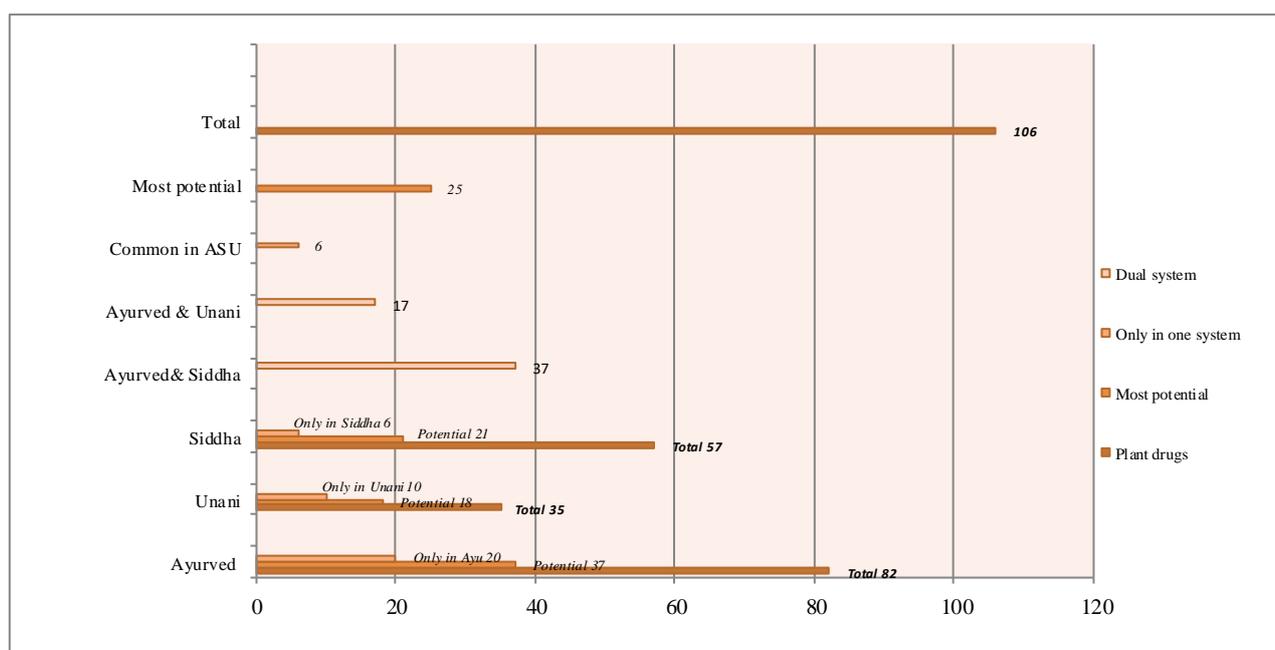
## **RATIONALE TO PRIORITIZE POTENTIAL MEDICINAL PLANTS FOR LIVER DISEASES FROM ASU SYSTEMS**

### **Classical and Textual Approach**

Ancient literature as referred earlier was critically reviewed to identify priority list. Multiple volumes of 'The National Ayurvedic<sup>[37]</sup>, Siddha<sup>[38]</sup> and Unani<sup>[39-40]</sup> Formularies', 'Pharmacopoeias'<sup>[41-44]</sup> and 'Essential Drug List of Ayurved, Sidhhda and Unani'<sup>[45,46,47]</sup>, - all published by Ministry of AYUSH, Government of

India for ASU system were screened for their prescribed uses in liver disorders. Potential plants as per our earlier review papers for each system and proprietary products were also considered<sup>[6-10]</sup>. 37 plants from Ayurveda, 21 from Siddha and 18 from Unani Systems are shortlisted.

It is observed that eighty-two, fifty-seven and thirty-five plants drugs are used in multiple ASU formulations, respectively. Repeated use in *alleviation* of liver dysfunctions underlines the importance of their specific medicinal value. Figure 1 summarizes the outcome of 106 medicinal plants that are more frequently used either singly or in various preparations for liver disorders in ASU systems.



**Fig. 1 Total plants and most potential plants in ASU system**

### Research Papers Published for Hepatoprotective Activities

Several reviews have provided major contributions to the current knowledge on herbal medicines for treatment of various types of Liver diseases. A thorough survey of scientific literature and review articles on prioritized medicinal plants used for liver disorders was undertaken using “PubMed” and “Google Scholar” searches engines to collect the published data. The MESH terms used for search included the following keywords: medicinal plants, ASU, liver diseases, Hepatoprotective, Hepatic disorders. More than 485 research papers have been reviewed to provide progression of the use of ASU plants in liver disorders.

### ICMR Monograph

It is noteworthy that Indian Council of Medical Research, the apex research body under Government of India has published a special monograph on ‘Perspectives of Indian Medicinal Plants in The Management of Liver Disorders’<sup>[48]</sup>. It has listed medicinal plants and products reported to have been used in various liver disorders by ISM. A detailed compilation of information on twelve of the important medicinal plants used traditionally has been assessed for their phytoconstituents, pharmacological, toxicological and clinical data.

### Proprietary Liver formulations

On Google, under the name of Ayurved manufactures, of more than 200 Ayurvedic pharmaceutical liver products 130 proprietary products available in the Indian markets were compiled. Twenty medicinal plants are extensively used in these liver products.

### Practitioners' choice

Hundreds of ASU practitioners using various formulations containing herbal or mineral ingredients to treat various liver diseases are source of knowledge and experience. Several of these practitioners shared their views and experiences about the formulations and ingredients used by them for liver disorders.

The polyherbal formulations commonly used by the practitioners included *Arogyavardhinivati*, *Phaltrikadikwath*, *Patoadikwath*, *Punanarvashtakkwath*, *Liv 52*, *Rohitakghrita*, *Amlakyaadighrit*, and *Vardhaman Pippali* for viral hepatitis, non-alcoholic fatty liver disease, cirrhosis of liver and hepato cellular carcinoma. *Haridra*, *Katuki*, *Kirattikta*, *Punnanava*, *Sharpunkha*, *Bhumyamalaki* is most common plants used by the Ayurvedic physicians and the *herbalists* in the treatment of various liver disorders.

### HIGH POTENTIAL MEDICINAL PLANTS

#### Liver Diseases in ASU Systems

As per Ayurved and Siddha systems of medicine; one or more of the six *rasa*, tastes, *guna* – biophysical attributes, either of two *veerya* – *ushana* or *sheeta* - stimulant or suppressive effect, *vipaka*- the resultant biological effect on one of the three functional systems and *prabhava*- the inherent potency are the properties that are considered embedded in each substance including a medicinal a part or whole plant to exhibit its biological or clinical performance. Unani medicine recognizes the four '*mizaj, the temperament*' as the main chrematistic - heat, coldness, moisture or dryness - of a substance for its effectiveness on the bodily functions.

Twenty-five medicinal plants are found to be extensively used in the treatment of specific liver disorders in ASU Systems of medicine are categorized in Table 3.

**Table 3: List of Medicinal plants for treatment of various chronic liver diseases**

No.	Medicinal Plant	Alcoholic Liver Diseases	Ascites	Cirrhosis	Drug induced toxicity	Hepatitis	Jaundice	Liver/spleen Enlargement	Liver Cancer
1	<i>Aloe vera</i> (L.) Burm.f. I / <i>Aloe barbadensis</i> Mill.	√	√				√	√	
2	<i>Amoora rohituka</i> (Roxb.) Wight & Arn.// <i>Tecoma undulata</i> (Sm.) G.Don		√					√	
3	<i>Andrographis paniculate</i> Nees				√		√	√	
4	<i>Azadirachta indica</i> A. Juss				√				
5	<i>Berberis aristata</i> DC. / <i>Berberis lyceim</i> Royle					√	√	√	
6	<i>Boerhaavia</i>		√				√	√	

	<i>diffusa</i> Linn.								
7	<i>Cichorium intybus</i> L.	√		√		√	√		
8	<i>Cinnamomum zeylanicum</i> Blume	√		√		√	√		
9	<i>Curcuma longa</i> L.	√	√	√	√	√	√		√
10	<i>Cuscutareflexa</i> Rob.	√		√	√	√	√		√
11	<i>Eclipta alba</i> f. <i>prostrata</i> (L.) Hassk.	√	√	√		√	√	√	
12	<i>Emblica officinalis</i> Gaertn.	√			√	√	√		√
13	<i>Glycyrrhiza glabra</i> L.	√			√	√	√		√
14	<i>Luffa echinata</i> Roxb.								
15	<i>Moringa oleifera</i> Lam								
16	<i>Nigella sativa</i> L.	√				√	√		
17	<i>Phyllanthus niruri</i> Linn / <i>Phyllanthus amarus</i> Schumacher & Thonn	√		√	√	√	√		
18	<i>Picrorhiza kurroa</i> Royle ex Benth DC.	√		√		√	√		
19	<i>Piper longum</i> L.	√		√	√	√		√	√
20	<i>Plumbago zeylanica</i> L.			√	√			√	√
21	<i>Swertiachirata</i> Buch Ham	√			√		√		
22	<i>Tephrosia purpurea</i> (L.) Pers.			√				√	√
23	<i>Terminalia chebula</i> Retz				√			√	
24	<i>Tinospora cordifolia</i> (Willd.) Miers.	√		√	√	√	√		√
25	<i>Zingiber officinale</i> Roscoe	√		√	√		√		√

The potential **twenty-five (25)** plants were screened again for their attributes based on ASU principles and were further scrutinized based on published literature for scientific assessment of clinical activities related to hepatic functions. The list of these selected **twenty-five** potential plants with botanical name, ASU names, useful part/s used, attributes as per ASU systems is given in table 4.

**Table 4: High Potential Medicinal Plants from ASU Systems**

Sr no.	Botanical name- Family- ASU name	Parts used	ASU attributes	Action
1.	<i>Aloe vera</i> (L.) Burm.f. I / <i>Aloe barbadensis</i> Mill. Liliaceae <i>Kumari, Kattrazhai, Sibr</i>	Leaf	<i>Bitter, Sweet, Heavy, Unctuous, Hot, dry Balancing all doshas</i>	Antifungal, Antidiabetic, Anti-inflammatory, Anti-Cancer, Disinfectant, immunomodulatory, Laxative
2.	<i>Amoora rohituka</i> (Roxb.) Wight & Arn./ <i>Tecoma undulata</i> (Sm.) G.Don Bignoniaceae <i>Rohitak, Cennaraki, Rohida</i>	Bark	<i>Pungent, Astringent Light, Dry, Cold, Pacify Kapha, Pitta Unani-Hot</i>	Hepatoprotective, Immunomodulatory, Anti-inflammatory
3.	<i>Andrographis paniculate</i> Nees Acanthaceae <i>Kalmedha, Nilavembu Quasabhuva</i>	Whole plant	<i>Bitter, Light, Dry, Pungent, Hot Pacify Vata pitta</i>	Antibacterial, Antioxidant, Anti-inflammatory, Anti-Cancer, Antimalarial, Antiviral, Antifungal, Hepatoprotective, Immunomodulatory
4.	<i>Azadirachta indica</i> A. Juss Meliaceae <i>Nimba, Vembu, Burg neem</i>	Seed, Bark, Leaves	<i>Bitter, Pungent Light, Dry, Cold Pacify Kapha, Pitta Unani-Hot</i>	Analgesic, Antifungal, Antipyretic, Antiviral, Antibacterial, Hepatoprotective
5.	<i>Berberis aristata</i> DC./ <i>Berberis lyceim</i> Royle Berberidaceae <i>Daruharidra Kasturimanjal, Zarishk</i>	Bark	<i>Bitter, Astringent Light, Dry Pungent, Hot Pacify Kapa, pitta</i>	Anti-Cancer, Anti-inflammatory, Antimicrobial, Antipyretic, Anti-Diabetic, Antioxidant, Antimalarial, Immunomodulatory
6.	<i>Boerhavia diffusa</i> L. Nyctaginaceae <i>Punarnava Caranai, Tukhm-i-ispast</i>	Root	<i>Bitter, Sweet Light, Dry Pungent Hot Pacify Kapha, Vata</i>	Anti-inflammatory, Appetizer, Digestive
7.	<i>Cichorium intybus</i> L. Compositae <i>Kasani, Kasni, Tukhm-e-kasni</i>	Whole plant	<i>Bitter, Light, Dry Pungent, Hot, Pacify Kapha, Vata Unani- Cold</i>	Antimicrobial, Analgesic, Antidiabetic, Gastroprotective Hepatoprotective,

8.	<i>Cinnamomum zeylanicum</i> Blume/ <i>Cassia Dalchini, Seeragam Darchini</i>	Bark	<i>Bitter, Light, Dry, Pungent, Hot Pacify Kapha, Vata</i>	Anti-allergenic, Anti-inflammatory, Anti-pyretic, Antibacterial, Anaesthetic, Antioxidant, Antifungal,
9.	<i>Curcuma longa</i> L. <i>Zingiberaceae Haridra, Manjal aurquussufr, haldizard</i>	Root tuber	<i>Pungent, Bitter, Light, Dry, Hot Pacify Kapha, Vata</i>	Anticarcinogenic, Antiviral, Antioxidant, Anti-cancer, Anti-ischemic, Apoptotic, Anti-inflammatory Antitumor, Hepatoprotective
10.	<i>Cuscuta reflexa</i> Roxb. <i>Cuscutaceae Akashbel, Afitmun</i>	Whole plant	<i>Light, Dry, Hot Pacify Kapha, Vata</i>	Anti-inflammatory, Anti-cancer, Antimicrobial, Antifungal, Hypotensive, Hypoglycemic
11.	<i>Eclipta alba f. prostrata</i> (L.) Hassk. <i>Compositae/ Asteraceae Bhrungaraj Karisalankanni, Bhangra</i>	Whole plant		Anti-hepatotoxic, Anti-hyperlipidemic, Antioxidant, Analgesic, Immunomodulatory, Anti-inflammatory, Antidiabetic, Anti-cancer
12.	<i>Embllica officinalis Gaertn / Phyllanthus emblica</i> <i>Phyllanthaceae. Amalaki, Nelli, Amla</i>	Fruit	<i>Sour Light, Sweet, Cold Pacify all dosha</i>	Antioxidant, Antispasmodic Chemo-preventive, Anti-Carcinogenic, Anti-mutagenic, Anti-allergic, Anti-inflammatory, Hepato Protective, Antitumor
13.	<i>Glycyrrhiza glabra</i> L. <i>Yashtimadhu Adhimathuram Aslussoos</i>	Root	<i>Sweet Heavy, Unctuous, Cold Pacify Vata, Pitta</i>	Antifungal, Hepatoprotective, Anticonvulsant, Anti-tussive, Neuroprotective, Tranquilizing, Antioxidant, Antidiabetic
14.	<i>Luffa echinata</i> Roxb. <i>Cucurbitaceae Devadali Peypirkku, Bindaal</i>	Fruits	<i>Pungent, Bitter, Light, Dry, Hot Pacify all dosha</i>	Antioxidant, Analgesic, Anti-Inflammatory, Antidepressant, Anxiolytic, Antiepileptic, Hepatoprotective, Antibacterial, Antifungal,
15.	<i>Moringa oleifera</i> Lam <i>Moringaceae Shigru, Moringkai Sahajan</i>	Root bark, stem bark, leaves, fruits and seeds	<i>Pungent, Bitter, Light, Dry, Hot Pacify Kapha-Vata</i>	Anti-asthmatic, Anti-Diabetic, Hepatoprotective, Anti-Inflammatory, Anti-Fertility, Anti-Cancer, Anti-Microbial, Anti-Oxidant, Anti-Allergic, Analgesic, Antipyretic

16.	<i>Nigella sativa</i> L. <i>Ranunculaceae</i> <i>Upakunchika</i> <i>Acaci, Kalonji</i>	Seeds	<i>Pungent, Bitter,</i> <i>Light, Hot, Dry</i> <i>Pacify Vata</i>	Antimicrobial, Antiviral, Anti-cancer, Antioxidant, Anti-inflammatory, Antitumor, Antitussive, Anti-anxiety, Gastroprotective, Hepatoprotective, Immunomodulatory
17.	<i>Phyllanthus niruri</i> Linn/ <i>Phyllanthus amarus</i> Schumach. & Thonn <i>Euphorbiaceae</i> <i>Bhumiamalaki</i> <i>Kizhanelli, Bhui-aml</i>	Whole plant	<i>Bitter, Astringent,</i> <i>Sweet, Light, Dry,</i> <i>Cold</i> <i>Pacify Kapa, pitta</i>	Anti-spasmodic, Analgesic, Anti-inflammatory, Antioxidant, Anti-cancer, Anti-ulcer, Anti-microbial, Liver protective, Immune modulatory
18.	<i>Picrorhiza kurroa</i> Royle ex Benth DC. <i>Scrophulariaceae</i> <i>Katuki</i> <i>Katurokini, Kutki</i>	Rhizomes	<i>Bitter, Dry, Light</i> <i>Pungent, Cold,</i> <i>Kapha – pittahara</i> <i>Unani- Hot</i>	Anti-microbial, Antioxidant, Anti-bacterial, Anti-mutagenic, Anti-cancer, Hepatoprotective
19.	<i>Piper longum</i> L. <i>Piperaceae</i> <i>Pippali,</i> <i>Thippili, Darfilfil</i>	Fruit	<i>Pungent, Light,</i> <i>Unctuous Sweet,</i> <i>Hot, Dry</i> <i>Pacify</i> <i>Kapha, Vata</i>	Stimulant, Antibacterial, Anti-asthmatic, Hepatoprotective, Hypocholesterolaemic, Anti-inflammatory, Anti-aging, Anti-amoebic
20.	<i>Plumbago zeylanica</i> L. <i>Plumbaginaceae</i> <i>Chitrak, Chittiri, Sheetraj</i>	Root	<i>Pungent, Light, Dry,</i> <i>Hot, Pacify Kapha</i> <i>Vata</i>	Anticancer, Antitumor, Anti-inflammatory, Antioxidant, Anti-mycobacterial, Anti-atherogenic, Cardiotonic, Hepatoprotective, Neuroprotective
21.	<i>Swertia chirata</i> Buch Ham <i>Gentianaceae</i> <i>Kiratatikta</i> <i>Chirata</i>	Whole plant	<i>Pungent, Hot, Cold in</i> <i>Potency, Dry,</i> <i>Pacifying Vata &amp; pitta</i>	Antibacterial, Antiviral, Antifungal
22.	<i>Tephrosia purpurea</i> (L.) Pers <i>Fabaceae</i> <i>Sharpunkha</i> <i>Kollilai,</i> <i>kolunchi</i> <i>Sarphoka</i>	All parts, root	<i>Bitter, Astringent,</i> <i>Pungent, Light, Hot</i> <i>Pacify Vata Kapha</i>	Antioxidant, Anti-inflammatory, Hepatoprotective
23.	<i>Terminalia chebula</i> Retz. <i>Combretaceae</i> <i>Haritaki</i> <i>Kadukkai</i> <i>Post halelakabali</i>	Fruit	<i>Astringent, Bitter,</i> <i>Sweet, Pungent,</i> <i>Sour, Light, Dry, Hot</i> <i>Pacify all the doshas</i>	Antibacterial, Antifungal, Antiviral, Anti-mutagenic, Antioxidant, Antiulcer, Immunomodulatory, Cytoprotective, Anti-aging, Hepatoprotective, Chemopreventive

24.	<i>Tinospora Cordifolia</i> (Willd.) Miers <i>Menispermaceae</i> <i>Guduchi, Seendhil, gilo</i>	Stem	<i>Bitter, Pungent, Sweet, Heavy, Unctuous, Hot</i> <i>Pacify all three dosha</i>	Anti-diabetic, Anti-cancer, Anti-Oxidant, Immunomodulatory, Anti-Microbial, Anti-toxin, Hepatoprotective
25.	<i>Zingiber officinale</i> Roscoe <i>Zingiberaceae</i> <i>Sunthi, Inji, Zanjabeel</i>	Rhizome	<i>Pungent, Light, Dry, Sweet, Hot</i> <i>Pacify Vat Kapha</i>	Hepatoprotective, Nephron-Protective, Larvicidal, Antibacterial, Anti-diarrhoea, Antidiabetic, Antioxidant, Anti-fungal, Anti-inflammatory, Analgesic, Cytotoxic

### Clinical Trials

Several ASU products/ingredients have been clinically studied in different liver diseases. These studies with different clinical trial designs, covering small to large number of sample size and supported by biochemical parameters are listed.

**Table 05-Clinical studies in Liver Diseases with ASU Plants and /or Phyto-Constituents**

Diseases/ action	Source	Study design	Assessment/Results
Autoimmune hepatitis (AIH) <sup>[49]</sup>	Glycyrrhizin SNMC 200 mg+ NaCl 100ml, intra venous, Q.D. for 8 weeks	17 patients (100 ml/day) of intravenous glycyrrhizin (SNMC) at an early stage and treated 14 patients of severe disease with intravenous glycyrrhizin and corticosteroids (CS) (SNMC + CS group)	ALT decrease 26 % and 47 %
Chronic hepatitis C <sup>[50]</sup>	Glycyrrhizin in interferon + ribavirin-based therapy non-responders	379 patients, a randomised, double-blind, placebo-controlled, comparison of glycyrrhizin, administered intravenously for 12 weeks	Reduces ALT, prevents disease progression
Chronic Hepatitis, Liver cirrhosis <sup>[51]</sup>	Di-ammonium Glycyrrhizinate Intravenous, Q.D	629 patients with 150 mg+ 5-10 % glucose injection liquid 250 ml for one month, 1-2 cycles	After 17 day therapy, 93.3 % with ALT normal level, at day 10, SB 86.7 %
Hang over symptoms <sup>[52]</sup>	PHYLLPRO™ standardized ethanol extract of <i>P. amarus</i> leaves	15 subjects (21–50 years) crossover study, randomized placebo-controlled, [oxidative stress, liver damage, alleviating hangover symptoms], mood improvement	Remove blood alcohol more efficiently, resulting in reduced hangover symptoms, improved mood
HBV infection Cochrane	<i>phyllanthus</i> species with other antivirals	16 trials with 1326 patients	Significant effect on HBV DNA levels, hepatitis B antigen

meta-analysis <sup>[53]</sup>			seroconversion
Hepatic Cirrhosis complicated by Ascites <sup>[54]</sup>	<i>P.longum, P. kurro, PunarnavadiKwath, Compound powder, E. alba</i>	56 patients, non-randomized, uncontrolled, single group, open-label observational study	Significant clinically relevant improvements
Hepatitis C <sup>[55]</sup>	<i>Phyllanthus amarus</i>	50 (25-60 years) clinical diagnosed patients	Antioxidants, reduces lipid peroxidation of hepatic cellular, intracellular membranes, protects liver damage due to free radicals
Hepatocellular jaundice <sup>[56,57]</sup>	Decoction of <i>A.Panniculata</i>	60 patients-60 ml/day for 23 to 27 days	A marked symptomatic & statistically highly significant
	<i>Eclipta prostrata</i> powder, Livercare Churna, Hepatogard forte Tablets	90 patients, orally for the period of 1-3 weeks, to 4-6 weeks, as per severity and recovery	<i>E. prostrate</i> & marketed formulation Livercare showed better hepatoprotective effects than Hepatogard forte Tablet
Hepatocellular carcinoma [ HCC] in patients with Hepatitis C virus- RNA positive chorin liver diseases <sup>[58]</sup>	Stronger Neo-Minophagen C, a glycyrrhizin-containing preparation, SNMC200MG+NAC L 100ml IV	453 patients (2-16 years)diagnosed with chronic hepatitis C, QD for 8 weeks then 2-7 week	Long term administration in chronic hepatitis C effective in preventing liver carcinogenesis
Infective Hepatitis <sup>[59]</sup>	<i>A. paniculata</i>	20 patients- 24 days - 40 gram/day	Symptomatic & statistically highly significant
Interferon-resistant Hepatitis C <sup>[60]</sup>	Glycyrrhizin I/V	1249 patients with chronic hepatitis with or without cirrhosis- Retrospective study	Significantly decreased the incidence of hepatocellular carcinoma
Jaundice <sup>[61]</sup>	<i>E. alba</i> powder 50mg/kg with honey	Three divided dose for 1-5 weeks	Statistically highly significant
Liver disorders <sup>[62]</sup>	Herbal formulation	01 capsule of 500mg- twice a day for 30 days	Safe, effective medication, well tolerated without any adverse effects
Liver diseases <sup>[63]</sup>	<i>Phyllanthus amarus</i> – powder	107 patients, thrice a day orally with water for 30-45 days	Significant decrease in SGPT, Bilirubin,

		depending on the severity	increase in haemoglobin
NAFLD <sup>[64]</sup> Non-Alcoholic Fatty Liver Disease	Curcumin 1000 mg/day for 8 weeks	87 patients assigned (n = 44) or placebo group (n = 43)	Decreased the body mass index, AST, ALT, SGOT, SGPT
NAFLD <sup>[65]</sup>	Curcumin 500 mg/day for 8 weeks	80patients (n = 40) or placebo group (n = 40)	Decreased Total cholesterol, LDL-C, ALT, AST

## DISCUSSION

ASU medicinal plant and products reveal significant potential of their role in several specific conditions such as Jaundice, Hepatitis, Alcoholic liver, fatty liver, Drug induced hepatotoxicity, Hepato carcinoma etc. Various Ayurvedic Liver products are act on the base of synergism as phenomenon of positive herb-herb interaction. The use of herbal remedies for various ailments, folkloric or scientific has been of great usefulness to humankind.

### Studies and outcome

Many polyherbal formulations/ products containing three or more, mostly seven to nine and even more of the above listed plants or their extracts are observed to have hepatoprotective activities in clinical studies.

*Emblica officinalis Gaertn* and *Tinospora cordifolia (Willd) Hook.f & Thomson* having rejuvenates (rasayana) action and acts at various level, establish physical strength, and protect the body against deleterious effect of radiotherapy & chemotherapy. It brings proper uptake, growth and improvement of essential seven vital tissues. While simultaneously being a powerful blood and liver cleanser, both the drugs as being useful in conditions of hepatitis and jaundice due to its ability to detoxify the liver and act antioxidant, hypoglycemic, and cardio-protective activities.

In a comparative study on 90 patients suffering from Hepatocellular jaundice when treated with *Eclipta prostrata* and marketed hepatoprotective formulations (Hepatogaurd forte Tablet and Livercare Churna) over 1 to 3 weeks, to 4 and 6 weeks, *Eclipta prostrata*, and marketed formulation Liver care powder showed better hepatoprotective effects and recovery than the other marketed formulation Hepatogaurd forte Tablet<sup>[53]</sup>.

56 patients of Hepatic Cirrhosis complicated by Ascites showed significant clinically relevant improvements when treated with standardized treatment protocol consisting of oral administration of single and compound herbal preparations combined with purification measures as well as dietary and lifestyle regimens in an open-label observational clinical study. Herbal intervention included *P. longum*, *P. kurro*, *E. alba*, *PunarnavadiKwath*, Compound powder of *Phyllanthus niruri Sensu Hook. F. non Linn.*, *Shveta-Parpati( Herbomineral combination)*, *Ammonium chloride [NH<sub>4</sub>Cl]*, *Potassium nitrate [KNO<sub>3</sub>]*, *Potash alum [KAl(SO<sub>4</sub>)<sub>2</sub>12H<sub>2</sub>O]<sup>[54]</sup>.*

A 'Herbal formulation' (Extracts of *Capparis spinosa Root*, *Cichorium intybus Seed*, *Solanum nigrum Whole plant*, *Terminalia arjuna Bark*, *Cassia occidentals Seed*, *Achillea millefolium Aerial part*, *Tamarix gallica Whole plant*) 500 mg capsule given twice a day for 30 days was found to be safe and effective medication in liver disorders without any adverse effects<sup>[62]</sup>.

Majority of formulations contained one or three of *Trikatu*, the 'three pungent' namely ginger, black pepper and long pepper. Ginger (*Z. officinale*) has a powerful effect on gastro-intestinal mucous membrane. In ASU systems these are used to increase the bioavailability. Piperine, the active constituent from *Piper nigrum* and

*Piper longum* inhibits drug metabolizing enzymes, stimulates absorption by stimulating gut amino acid transporters, inhibits the cell pump responsible for drug elimination from cells and inhibits intestinal production of glucuronic acid<sup>[66-67]</sup>.

Though polyherbal formulations are found to be effective in clinical studies the challenges of standardization and quality control leads to opt for minimum number of plants.

**Parts, Formulations** - Juice or fresh leaves of a plant each, six whole plants mostly shrubs, powders of six plants, eight roots or rhizomes, four each of leaves, fruits, stems, bark of two and seeds of a plant have been studied variably for their hepatoprotective activities. Different parts of plants *Phyllanthus niruri*, *Aloe vera* and *Tinospora cordifolia* have been extensively studied. Studies on Kalaunji - *Nigella sativa* as a diet article and Turmeric - *Curcuma longa* as a kitchen spice have also been tested. Use of Specific as suggested in Ayurveda authenticated plant parts are important as parts of plants can contain different active ingredients within one plant. One part of the plant could be toxic while another portion of the same plant could be harmless.

**Clinical Studies** - Clinical trials on many Ayurvedic pharmaceuticals and few classical dosage forms have shown hepatoprotective effects. The hepatic disorders studied vary from simple jaundice, chronic or acute hepatitis 'B' and 'C', NASH, Hepatic amoebiasis, fibrotic or cirrhotic situations and hepatocellular carcinoma and even hang over or mood swing symptoms. *Andrographis paniculata*, *Glycyrrhiza glabra* and *Phyllanthus niruri* or their phytoconstituents are the clinically studied plants for variety of liver conditions including cirrhotic conditions and HCC. *Picrorrhiza kurroa* and *Eclipta alba* are studied more for hepatitis and amoebiasis and *Curcuma longa* for NASH and *Piper longum* for fibrosis.

#### **ASU approach for products development- synergetic effect<sup>[68]</sup>**

ASU formulations and product development are based used in two ways - as single ingredients and as combinations of more than one ingredient. This key therapeutic herbal strategy based on indigenous systems of medicine exploits the polyingredient dosage forms to achieve therapeutic effectiveness. Herbal, herbomineral and mineral ASU formulas effectively recognize the obvious synergistic therapeutic benefits. These multi-ingredient dosage forms may increase the potency, reduce unwanted effects, make the formulation more palatable and stable, and avoid any toxicity. Due to synergism, best combination of polyherbal provides higher activity against a disease. Formulations having multiple ingredients have various types of molecules to act against a disease complex as in liver dysfunctions by different mechanisms to provide a complete therapy against an intricate condition.

#### **COCLUSION**

ASU systems provide an opportunity to innovate new therapeutic approaches to effectively treat different types of liver disorders. Ancient classical literatures suggest that natural origin ingredients, mainly plants have been extensively used in ASU traditional medicine for the treatment of liver diseases. In this review, we have carefully examined the presently available clinical information and research data on ASU formulations and ingredients. A list of 106 plants is provided with a priority list of 25 plants.

These plants can be used both preventively and clinically to manage a spectrum of liver-related imbalances. The compiled information will be of use to identify individual ingredients that are used in maximum formulation and may be of most value in reversal or treatment of liver dysfunctions.

## REFERENCES

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