Chapter 2
Review of Literature

2.1 Review of Literature:

The liver is essential for maintaining several physiological functions in the body. The organelle has a role in several processes, including metabolism, secretion, and storage (Sultana et al., 2018; Boro et al., 2022). It controls the process of removing and eliminating different substances that come from outside the body or are produced inside the body. In addition, any harm or impairment to the liver serves as evidence of a person's declining health. According to research, around 2 million individuals worldwide succumb to liver disease annually (Asrani et al. 2019). Liver disease is a very lethal condition that continues to increase in prevalence, despite recent advancements in the area of hepatology. Jaundice and hepatitis are two liver disorders that contribute significantly to the high mortality rate (Shresta and Babu, 2018).

Alternative and complementary systems, such as the Indian traditional system, sometimes referred to as Ayurvedic, as well as European and Chinese alternative systems, are well recognised as popular therapeutic methods within local communities. Throughout history, plants have served as the cornerstone of medicinal practices. Medicinal herbs provide as a significant reservoir of hepatoprotective drugs. Over 700 mono and polyherbal medications, in the form of decoction, tincture, and tablets, have been used to treat various liver disorders. It has been claimed that several herbs and preparations have hepatoprotective effects. Reportedly, there are 160 active components derived from 101 plants that possess post-liver protecting effects. There are 33 patented plant mixtures with unique features that consist of around 87 plants from India. In current medicine, there is a lack of major and secure hepatoprotective medications, despite the substantial advances made. The worldwide focus on the discovery of hepatoprotective medicines, mostly derived from plants, that may effectively treat various liver diseases has increased significantly (Casas and Muriel 2015).

Polyherbal formulations (PHFs) are made by mixing many herbs in various ratios to provide a broad variety of indications against different conditions. These formulations are known for their affordability and little adverse effects (Brahma et al., 2023). There are almost 600 pharmaceuticals (PHFs) that are marketed globally as liver protectors (Bera et al., 2011). Due to the lack of scientific testing, most newly introduced polyherbal combinations raise concerns about their efficacy, safety, and potential health risks upon entering the market (Teschke and Eickhoff, 2015; Mochahary et al., 2022). Oxidative stress, also known as oxidative damage, plays a significant role in the development of several chronic liver diseases such as alcoholic liver disease (ALD), non-alcoholic fatty liver disease (NAFLD) (Chachay et al., 2014), drug-induced liver injury (DILI), and fibrosis (Muriel and Arauz., 2012). Comparing the antioxidant activity of various PHFs may help identify a formulation that is high in antioxidants for the treatment of liver disorders (Yoshikawa and Kaito, 2002). The present research aims to elucidate the various in-vitro antioxidant scientific approaches used to support the therapeutic claims of the hepatoprotective PHFs developed in the last decade. The time period is from 2013 to 2023.

Hepatotoxicity can be defined as liver damage or poisoned liver and considered as one of the major health problems (Fatima and Nayeem, 2016; Middha et al., 2013). Hepatotoxicity of the liver primarily results from exposure to toxic substances, including chemotherapeutic agents, paracetamol, chronic alcohol consumption, carbon tetrachloride (CCl_4), hepatitis viruses (A, B, C, and D), obesity, genetic defects such as Haemochromatosis, Wilson's disease, and alpha-1 antitrypsin deficiency, as well as certain drugs like aspirin, ibuprofen, amiodarone, valproic acid, and rifampin. Modern medicines are ineffective and give unsatisfactory results because of additional adverse drug reactions (ADRs) to liver problems and cost much higher compared to herbal drugs (Middha et al., 2013; Kamala et al., 2018). There are hundreds of plants which are reported to possess a hepatoprotective activity that can be used as potential alternative drugs in various parts of the world, but most of them are yet to be scientifically validated (Rasal and Ugare, 2018).

2.2 The herb-herb amalgamation:

An herb-herb combination is a compilation of herbs utilised for their synergistic effects in the management of various ailments. Although a solitary plant may

possess therapeutic properties, their efficacy is comparatively diminished in contrast to PHFs, which derive their influence from a composite of multiple plants. In recent decades, empirical evidence on herb-herb combinations has contributed to a growing interest in the possibility of treating diseases with herb-herb combinations as opposed to the one-to-one target model. It is noteworthy that herb-herb combinations have been utilised in Chinese medicine for millennia (Xie, 2000; Che et al., 2013). Traditional Chinese medicine (TCM) frequently employs herbal combinations to enhance the efficacy of a formulation and reduce toxicity. Without compromising their fundamental therapeutic properties, the herb-herb combinations are less intricate than complex (Wang et al., 2012; Shi et al., 2015). PHFs have mutualistic interaction effects in tackling the various diseases under observation. Currently, a significant number of PHFs are commercially available in different countries for the treatment of liver disorders *(*Aslam et al., 2016). For instance, an herb-herb combination is proven to work synergistically against hepatotoxicity, as reported by Fan et al., (2016). Supported by the nature of the interactions, the action of synergism is divided into two mechanisms, i.e., pharmacokinetic and pharmacodynamic. Pharmacokinetic synergism focuses on the competence of herbs to effortlessly absorb, distribute, metabolize and eliminate the harmful effects of other herbs. On the other hand, pharmacodynamic synergism deals with the collaborative action of the active components of similar herbs and their mechanism (s) of action (Mishra et al., 2020).

2.3 Advantage of polyherbal formulations:

a. Have a plethora of applications for the treatment of diseases.

b. Offers better patient tolerance compared to synthetic drugs.

c. Comparatively cheaper than synthetic drugs.

c. Have fewer side effects compared to synthetic drugs.

d. Provides a natural and sustainable source of medicine.

e. Improved acceptability of herbal medicine in modern society in recent years.

f. The quality, efficacy and safety of PHFs have immensely improved with the advancement of science and technology.

g. Above all, polyherbal medicines form the basis for the development of modern medicines.

2.4 Disadvantages of polyherbal formulation:

a. There is no or very limited scientific evidence to support the effectiveness of many PHFs.

b. PHFs take a longer time to act than synthetic drugs, and the entire process behind the effect of the formulation is very slow.

c. Lack of appropriate/specified dosage of the PHFs in most of the cases.

d. Even at a low degree, some PHFs are prone to side effects.

2.5 The need of standardization:

The establishment of standardised protocols serves as the fundamental basis for the advancement of pharmaceutical research and development. Therefore, this particular procedure has emerged as a crucial measure in assessing the efficacy and consistency of polyherbal medications, thereby mitigating the potential for batch-to-batch variability. Standardized herbal medicines are more popular and desirable than non-standardized extracts (Pattanayak *et al*., 2010; Kumari *et al.,* 2020). Standardization is still in the stage where the guideline for standardization of polyherbal formulation in Ayurveda and traditional systems is ambiguous. Identifying and developing the reference standard(s) to control the quality of PHFs is an immediate necessity, which should be the focus of future studies in PHF development. The traditional ways of standardization need to be improved, and hence, the implementation of modern techniques is the need of the hour to retain the quality of PHFs. An increase in safety, effectiveness and product acceptance is the ultimate goal for standardization (Bijauliya*et al*., 2017). Accordingly, the World Health Organization (WHO) has issued general guidelines for the standardization of herbal medicines in 1992, and most countries in the world abide by the same guidelines in formulating and standardizing PHFs (Pradhan *et al*., 2015). The standardization of polyherbal formulation is a tedious task and must be carried out carefully with quality control since the chemical composition of plant materials vary considerably with the season, time and location (Meena *et al*., 2011). Quality control is an essential step in formulating PHFs as it helps to retain the quality and consistency of the drug from batch to batch (Kumar *et al*., 2016).

Some standardized PHFs with hepatoprotective activity are available today with appreciable formulation standards. Padmanabhan and Jangle (2014) reported an Herbal Preparation (HP-4) comprising of 80% alcoholic extract of four ingredients: *Zingiber officinale* (rhizome), *Aloe vera* (leaf)*, Moringa oleifera* (leaf), and *Bacopa*

monnieri(leaf)in equal amount. This preparation showed effective protection against hepatotoxicity in alcohol-fed mice. In their 2018 study, Huda and Mosaddik (2018) documented the potential protective properties of Sharbat Chylosin, a polyherbal formulation (PHF) commonly found in the local markets of Bangladesh. Specifically, they investigated its effects on hepatotoxicity induced by carbon tetrachloride (CCl4) in male Long-Evans albino rats. The PHF consisted of a combination of indigenous herbs viz. *Foeniculum vulgare*, *Carum roxburghianum* (seed), *Carum roxburghianum*(root), *Cichorium intybus*, *Cassia fistula*, *Hygrophila auriculata*, *Boerhaviadiffusa*, *Andrographis paniculata*, *Terminalia chebula*, *Artemisia absinthium*, *Leonurus cardiaca*in the ratio 1:1.5:2:1.5:1.5:1:1:1:1:1:1, respectively.

2.6 Polyherbal formulations for liver diseases:

In this review, 95 standardized PHFS in the management of liver diseases are documented. The names of those formulations, their herbal constituents (i.e., plant names), animal models used to test the efficacy of the formulation and the resultant effects of those herbal formulations in comparison with some reference drugs are mentioned in table 2.1. According to the World Health Organization (WHO), deaths due to liver diseases in India reached 264,193 as per data published in 2018 and ranked 62nd in the world and thus become a necessity to find new plant-based therapeutic agents to deal with it (https://www.worldlifeexpectancy.com/india-liver-disease/20-01-2021). Recently, the application of herbal medicine in dealing with various diseases has been gaining popularity, especially in many developed countries, with complementary and alternative medicines (CAMs) now becoming mainstream worldwide and not overlooking developing nations as well (Ekor, 2014). India has a vast lexicon of herbal formulations and medicinal plants and is considered the medicinal garden of the world (Sen and Chakraborty, 2015; Dukare et al., 2017). Among the PHFs discussed in this review, India has contributed to the highest number of PHFs, with 85 out of 95 PHFs, which are supported by studies, followed by South Korea, Nigeria, Pakistan, and Saudi Arabia.

***2.6.1 In vitro* analysis**

Among the 93 PHFs, only LIVT, Khamira Gaozaban Ambri JadwarOod Saleeb Wala, Purnarnavashtakkwath, Liv-Pro-08, F1 and F2, and HEPIN were subjected to *in-vitro* analyses. The hepatoprotective activity of LIVT has been investigated on a D-galactosamine-induced cell toxicity model using human hepatic cell line (HepG2). The formulation composed of *Boerhavia diffusa, Tinospora cordifolia,*

Table 2.1: List of polyherbal formulations and its constituents along with experimental model and effect on various parameters related to liver disorders

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Huda and Msaddik, 2018	Sharbat Chy-losin	*Foeniculum vulgare, Carum roxburghinum Cichorium intybus, Cassia fistula, Hygrophila auriculata, Boerhavia diffusa, Andrographis paniculata, Terminalia chebula, Artemisia absinthium* and *Leonurus cardiac*	CCl_4 induced hepatotoxicity in rats; injection of 1 mL/kg on14th days.	At 1 g/kg; ↓AST (39%) ↓ALT (37%) ↓ALP (41%) ↓Total Bilirubin (10%)	Silymarin (50 g/kg) ↓AST (35%) ↓ALT (29%) ↓ALP (44%) ↓Total Bilirubin (08%)	*In vivo*; Bangladesh
Sarkar et al., 2014	Heptoplus	*Phyllanthus amarus, Eclipta alba, Tephrosia purpurea, Curcuma longa, Picrorhiza kurroa, Withania somnifera, Pinius succinifera, Pistacia lentiscus, Orchis mascula* and *Cycas circinalis*	Isoniazid and rifampicin induced liver damage in rats; feeding of 50 g/kg.	At 100 g/kg; ↓AST (61%) ↓ALT (69%) ↓ALP (68%) ↓GGT (81%) ↓Total Bilirubin (36%)	Liv 52 (100 g/kg) ↓AST (72%) ↓ALT (76%) ↓ALP (79%) ↓GGT (84%) ↓Total Bilirubin (47%)	*In vivo*; India
Karunarathn et al., 2017	LINK LIVEC-ARE™	*Andrographis paniculata, Eclipta alba, Phyllanthus amarus, Phyllanthus emblica, Terminalia chebula, Terminalia bellirica, Tinospora codifolia, Curcuma longa, Glycyrrhiza glabra, Boerhavia diffusa, Osbekia octandra. Tephrosia purpurea, Piper longum* and *Vernonia cinerea*	CCl_4 induced hepatotoxici-ty in ICR mice; injecting of 0.08 mL/kg in olive oil.	At 240 g/kg; ↓AST (79%) ↓ALT (75%) ↓ALP (64%) ↓Total Bilirubin (78%)	Silymarin (50 g/kg) ↓AST (37%) ↓ALT (40%) ↓ALP (53%) ↓Total Bilirubin (52%)	*In vivo*; Sri Lanka
Golla, 2018	CURNA	*Alstonia scholaris, Ficus benghalensis, Pongamia pinnata* and *Ricinus communis*	Ethanol 3.7 g/kg for 7 days and on 8th day paracetamol 2 g/kg once daily from 8th day to 14th day induced hepatotoxicity in rats.	At 100 g/kg; Curative study ↑SGPT (72%) ↓SGOT (80%) ↓ALP (61%)	Silymarin (100 g/kg) ↑SGPT (39%) ↓SGOT (49%) ↓ALP (44%)	*In vivo*; India

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Nipanikar et al., 2017	AHPL/ AYTAB/0613	*Eclipta alba, Tinospora cordifolia,Berberis aristata, Solanum nigrum, Boerhavia diffusa, Phyllanthus niruri, Picrorhiza kurroa* and *Andrographis paniculata*	CCl_4 induced hepatotoxicity in rats; feeding daily 1 mL/ kg for 10 days	At 220 g/kg; ↓SGPT (61%) ↓SGOT (49%) ↓ALP (63%) ↓TB (26%)	Silymarin (25 g/kg) ↓SGPT (55%) ↓SGOT (43%) ↓ALP (59%) ↓TB (22%)	In vivo; India
Nipanikar et al., 2017	AHPL/ AYTAB/0613	*Eclipta alba, Tinospora cordifolia,Berberis aristata, Solanum nigrum, Boerhavia diffusa, Phyllanthus niruri, Picrorhiza kurroa* and *Andrographis paniculata*	Ethanol induced hepatotoxicity in rats; feeding of 2 mL daily for 14 days.	At 220 g/kg; ↓SGPT (43%) ↓SGOT (49%) ↓ALP (40%) ↓Total Bilirubin (22%)	Silymarin (25 g/kg) ↓SGPT (45%) ↓SGOT (43%) ↓ALP (41%) ↓Total Bilirubin (21%)	In vivo; India
Nipanikar et al., 2017	AHPL/ AYTAB/0613	*Eclipta alba, Tinospora cordifolia,Berberis aristata, Solanum nigrum, Boerhavia diffusa, Phyllanthus niruri, Picrorhiza kurroa* and *Andrographis paniculata*	Paracetamol induced hepatotoxicity in rats; feeding of 2 g/kg body weight for 14 days	At 220 g/kg; ↓SGPT (20%) ↓SGOT (32%) ↓ALP (56%) ↓Total Bilirubin (25%)	Silymarin (25 g/kg) ↓SGPT (19%) ↓SGOT (28%) ↓ALP (51%) ↓Total Bilirubin (22%)	In vivo; India
Sapkota et al., 2017	Arogya-vardhini Rasa	*Terminalia chebula, Terminalia bellirica, Phyllanthus emblica, Plumbago zeylanica, Picrorhiza kurroa, Azadirachta indica* and *Commiphora wightii,*	Paracetamol induced hepatoxicity in rats; feeding of 1% carboxymethylcellulose in a dose of 10 mL/kg for 7 days.	At 90 g/kg; ↓SGPT (64%) ↓SGOT (60%) ↑ALP (95%) ↓Total Bilirubin (62%)	Silymarin (100 g/kg) ↓SGPT (46%) ↓SGOT (65%) ↓ALP (77%) ↓Total Bilirubin (90%)	*In vivo*; India

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Kapur et al., 1994	Jigrine	*Cichorium intybus, Tamarix dioica, Solanum nigrum, Rheum emodii, Rubia cordifolia, Vitex negundo, Cassia occidentalis, Foeniculum vulgare, Cuscuta reflexa, Careya arborea, Phyllanthus niruri, Plantago major, Rosa damascene* and *Solanum xanthocarpum*	Paracetamol induced liver toxicity in rats; injecting of 750 g/kg on 7th day	At 1 mL/kg; ↓SGPT (77%) ↓SGOT (69%) ↓Total Bilirubin (37%)	NA	In vivo; India
Dhuley and Naik, 1997	Rhinax	*Withania somnifera, Asparagus racemosus, Mucuna pruriens, Phyllanthus emblica, Glycyrrhiza glabra, Terminalia chebula* and *Myristica fragrans*	CCl_4 induced liver damage in rats; injecting of 2.5 mL/ kg single dose.	At 80 g/kg; ↓AST (83%)	NA	In vivo; India
Venkateswaran et al., 1997	Livex	*Tephrosia purpurea, Aconitum heterophyllum, Solanum nigrum, Cichorium intybus, Cassia occidentalis, Tamarix gallica, Embelia ribes, Andrographis paniculata* and *Piper longum*	Erythromycin estolate induced hepatotoxicity in rats; feeding of 800 g/kg daily for 10 days.	At 121.25 gm/kg; ↓ALT (25%) ↓AST (14%) ↓ALP (14%) ↓Bilirubin (48%)	NA	In vivo; India
Saraswathy and Devi, 1999	Liv 100	*Cichorium intybus, Solanum nigrum, Phyllanthus amarus, Picrorhiza kurroa,* and *Embelica officinalis*	Anti-Tubercular drugs induced liver damage in rats; feeding anti-TB drugs 15 g/ kg, RMP 20 g/kg and PZA 35 g/kg daily for 42 days.	At 400 g/kg; ↓LDH (46%) ↓AST (42%) ↓ALT (35%) ↓ALP (48%)	Liv 100 (400 g/kg) ↓LDH (52%) ↓AST (54%) ↓ALT (39%) ↓ALP (51%)	In vivo; India

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Mitra et al., 2000	HD-03	*Solanum nigrum, Cichorium Intybus, Picrorrhiza kurroa, Tephrosia purpurea* and *Andrographis paniculata*	Galactosamine induced liver damage in rats; feeding of 400 g/kg on 15th day.	At 500 g/kg; ↓SGOT (70%) ↓SGPT (83%) ↓Total Bilirubin (39%)	NA	In vivo; India
Ahmad et al., 2001	Jigrine	*Cichorium intybus, Tamarix dioica, Solanum nigrum, Rheum emodii, Rubia cordifolia, Vitex negundo, Cassia occidentalis, Foeniculum vulgare, Cuscuta reflexa, Careya arborea, Phyllanthus niruri, Plantago major, Rosa damascene* and *Solanum xanthocarpum*	Thioacetamide-intoxicated rats; injecting of 100 g/kg on 1st day of experiment.	At 0.5 mL/kg; ↓ALT (69%) ↓AST (82%) ↓Serum Na+ (17%) ↓Serum K+ (40%)	Silymarin (25 g/kg) ↓ALT (54%) ↓AST (77%) ↓Serum Na+ (14%) ↓Serum K+ (33%)	In vivo; India
Achliya et al., 2003	Amalkadi Ghrita	*Emblica officinalis, Glycyrrhiza glabra* and cow's ghee	CCl_4 induced liver damage in rats; feeding of 1 mL/kg 24 hrs before the start of treatment.	At 300 g/kg; ↓SGOT (41%) ↓SGPT (53%) ↓ALP (48%) ↓Total Bilirubin (58%)	Silymarin (100 g/kg) ↓SGOT (54%) ↓SGPT (70%) ↓ALP (48%) ↓Total Bilirubin (62%)	In vivo; India
Satturwar et al., 2003	Haridradi ghrita	*Terminalia chebula, Terminalia belerica, Azadirachta indica, Sida cordifolia* and *Glycyrrhiza glabra*	CCl_4 induced liver damage in rats; injecting of 0.7 mL/kg every alternate day for 7 days.	At 300 g/kg; ↓SGOT (49%) ↓SGPT (52%) ↓ALP (23%) ↓Bilirubin (25%)	Silymarin (20 g/kg) ↓SGOT (51%) ↓SGPT (52%) ↓ALP (24%) ↓Bilirubin (14%)	In vivo; India

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Khaliq et al., 2017	Bonjigar®	*Silybum marianum, Eclipta alba, Cichorium intybus, Berberis aristata, Picrorhiza kurroa, Tamarix gallica, Boerhavia diffusa, Solanum nigrum* and *Raphanus sativu.*	Diclofenac sodium induced hepatotoxicity in albino rabbits; feeding of 20 g/ mL/kg body weight for 15 days	At 1.5 mL/kg; ↓ALT (91%) ↓AST (92%) ↓Bilirubin (86%)	Silymarin (100 g/kg) ↓ALT (86%) ↓AST (90%) ↓Bilirubin (82%)	*In vivo;* Pakistan
Iqbal and Khan, 2019	NPCF	*Rosa damascene, Cinnamomum cassia Blume, Nardostachys jatamansi, Cichorium intybus, Boerhavia diffusa, Asarum europaeum, Iris ensata, Crocus sativus* and *Laccifer lacca*	CCl_4 induced liver damage in rats; injecting of 0.2 mL/100g on 6^{th} day.	At 140 g/ 100g; ↓SGPT (68%) ↓SGOT (68%) ↓ALP (74%) ↓Serum Bilirubin (32%)	Silymarin (10 g/ 100g) ↓SGPT (43%) ↓SGOT (55%) ↓ALP (52%) ↓Serum Bilirubin (23%)	*In vivo*; India
Singh et al., 2015	PHE	*Andrographis paniculata, Tinospora cordifolia* and *Solanum nigrum*	Paracetamol induced liver toxicity in rats; injecting of 500 g/kg on 7^{th} day.	At 500 g/kg; ↓AST (62%) ↓ALT (64%) ↓ALP (80%) ↓Bilirubin (61%)	Liv-52 (5.2 mL/kg) ↓AST (55%) ↓ALT (61%) ↓ALP (76%) ↓Bilirubin (55%)	*In vi-vo*;India
Joseph et al., 2014	HEPIN	NR.	Alcohol induced hepatotox-icity in rats; feeding of 40% ethanol (2 mL/kg) daily for 28 days.	At 500 g/kg; ↓SGPT (44%) ↓SGOT (53%) ↓ALP (64%) ↓Total Bilirubin (54%)	Silymarin (25 g/kg) ↓SGPT (29%) ↓SGOT (37%) ↓ALP (60%) ↓Total Bilirubin (34%)	*In vi-vo*;India

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Sreshta and Babu, 2018	PHF	*Tinospora cordifolia* and *Curculigo orchioides*	CCl_4 induced liver damage in rats; injecting of 1 mL on 7^{th} day.	At 400 g/kg; ↓SGOT (87%) ↓SGPT (75%) ↓ALP (48%) ↓Bilirubin (27%)	Silymarin (100 g/kg) ↓SGOT (70%) ↓SGPT (70%) ↓ALP (45%) ↓Bilirubin (22%)	*In vivo*; India
Sreshta and Babu, 2018	PHF	*Tinospora cordifolia* and *Curculigo orchioides*	Paracetamol induced liver toxicity in rats; feeding of 2 gm/kg on 7^{th} day.	At 400 g/kg; ↓SGOT (80%) ↓SGPT (69%) ↓ALP (61%) ↓Bilirubin (35%)	Silymarin (100 g/kg) ↓SGOT (70%) ↓SGPT (65%) ↓ALP (55%) ↓Bilirubin (29%)	*In vivo*; India
Shailajan et al., 2015	Jawarish-e-AmLa Sada	*Emblica officinalis, Citrus medica, Santalum album, Pistacia lentiscus, Elettaria cardamomum Punica granatum,* Asal (Honey) and Qand safaid (Sugar)	CCl_4 induced liver damage in rats; injecting of 1.2 mL/kg on 1^{st} day.	At 1 g/kg; ↓SGPT (49%) ↓SGOT (54%) ↓Bilirubin (65%)	Silymarin (0.07 g/kg) ↓SGPT (54%) ↓SGOT (49%) ↓Bilirubin (64%)	*In vivo*; India
Khan et al., 2018	Kumaryasava	NR.	CCl_4 induced liver damage in rats; feeding of 1 mL on 10^{th} day.	At 1.6 mL/kg; ↓SGPT (41%) ↓SGOT (40%) ↓ALP (39%) ↑Albumin (52%)	Livfit (100 g/kg) ↓SGPT (45%) ↓SGOT (37%) ↓ALP (56%) ↑Albumin (61%)	*In vivo*;India

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Maheshwari et al., 2015	Livplus	*Boerhavia diffusa, Andrographis paniculata, Cichorium intybus, Eclipta alba, Berberis aristata, Phyllanthus niruri* and *Picrorhiza kurroa*	CCl_4 induced liver damage in rats; injecting of 1 mL/kg every 72 h for 14 days.	↓ALT, ↓AST, ↓ALP, ↓Bilirubin (direct and total), ↓GGT, ↓TC, ↓TG&↓TP	↓↓ALT, ↓↓AST, ↓↓ALP, ↓↓Bilirubin (direct and total), ↓↓GGT, ↓↓TC, ↓↓TG&↓↓TP	*In-vivo*; India
Khan et al., 2018	PHF	*Solanum nigrum, Silybum marianum, Atrmesia absinthium, Achillea millefolium* and *Cichorium intybus*	CCl_4 induced liver damage in rats; injecting of 1mL/kg.	At 500 g/kg; ↓AST (17%) ↓ALT (12%) ↓ALP (54%) ↓Bilirubin (17%)	Silymarin (200 g/kg) ↓AST (17%) ↓ALT (11%) ↓ALP (53%) ↓Bilirubin (17%)	*In vivo*;Pakistan
Lu et al., 2011	Ginseng essence	*Panax ginseng, Panax quinquefolius, Nelumbo nucifera* and *Lilium longiflorum*	CCl_4 induced liver damage in rats; feeding of 1.5 g/kg two times a week for 8 weeks.	At 3.125 g/kg; ↑Glutathione (57%) ↑GST (38%) ↑SOD (57%) ↑CAT (60%)	Silymarin (0.5 g/kg) ↑Glutathione (56%) ↑GST (32%) ↑SOD (59%) ↑CAT (59%)	*In vivo*;Taiwan
Fathima et al. 2015	Herbal formulation	*Andrographis paniculata*, *Boerhavia diffusa*, *Eclipta alba* and *Picrorhiza kurroa,* Sorbitol, Sucrose, Carbox methyl cellulose (CMC) and Olive oil	CCl_4 induced liver damage in rats; feeding of 1 mL/kg on 4^{th} day.	At 400 g/kg; ↓SGOT (57%) ↓SGPT (65%) ↓Albumin (67%) ↑Bilirubin (87%)	Liv 52 (50 mL/kg) ↓SGOT (48%) ↓SGPT (58%) ↓Albumin (58%) ↑Bilirubin (81%)	*In vivo*;India

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Fiaz et al., 2017	PoHF	*Zingiber officinale*, *Peganum harmala*, *Cassia angustifolia* and *Operculina turpethum*	Paracetamol induced hepatic damage in rabbits	At 500 mg/kg; ↓ALT (32%) ↓AST (42%) ↓ALP (48%)	Ascorbic Acid (200 mg/kg) ↑ALT (12%) ↑AST (17%) ↑ALP (16%)	In vivo; India
Gawate et al., 2016	MandurBhasma	NR.	Paracetamol induced liver toxicity in rats; feeding of 3 gm/kg on 8th day.	At 1 gm/100gm; ↓SGOT (82%) ↓SGPT (88%) ↓ALP (74%) ↓Bilirubin (46%)	NA	*In vivo*; India
Dey et al., 2020	BV-7310	*Phyllanthus niruri, Tephrosia purpurea, Boerhavia diffusa,* and *Andrographis paniculata*	CCl_4 induced liver damage in rats; feeding of 0.1 mL/kg of CCl_4 on 20th day.	At 500 g/kg; For male rats ↓AST (63%) ↓ALT (38%) ↓ALP (60%) ↑Total Protein (96%) ↓Serum Bilirubin (62%)	NA	*In vivo*;India
Rouf et al., 2021	Arogyavardhini	*Terminalia chebula, Terminalia Bellerica, Emblica Officinalis, Commiphora wightii, Plumbago zeylanica Linn, Picrorrhiza kurroa, Azadirachta indica*, Parada, Gandhaka, Iron, Mica, Copper and Asphaltum	D-Galactosamine induced liver toxicity in rats; injecting of 270 mg/kg on the 14th day	At dose 50 mg/kg; ↓ALT (92%) ↓AST (91%) ↓ALP (72%) ↓Bilirubin (89%)	Silymarin 100 mg/kg ↓ALT (94%) ↓AST (92%) ↓ALP (69%) ↑Bilirubin (86%)	*In vivo;* India

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Tasaduq et al., 2003	HP-1	*Tinospora cordifolia, Terminalia belerica, Terminalia chebula, Phyllanthus emblica* and *Phyllanthus niruri*	CCl_4 induced liver damage in rats; feeding of 0.2 mL/100gm on 7th day.	At 100 g/kg; ↓SGPT (34%) ↓SGOT (37%)	Silymarin (50 g/kg) ↓SGPT (52%) ↓SGOT (41%)	In vivo; India
Kumar and Mishra, 2004	Trikatu Churna	*Piper longum, Piper nigrum* and *Zingiber officinale*	CCl_4 induced liver damage in mice; injecting of 1 mL/kg single dose.	At 150 g/kg; ↓SGOT (40%) ↓SGPT (36%) ↓ALP (18%) ↓Total Bilirubin (28%)	Liv 52 ↓SGOT (2%) ↓SGPT (42%) ↓ALP (29%) ↓Total Bilirubin (39%)	In vivo; India
Rajesh and Latha, 2004	Kamilari	*Berberis aristata, Cordia myxa, Curculigo orchioides, Elettaria cardamomum, Glycyrrhiza glabra, Piper longum, Thespesia populnea* and *Zingiber offcinale*	CCl_4 induced liver damage in rats; feeding of 0.1 mL/100 gm twice a week for 2 months.	At 750 g/kg; ↓ALT (60%) ↓AST (25%) ↓ALP (31%) ↓Total Bilirubin (79%)	NA	In vivo; India
Gupta et al., 2004	New Livfit®	*Eclipta alba, Phyllanthus niruri, Rheum emodi, Tephrosea purpurea, Cichorium intybus, Tinospora cordifolia, Terminalia chebula, Boerrhaavia diffusa, Andrographis paniculata, Picorrhiza kurroa* and *Fumaria officinalis*	Pyrogallol induced liver damage in rats; injection of 100 g/kg.	At 50 g/kg; ↓AST (25%) ↓ALT (37%)	NA	In vivo; India

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Naraya-nasamy and Selvi, 2005	AYUSH-LIV.04	*Eclipta alba, Clitoria ternatea, Asparagus racemosus* and *Alpinia galangal.* Milk tuttam (Copper containing stone)	CCl_4 induced hepatotoxicity in rats; feeding of single dose of CCl_4 in liquid paraffin on 20th day.	At 4 mL/100g; ↓AST (67%) ↓ALT (69%) ↓ALP (28%) ↓Bilirubin (18%)	LIV 52 (2 mL/100g) ↓AST (83%) ↓ALT (64%) ↓ALP (49%) ↓Bilirubin (15%)	In vivo; India
Bhar et al., 2005	Enliv®	*Aphanamixis polystachia, Phyllanthus niruri, Eclipta alba, Andrographis paniculata, Picrorhiza kurroa, Tinospora cordifolia, Naregamia alata,* and *Emblica officinalis.*	Paracetamol-induced liver damage in broiler chicks; feeding of 250 g/kg on 21st day.	At 1 kg/ton; ↑AST (33%) ↑ALT (63%) ↑Reduced GSH (37%)	NA	In vivo; India
Lal et al., 2007	HM	*Glycyrrhiza glabra, Hemidesmus indicus, Phyllanthus amarus (Syn Phyllanthus niruri), Phyllanthus emblica, Picrorhiza scrophulariiflora, Ricinus communis* and *Tinospora cordifolia*	CCl_4 induced liver damage in mice; injecting of 2 mL/kg once every 48 hrs for 9 days.	At 1000 g/kg; Male mice ↓ALT (27%) ↓AST (80%)	Liv 52 (1000 g/kg) Male mice ↓ALT (35%) ↓AST (84%)	In vivo; India
Rasool et al., 2007	Triphala	*Terminalia chebula , Terminalia bellerica* and *Emblica officinalis*	Acetaminophen induced liver damage in rats; injection of 900 g/kg singles dose.	At 100 g/kg; ↓ALT (44%) ↓AST (53%) ↓ALP (62%)	Silymarin (50 g/kg) ↓ALT (51%) ↓AST (63%) ↓ALP (74%)	In vivo; India

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Dandagi et al., 2008	F1	*Ferula asafetida* (chloroform extract), *Momordica charantia* (Pet ether extract), *Nardostachys jatamansi* (Pet ether extract), Tween 80, sodium CMC, Sucrose, Sorbitol and Methyl parabeen	CCl_4 induced hepatotoxicity in rats; Injections of 0.7 mL/kg on 3rd, 6th and 10th	F1 at 10 g/kg; ↓SGPT (61%) ↓SGOT (35%) ↓ALP (56%)	LIV- 52 (1 mL/kg) ↓SGPT (23%) ↓SGOT (45%) ↓ALP (22%)	In vivo; India
Dandagi et al., 2008	F2	*Ferula asafetida* (water and Pet extract), *Momordica charantia* (alcohol extract), *Nardostachys jatamansi* (alcohol extract), Tween 80, sodium CMC, Sucrose, Sorbitol and Methyl parabeen		F2 at 10 g/kg; ↓SGPT (67%) ↓SGOT (33%) ↓ALP (76%)	LIV- 52 (1 mL/kg) ↓SGPT (23%) ↓SGOT (45%) ↓ALP (22%)	In vivo; India
Dandagi et al., 2008	F3	*Ferula asafetida* (chloroform extract), *Momordica charantia* (Pet ether extract), *Nardostachys jatamansi* (Pet ether extract), *Ferula asafetida* (water and Pet extract), *Momordica charantia* (alcohol extract), *Nardostachys jatamansi* (alcohol extract), Tween 80, sodium CMC, Sucrose, Sorbitol and Methyl paraben		F3 at 10 g/kg; ↓SGPT (34%) ↓SGOT (60%) ↓ALP (22%)	LIV- 52 (1 mL/kg) ↓SGPT (23%) ↓SGOT (45%) ↓ALP (22%)	In vivo; India

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Satyapal et al., 2008	Livobond	*Salvadora persica, Eclipta alba, Tecoma undulate, Boerhavia diffusa, Embelia ribes, Aloe barbadensis, Vitis venifera, Coriandrum sativum, Cassia accidentalis, Andrographis paniculata, Cissumpelos periera, Picrorhiza kurroa, Terminalia arjuna, Berberis aristata, Piperum longum, Cichorium intyns* and *Tefrosia purpurea*	CCl_4 induced liver damage in rats; injecting of 1.5 mL/kg on 7th day single dose.	At 750 g/kg; ↓AST (72%) ↓ALT (52%) ↓ALP (39%) ↓Total Bilirubin (57%)	Silymarin (50 g/kg) ↓AST (27%) ↓ALT (44%) ↓ALP (38%) ↓Total Bilirubin (66%)	In vivo; India
Kamble et al., 2008	F1	*Acacia catechu, Allium sativum, Andrographis paniculata, Azadirachta indica, Boerhaavia diffusa, Curcuma longa, Eclipta alba, Emblica officinalis, Luffa echinata, Picrorrhiza kurroa* and *Phyllanthus amarus*	CCl_4 induced liver damage in rats; feeding of 1.5 mL/kg daily for 5 days.	F1 at 400 g/kg; ↓SGOT (32%) ↓SGPT (41%) ↓ALP (44%) ↓Total Bilirubin (50%)	Silymarin (6 g/kg) ↓SGOT (42%) ↓SGPT (52%) ↓ALP (55%) ↓Total Bilirubin (57%)	In vivo; India
Kamble et al., 2008	F1	*Acacia catechu, Allium sativum, Andrographis paniculata, Azadirachta indica, Boerhaavia diffusa, Curcuma longa, Eclipta alba, Emblica officinalis, Luffa echinata, Picrorrhiza kurroa* and *Phyllanthus amarus*	Paracetamol induced liver toxicity in rats; feeding of 2 g/kg	F1 at 400 g/kg; ↓SGOT (38%) ↓SGPT (39%) ↓ALP (48%) ↓Total Bilirubin (17%)	Silymarin (6 g/kg) ↓SGOT (59%) ↓SGPT (64%) ↓ALP (42%) ↓Total Bilirubin (58%)	In vivo; India

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Kamble et al., 2008	F2	*Acacia catechu, Allium sativum, Andrographis paniculata, Azadirachta indica, Boerhaavia diffusa, Curcuma longa, Eclipta alba, Emblica officinalis, Luffa echinata, Picrorrhiza kurroa* and *Phyllanthus amarus* [Composition weight differ from F1]	CCl_4 induced liver damage in rats; feeding of 1.5 mL/kg daily for 5 days.	F2 at 400 g/kg; ↓SGOT (42%) ↓SGPT (20%) ↓ALP (57%) ↓Total Bilirubin (54%)	Silymarin (6 g/kg) ↓SGOT (58%) ↓SGPT (48%) ↓ALP (45%) ↓Total Bilirubin (43%)	In vivo; India
Kamble et al., 2008	F2	*Acacia catechu, Allium sativum, Andrographis paniculata, Azadirachta indica, Boerhaavia diffusa, Curcuma longa, Eclipta alba, Emblica officinalis, Luffa echinata, Picrorrhiza kurroa* and *Phyllanthus amarus* [Composition weight differ from F1]	Paracetamol induced liver toxicity in rats; feeding of 2 g/kg	F2 at 400 g/kg; ↓SGOT (36%) ↓SGPT (34%) ↓ALP (54%) ↓Total Bilirubin (42%)	Silymarin (6 g/kg) ↓SGOT (41%) ↓SGPT (34%) ↓ALP (58%) ↓Total Bilirubin (42%)	In vivo; India

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Patere 2009	Normeta	*Withania somnifera, Tinospora cordifolia, Tribulus terrestris, Emblica officinalis, Asparagus racemosus, Zingiber officinale, Piper longum, Piper nigrum, Glycyrrhiza glabra, Mucuna pruriens, Argyreia speciosa, Vitis vinifera, Cinnamomum zeylanicum, Eugenia caryophyllus* and *Syzygium aromaticum*	Alcohol, carbonyl iron and polyunsaturated fatty acids-induced liver damage in rats feeding daily for 30 days.	At 4 mL/kg; ↓SGPT (66%) ↑Total Protein (75%) ↓ Iron (16%) ↑SOD (20%) ↑CAT (25%)	Silymarin (50 g/kg) ↓SGPT (34%) ↑Total Protein (28%) ↓ Iron (19%) ↑SOD (24%) ↑CAT (24%)	In vivo; India
Najmi et al., 2009	Jigrine	*Cichorium intybus, Tamarix dioica, Solanum nigrum, Rheum emodii, Rubia cordifolia, Vitex negundo, Cassia occidentalis, Foeniculum vulgare, Cuscuta reflexa, Careya arborea, Phyllanthus niruri, Plantago major, Rosa damascene* and *Solanum xanthocarpum*	D-galactosamine induced liver toxicity in rats; injecting of 400 g/kg on 21st day.	At 1 g/kg; ↓ALT (77%) ↓ALP (57%) ↓Bilirubin (44%)	Silymarin (25 g/kg) ↓ALT (80%) ↓ALP (53%) ↓Bilirubin (36%)	In vivo; India
Desai et al., 2010	PHF08	*Tinospora cordifolia, Emblica officinalis, Withania somnifera, Curcuma longa, Glycyrrhiza glabra, Bacopa monnieri, Terminalia chebula, Asparagus racemosus, Terminalia arjuna* and *Aloe barbadensis*	CCl_4 induced hepatotoxicity in rats; injecting of 0.7 mL/kg on 1st, 4th and 7th day.	At 200 g/kg; ↓SGPT (19%) ↓SGOT (17%) ↓ALP (26%) ↑Total Protein (12%)	Silymarin (100 g/kg) ↓SGPT (45%) ↓SGOT (26%) ↓ALP (34%) ↑Total Protein (17%)	In vivo; India

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Keche et al., 2010	Livwin	Ashwagandha (*Withania somnifera*), Arjuna (*Terminalia arjuna*), Bhumyamalaki (*Phyllanthus niruri*), Daruharidra (*Berberis aristata*), Guduchi (*Tinospora cordifolia*), Kutki (*Picrorhiza kurrooa*) and Punarnava (*Boerhavia diffusa*)	Patients' diagnosis with symptomatic acute viral hepatitis (Less than 6 months).	At 500 mg in 2, 4, 8, 12 weeks; Tender and Enlarged Liver recovered ↓83%, ↓100%, ↓100%, ↓100% Serum Bilirubin ↓37.39%, ↓62.06%, ↓96.55%, ↓89.66 AST ↓27.59%, ↓48.28%, ↓65.52%, ↓82.76% ALT ↓27.59%, ↓89.66%, ↓100%, ↓100% Serum Alkaline ↓37.93%, ↓68.97%, ↓75.86%, ↓82.76%	Placebo (500 mg) in 2, 4, 8, 12 weeks; Tender and Enlarged Liver recovered ↓48%, ↓79%, ↓96.55%, ↓100% Serum Bilirubin ↓6.90%, ↓34.48%, ↓58.62%, ↓79.31% AST ↓0%, ↓10.34%, ↓58.62%, ↓82.76% ALT ↓0%, ↓17.24%, ↓51.72%, ↓93.10% Serum Alkaline ↓24.13%, ↓48.28%, ↓79.31%, ↓82.76%	Clinical trial; India
Kandasamy et al., 2010	RVSPHF567	*NR.*	CCl_4 induced liver damage in rats; injecting single dose of 2 mL/kg.	At 1 mL/kg; ↓SGOT (77%) ↓SGPT (79%) ↓ALP (55%) ↓Bilirubin (71%)	Liv-52 (1 mL/kg) ↓SGOT (77%) ↓SGPT (78%) ↓ALP (48%) ↓Bilirubin (62%)	In vivo; India

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Lima et al., 2010	LIV-first	*Eclipta alba, Andrographis paniculata, Tinospora cordifoli, Picrorhiza kurroa, Boerhavia diffusa* and *Berberis aristata*	CCl_4 induced liver damage in rats; injecting of 1 mL/kg for 7 days.	At 1 mL/kg; ↓SGOT (63%) ↓SGPT (52%) ↓ALP (64%) ↓Bilirubin (37%)	Silymarin (25 g/kg) ↓SGOT (74%) ↓SGPT (76%) ↓ALP (77%) ↓Bilirubin (62%)	In vivo; India
Mayuren et al., 2010	Livactine	*Boerrhavia diffusa, Tinospora cordifolia, Andrographis paniculata, Emblica officianalis* and 5 more undisclosed plants.	CCl_4 induced liver damage in rats; injecting of 1 mL/kg every 72 hrs for 10 days.	At 2 mL/kg; ↓SGOT (52%) ↓SGPT (59%) ↓ALP (59%) ↓Total Bilirubin (28%)	Liv-52 (1 mL/kg) ↓SGOT (73%) ↓SGPT (84%) ↓ALP (64%) ↓Total Bilirubin (39%)	In vivo; India
Mayuren et al., 2010	Livactine	*Boerrhavia diffusa, Tinospora cordifolia, Andrographis paniculata, Emblica officianalis* and 5 more undisclosed plants.	Paracetamol induced liver toxicity in rats; feeding of 3 gm/kg for 10 days.	At 2 mL/kg; ↓SGOT (15%) ↓SGPT (47%) ↓ALP (18%) ↓Total Bilirubin (21%)	Liv-52 (1 mL/kg) ↓SGOT (25%) ↓SGPT (52%) ↓ALP (55%) ↓Total Bilirubin (25%)	In vivo; India
Arsul et al., 2010	Polyherbal tablet	*Phyllanthus niruri, Eclipta alba, Cichorium intybus, Boerhaavia diffusa, Embelia ribes, Berberis aristata* and *Picrorhiza kurroa*	CCL_4 induced liver damage in rats; injecting of 0.7 mL/kg for 5 days	At 300 g/kg; ↓SGOT (36%) ↓SGPT (30%) ↓ALP (54%)	Silymarin (100 g/kg) ↓SGOT (36%) ↓SGPT (27%) ↓ALP (56%)	In vivo; India

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Prakash and Mukherjee, 2010	Prak-20	*Zingiber officinale, Piper nigrum, Piper longum, Terminalia chebula, Terminalia bellerica, Emblica officinalis, Plumbago zeylanica, Cyperus rotundus, Picrorhiza kurroa, Cedrus deodara, Embellia ribes, Saussuria lappa, Curcuma longa, Berberis aristata, Baliospermum montanum, Holarrhena antidysentrica, Ipomoea turpethum, Boerhavia diffusa* and *Mandoor Bhasma* (Ferric Oxide)	CCL_4 induced liver damage in rats; injection of 0.5 mL/kg for 7 days.	At 1.8 gm/kg; ↓AST (54%) ↓ALT (83%)	NA	In vivo; India
Shah et al., 2010	Punarnavashtak kwath	*Boerhaavia diffusa, Picrorhiza Kurroa, Tinospora cordifolia, Zingiber officinalis, Berberis aristata, Terminalia chebula, Azadirachta indica* and *Tricosanthes dioica*	Paracetamol induced liver toxicity in rats; feeding of 3 gm/kg on 8th day.	At 100 g/kg; ↓AST (43%) ↓ALT (49%) ↓ALP (54%) ↓Bilirubin (82%)	Silymarin (50 g/kg) ↓AST (32%) ↓ALT (42%) ↓ALP (42%) ↓Bilirubin (60%)	In vivo; India
Kandasamy et al., 2010	PHF	*NR.*	CCl_4 induced liver damage in rats; injecting of 2 mL/kg single dose.	At 1 mL/kg; ↓SGOT (77%) ↓SGPT (79%) ↓ALP (74%) ↓Bilirubin (71%)	Liv 52 (1 mL/kg) ↓SGOT (76%) ↓SGPT (78%) ↓ALP (48%) ↓Bilirubin (62%)	In vivo; India

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Devaraj et al., 2011	Hepax	*Plumbago zeylanica, Picrorrhiza kurroa, Piper nigrum, Zingiber officinale, Phyllanthus emblica,Terminalia chebula, Potassii carbonas, Sodii carbonas impure* and *Calcii oxidum*	CCl_4 induced hepatotoxicity in rats; injecting of 1 mL on 7th day.	At 200 g/kg; ↓SGPT (89%) ↓SGOT (58%) ↓ALP (34%) ↑Bilirubin (06%)	Siylmarin (100 g/kg) ↓SGPT (70%) ↑SGOT (39%) ↓ALP (25%) ↓Bilirubin (05%)	In vivo; India
Devaraj et al., 2011	Hepax	*Plumbago zeylanica, Picrorrhiza kurroa, Piper nigrum, Zingiber officinale, Phyllanthus emblica,Terminalia chebula, Potassii carbonas, Sodii carbonas impure* and *Calcii oxidum*	Paracetamol induced hepatotoxicity in rats; feeding of 100 g/gm on 7th day.	At 200 g/kg; ↓SGPT (82%) ↓SGOT (74%) ↓ALP (46%) ↓Bilirubin (71%)	Siylmarin (100 g/kg) ↓SGPT (80%) ↓SGOT (70%) ↓ALP (43%) ↓Bilirubin (86%)	In vivo; India
Devaraj et al., 2011	Hepax	*Plumbago zeylanica, Picrorrhiza kurroa, Piper nigrum, Zingiber officinale, Phyllanthus emblica,Terminalia chebula, Potassii carbonas, Sodii carbonas impure* and *Calcii oxidum*	Thioacetamide induced hepatotoxicity in rats; feeding of 100 g/gm on 7th day.	At 200 g/kg; ↓SGPT (42%) ↓SGOT (34%) ↓ALP (36%) ↓Bilirubin (51%)	Siylmarin (100 g/kg) ↓SGPT (47%) ↓SGOT (59%) ↓ALP (46%) ↓Bilirubin (73%)	In vivo; India
Sonkusale et al., 2011	Superliv Liquid	*Boerhavia diffusa, Andrographis paniculata, Phyllanthus emblica* and *Picrorrhiza kurroa*	CCl_4 induced liver damage in chicks; feeding of 1 mL/kg on every 3rd day during 15-28 days of trial.	At 5 mL/100 chicks/day; ↓SGOT (10%) ↓SGPT (35%) ↑Albumin (07%) ↑Protein (09%)	NA	In vivo; India

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Arsul et al., 2011	Livergen	*Andrographis paniculata, Apium graveolens, Berberis lyceum, Carum copticum, Cichorium intybus, Cyperus rontundus, Eclipta alba, Ipomoe turpethum, Oldenlandia corymbosa, Picrrorhiza kurroa, Plumbago zeylanica, Solanum nigrum, Tephrosia purpurea, Terminalia arjuna, Terminalia chebula* and *Trigonella foenugraecum*	CCl_4 induced hepatotoxicity in rats; injection of 0.7 mL/kg daily for 5 days	At 2.60 mL/kg; ↓SGPT (41%) ↓SGOT (46%) ↓ALP (55%) ↓Bilirubin (50%)	Siylmarin (100 g/kg) ↓SGPT (46%) ↓SGOT (46%) ↓ALP (56%) ↓Bilirubin (61%)	In vivo; India
Nehal, 2011	No name	*Apium graveolens, Cichorium intybus* and *Hordeum vulgare*	Cholesterol induced hypercholesterolemia in rats; feeding of 3% along with basal diet.	At 15% mixture of all feed; ↓AST (13%) ↓ALT (26%) ↓ALP (12%)	NA	In vivo; Egypt
Kenjale et al., 2011	Livomyn	*Boerrhavia diffusa, Tinospora cordifolia,Phyllanthus niruri, Andrographis paniculata, Cichorium intybus* and *Picrorhiza kurroa*	Ethanol induced hepatotoxicity in rats; feeding of 1 mL of 6% ethanol for 21 days.	At 2 TD (therapeutic dose); ↓SGOT (12%) ↓SGPT (15%) ↓ALP (07%) ↓Bilirubin (26%)	NA	In vivo; India

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Kenjale et al., 2011	Livomyn	*Boerrhavia diffusa, Tinospora cordifolia,Phyllanthus niruri, Andrographis paniculata, Cichorium intybus* and *Picrorhiza kurroa*	CCl_4 induced liver damage in rats; injecting of 0.8 mL/kg thrice a week.	At 2 TD (therapeutic dose); ↓SGOT (17%) ↓SGPT (16%) ↓ALP (13%) ↓Bilirubin (04%)	NA	In vivo; India
Kenjale et al., 2011	Livomyn	*Boerrhavia diffusa, Tinospora cordifolia,Phyllanthus niruri, Andrographis paniculata, Cichorium intybus* and *Picrorhiza kurroa*	D-galactosamine induced liver toxicity in rats; injecting of 700 g/kg on 1st day of experiment.	At 2 TD (therapeutic dose); ↓SGOT (16%) ↓SGPT (21%) ↓ALP (35%) ↓Bilirubin (18%)	NA	In vivo; India
Shah et al., 2011	Punarnavashtak kwath	*Boerhaavia diffusa, Picrorhiza Kurroa, Tinospora cordifolia, Zingiber officinalis, Berberis aristata, Terminalia chebula, Azadirachta indica* and *Tricosanthes dioica*	CCl_4 induced liver damage in rats; injecting of 1 mL/kg for two days.	At 150 g/kg; ↓AST (60%) ↓ALT (66%) ↓ALP (52%) ↓Bilirubin (43%)	Silymarin (50 g/kg) ↓AST (66%) ↓ALT (66%) ↓ALP (56%) ↓Bilirubin (47%)	In vivo; India
Shah et al., 2011	Punarnavashtak kwath	*Boerhaavia diffusa, Picrorhiza Kurroa, Tinospora cordifolia, Zingiber officinalis, Berberis aristata, Terminalia chebula, Azadirachta indica* and *Tricosanthes dioica*	CCl_4 induced hepatotoxicity activity on HepG2 cell line	At 15 µg/mL; ↑viability of HepG2 cell (87.84%)	Silymarin (50 µg/mL) ↑ viability of HepG2 cell (84.48%)	In vitro; India

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Shakya et al., 2012	Majoon-e-Dabeed-ul-ward	*Nardostachys, Pistacia lentiscus, Crocus sativus, Bambusa bambos, Cinnamomum zeylanicum, Cymbopogon jwarancusa, Asarum europaeum, Saussurea hypoleuca, Gentiana olivieri, Cuscuta reflexa, Rubia cordifolia, Coccus lacca, Cichorium intybus, Apium graveolens, Aristolochia donga, Commiphora opobalsamum, Aquilaria agalocha, Syzygium aromaticum, Elettaria cardamom, Rosa damascene* and *Qand Safed (granular sugar)*	CCl_4 induced liver damage in rats; injecting of 1.5 mL/kg only once.	At 1000 g/kg; ↓AST (56%) ↓ALT (85%) ↓Albumin (27%) ↓Urea (40%)	Silymarin (50 g/kg) ↓AST (58%) ↓ALT (87%) ↓Albumin (28%) ↓Urea (58%)	In vivo; India
Anturlikar et al., 2012	HD-03/ES	*Cyperus rotundus* and *Cyperus scariosus*	CCl_4 induced liver damage in rats; feeding of 1 mL/kg on 14^{th} day.	At 1000 g/kg Significant dose-dependent protection ↓↓SGPT ↓↓SGOT	NA	In vivo; India
Tatiya et al., 2012	HHF	*Andrographis paniculata, Phyllanthus niruri* and *Phyllanthus emblica*	Paracetamol induced liver toxicity in rats; feeding of 3 gm/kg on 3rd day.	At 400 g/kg; ↓SGOT (54%) ↓SGPT (48%) ↓ALP (41%)	Silymarin (50 g/kg) ↓SGOT (58%) ↓SGPT (59%) ↓ALP (47%)	In vivo; India

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Fulzele et al., 2012	Liv.52	*Capparis spinosa, Cichorium intybus, Solanum nigrum, Cassia occidentalis, Terminalia arjuna, Achillea millefolium* and *Tamarix gallica*	Antiandrogen – bicalutamide induced liver damage in rats; feeding of 25 g/kg daily for 14 days.	At 2 mL/100gm: ↓SGPT (04%) ↓SGOT (14%)	Silymarin (50 g/kg) ↓SGPT (01%) ↓SGOT (31%)	In vivo; India
Bera et al., 2012	Livshis	*Aloe barbadensis, Andrographis paniculata, Asteracantha longifolia, Berberis chitria, Fumaria parviflora, Phyllanthus fraternus* and *Picrorhiza kurroa*	CCl_4 induced liver damage in rats; injecting of 0.5 mL/kg on 28th day.	At 5 mL/kg; ↓SGOT (53%) ↓SGPT (60%) ↓ALP (41%) ↓Total Bilirubin (63%)	Silymarin (20 g/kg) ↓SGOT (50%) ↓SGPT (55%) ↓ALP (38%) ↓Total Bilirubin (61%)	In vivo; India
Mistry et al., 2012	PHF	*Coccinia indica, Sida cordata* and *Scoparia dulcis*	CCl_4 induced liver damage in rats; injection of 1 mL on 7th day	At 200 g/kg; ↓SGOT (59%) ↓SGPT (88%) ↓ALP (35%) ↑Bilirubin (05%)	Silymarin (100 g/kg) ↑SGOT (39%) ↓SGPT (70%) ↓ALP (25%) ↓Bilirubin (07%)	In vivo; India
Mistry et al., 2012	PHF	*Coccinia indica, Sida cordata* and *Scoparia dulcis*	Paracetamol induced liver toxicity in rats; feeding of 2 gm/kg on 7th day.	At 200 g/kg; ↓SGOT (74%) ↓SGPT (82%) ↑ALP (59%) ↓Bilirubin (69%)	Silymarin (100 g/kg) ↓SGOT (71%) ↓SGPT (80%) ↑ALP (62%) ↓Bilirubin (85%)	In vivo; India

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Goyal et al., 2012	Rohitaka ghrita	*Tecomella undulate, Ziziphus jujube, piper longum, Piper retrofractrum, Plumbago zeylanica* and *Zingiber officinalis*	Paracetamol induced liver toxicity in rats; feeding of 3 gm/kg on 3rd and 5th day.	At 3.6 gm/kg; ↓SGOT (36%) ↓SGPT (36%) ↓ALP (26%) ↓Bilirubin (33%)	Silymarin (25 g/kg) ↓SGOT (49%) ↓SGPT (41%) ↓ALP (45%) ↓Bilirubin (45%)	In vivo; India
Shakya et al., 2012	Sharbat-e-Deenar	*Cichorium intybus, Cuscuta reflexa, Rosa damascene, Rheum emodi, Borago officinalis* and *Nymphaea alba*	CCl_4 induced liver damage in mice; injecting of 1.5 mL/kg once.	At 4 g/kg; ↓ALT (81%) ↓AST (54%) ↓Urea (35%)	Silymarin (50 g/kg) ↓ALT (87%) ↓AST (61%) ↓Urea (44%)	In vivo; India
Saroj et al., 2012	PHF	*Emblica officinalis, Terminalia chebula, Terminalia bellirica, Picrorhiza kurroa, Tinospora cordifolia, Swertia chirata, Azadirachta indica, Adhatoda vasica.*	Paracetamol induced liver toxicity in rats; injecting of 300 g/kg on 8th day.	At 300g/kg; ↓ALT (26%) ↓AST (59%) ↓ALP (26%) ↓Total Bilirubin (34%)	Liv 52 (standard) ↓ALT (34%) ↓AST (26%) ↓ALP (06%) ↓Total Bilirubin (11%)	In vivo; India
Yang et al., 2012	AEF	*Artemisia capillaris, Lonicera japonica* and *Silybum marianum*	CCl_4 induced liver damage in rats; feeding of 20% CCl_4 dissolved in olive oil.	At 1.4 gm/kg; ↓AST (32%) ↓ALT (49%) ↓TG (10%)	Silymarin (200 g/kg) ↓AST (46%) ↓ALT (72%) ↓TG (6%)	In vivo; Taiwan
Bafna and Balaraman, 2013	DHC-1	*Bacopa monnieri, Emblica officinalis, Glycyrrhiza glabra, Mangifera indica* and *Syzygium aromaticum*	CCl_4 induced Liver damage in rats; injection of 2.5 mL/kg for 15 days.	At 1000 g/kg; ↓SGPT (59%) ↓SGOT (36%) ↓ALP (44%) ↓Total Bilirubin (92%)	NA	In vivo; India

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Kumar et al., 2013	Clearliv	*Phyllanthus niruri, Eclipta alba, Boerhaavia diffusa, Tinospora cordifolia, Tribulus terrestris, Tephrosia purpurea, Indigofera tinctoria, Aconitum heterophyllum, Andrographis paniculata, Rubia cordifolia, Terminalia chebula, Curcuma longa,* and *Ricinus cummunis*	Thioacetamide-intoxicated rats; Feeding of 500 g/kg for 3 days	At 1000g/kg; ↓AST (46%) ↓ALT (32%) ↓ALP (34%)	Liv 52 (20 mL/kg) ↓AST (59%) ↓ALT (38%) ↓ALP (34%)	In vivo; Malaysia
Kumar et al., 2013	Clearliv	*Phyllanthus niruri, Eclipta alba, Boerhaavia diffusa, Tinospora cordifolia, Tribulus terrestris, Tephrosia purpurea, Indigofera tinctoria, Aconitum heterophyllum, Andrographis paniculata, Rubia cordifolia, Terminalia chebula, Curcuma longa,* and *Ricinus cummunis*	CCl_4 induced hepatotox-icity in rats; injection of 50 mL/kg.	At 1000g/kg; ↓AST (42%) ↓ALT (39%)	Liv 52 (20 mL/kg) ↓AST (68%) ↓ALT (76%)	In vivo; Malaysia
Kumar et al., 2013	Clearliv	*Phyllanthus niruri, Eclipta alba, Boerhaavia diffusa, Tinospora cordifolia, Tribulus terrestris, Tephrosia purpurea, Indigofera tinctoria, Aconitum heterophyllum, Andrographis paniculata, Rubia cordifolia, Terminalia chebula, Curcuma longa,* and *Ricinus cummunis*	Galactosamine-intoxicated rats; feeding of 400g/kg for 3 days	At 1000g/kg; ↓AST (64%) ↓ALT (65%)	Liv 52 (20 mL/kg) ↓AST (72%) ↓ALT (69%)	In vivo; Malaysia

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Akhtar et al., 2013	Khamira Gaozaban Ambri Jadwar Ood Saleeb Wala	*Borago officinalis, Coriandrum sativum, Bombyx mori, Salvia haematodes, Centaurea behen, Santalum album, Mellisa parviflora, Lallemantia royleana, Ocimum gratissimum, Lavendula stoechas, Cheiranthus cheiri, Mathiola incana, Ambra grasea, Delphinium denudatum, Paeonia emodi* and *Pandanus tectorius*	CCl_4 induced liver damage in rats; injecting of 0.7 mL for 5 days.	At 300 g/kg; ↓SGPT (36%) ↓SGOT (38%) ↓ALP (56%)	Silymarin (100 g/kg) ↓SGPT (29%) ↓SGOT (33%) ↓ALP (59%)	In vitro; Pakistan
Ganapaty et al., 2013	Indian folklore medicine	*Begonia laciniata, Cuscuta epithymum* and *Dendrobium ovatum*	CCl_4 induced liver damage in rats; feeding of 1 mL/kg daily for 5 days.	At 150 g/kg; ↓SGOT (33%) ↓SGPT (50%) ↓ALP (32%) ↓Total Bilirubin (49%)	Silymarin (50 g/kg) ↓SGOT (13%) ↓SGPT (19%) ↓ALP (10%) ↓Total Bilirubin (27%)	In vivo; India
Patel et al., 2013	PHF	*Allium sativum, Rubus fruticosus, Curcuma longa* and *Viscum articulatum*	Paracetamol induced liver toxicity in rats; feeding of 2 gm/kg daily for 7 days.	At 500 g/kg; ↓ALT (20%) ↓AST (35%) ↓ALP (31%) ↓Total Bilirubin (56%)	Liv 52 (5.2 mL/kg) ↓ALT (23%) ↓AST (44%) ↓ALP (33%) ↓Total Bilirubin (63%)	In vivo; India
Padmanabhan and Jangle, 2014	HP-4	*Aloe vera, Bacopa monnieri, Moringa oleifera* and *Zingiber officinale*	Alcohol (25%) induced liver damaged in rats; feeding of 5 g/kg for 6 days	At 500 g/kg; ↓AST (32%) ↓ALT (47%) ↓ALP (36%) ↓LDH (31%) ↑SOD (36%)	Silymarin (100 g/kg) ↓AST (43%) ↓ALT (42%) ↓ALP (27%) ↓LDH (24%) ↑SOD (64%)	In vivo; India

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Gupta et al., 2014	PTF-1	*Butea monosperma, Bauhinia variegate* and *Ocimum gratissimum*	Paracetamol induced liver toxicity in rats; feeding of 2 g/kg for 5th day to 7th day.	PTF-1 at 100 g/kg; ↓SGPT (27%) ↓SGOT (36%) ↓ALP (39%) ↓Total Bilirubin (40%)	Silymarin (100 g/kg) ↓SGPT (28%) ↓SGOT (34%) ↓ALP (38%) ↓Total Bilirubin (33%)	In vivo; India
Gupta et al., 2014	PTF-2	*Butea monosperma, Bauhinia variegate* and *Ocimum gratissimum* (differ in quantity from PTF-1)		PTF-2 at 200 g/kg ↓SGPT (23%) ↓SGOT (36%) ↓ALP (36%) ↓Total Bilirubin (39%)		In vivo; India
Dinesh et al., 2014	F-I	*Tinospora cordifolia, Boerhavia diffuse, Phyllanthus amaraus,* Sarbitol, Sucrose, Carbox Methyl Cellulose (CMC), Olive Oil and Distilled Water	Paracetamol induced liver toxicity in rats; feeding of 3 g/kg as a single dose on day 8.	At 200 g/kg; ↓SGOT (64%) ↓SGPT (72%) ↓ALP (72%) ↓Total Bilirubin (23%) ↑Plasma protein (57%)	Silymarin (25 g/kg) ↓SGOT (60%) ↓SGPT (80%) ↓ALP (75%) ↓Total Bilirubin (42%) ↑Plasma protein (45%)	In vivo; India
Dinesh et al., 2014	F-II	*Boerhavia diffuse, Euphorbia hirta, Wedelia chinesis,* Sarbitol, Sucrose, Carbox Methyl Cellulose (CMC), Olive Oil and Distilled Water	Paracetamol induced liver toxicity in rats; feeding of 3 g/kg as a single dose on day 8.	F-II at 200 g/kg; ↓SGOT (70%) ↓SGPT (74%) ↓ALP (74%) ↓Total Bilirubin (36%) ↑Plasma protein (46%)	Silymarin (25 g/kg) ↓SGOT (60%) ↓SGPT (80%) ↓ALP (75%) ↓Total Bilirubin (42%) ↑Plasma protein (45%)	In vivo; India

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Dinesh et al., 2014	F-III	*Tinospora cordifolia, Boerhavia diffuse, Phyllanthus amaraus, Euphorbia hirta, Wedelia chinesis,* Sarbitol, Sucrose, Carbox Methyl Cellulose (CMC), Olive Oil and Distilled Water	Paracetamol induced liver toxicity in rats; feeding of 3 g/kg as a single dose on day 8.	F-III at 200 g/kg; ↓SGOT (75%) ↓SGPT (80%) ↓ALP (76%) ↓Total Bilirubin (43%) ↑Plasma protein (48%)	Silymarin (25 g/kg) ↓SGOT (60%) ↓SGPT (80%) ↓ALP (75%) ↓Total Bilirubin (42%) ↑Plasma protein (45%)	In vivo; India
Gite et al., 2014	F1	*NR*	CCl_4 induced liver damage in rats; injection of 2 mL/kg on 31st days.	F1 formulation; ↓ALP (38%) ↓LDH (24%) ↓SGOT (28%) ↓SGPT (50%) ↓Total Bilirubin (32%)	NA	In vivo; India
Gite et al., 2014	F2	*NR*	CCl_4 induced liver damage in rats; injection of 2 mL/kg on 31st days.	F2 formulation; ↓ALP (31%) ↓LDH (20%) ↓SGOT (20%) ↓SGPT (16%) ↓Total Bilirubin (61%)	NA	In vivo; India
Gite et al., 2014	F1 and F2	*NR*	CCl_4 induced radical toxicity to HepG2 cells: 4 mM concentration of CCl_4	F1 and F2 at 0.1 g in 10 ml PBS pH 7.4 ↓↓SOD ↓↓GPx ↓↓LDH ↓↓ALP	NA	In vitro; India

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Gengiah et al., 2014	Gluconorm-5	*Camellia sinensis, Punica granatum, Macrotyloma uniflorum, Foeniculum vulgare* and *Trigonella foenum-graecum*	Steptozotocin Induced hyperglycemic rats; Injecting of 60 g/kg.	At 600 g/kg; ↓AST (32%) ↓ALT (23%) ↓ALP (22%) ↓LDH (14%)	Glibenclamide (1g/kg) ↓AST (32%) ↓ALT (31%) ↓ALP (31%) ↓LDH (24%)	In vivo; India
Bigoniya and Singh, 2014	LivPro	*Achillea millefolium, Cichorium intybus* and *Picrorhiza kurroa*	CCl_4 induced liver damage in rats; injecting of 1 mL/kg on 7th day afterwards alternate days for a week.	At 15 mL/kg; ↓SGOT (34%) ↓SGPT (30%) ↓ALP (44%) ↓Bilirubin (33%)	Silymarin (20 g/kg) ↓SGOT (50%) ↓SGPT (44%) ↓ALP (61%) ↓Bilirubin (15%)	In vivo; India
Chung et al., 2014	F1	*Hovenia dulcis, Oryza sativa* and *Glycine max*	Alcohol induced hepatotoxicity in rats; feeding of 5 gm/kg ethanol six times per week for 12 weeks.	F1 at 200 µg/mL; ↓AST (19%) ↓ALT (07%) ↓ALP (18%) ↓TG (09%)	Hepakhan (100 µg/mL) ↓AST (20%) ↓ALT (02%) ↓ALP (23%) ↓TG (26%)	In vivo; South Korea
Chung et al., 2014	F2	*Hovenia dulcis, Oryza sativa* and *Glycine max* extract with powder of *Hovenia dulcis*	Alcohol induced hepatotoxicity in rats; feeding of 5 gm/kg ethanol six times per week for 12 weeks.	F2 at 200 µg/mL; ↓AST (14%) ↓ALT (01%) ↓ALP (18%) ↓TG (30%)	Hepakhan (100 µg/mL) ↓AST (20%) ↓ALT (02%) ↓ALP (23%) ↓TG (26%)	In vivo; South Korea

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Yadav and Kumar, 2014	Sarvakalp kwath	*Boerhavia diffusa, Phyllanthus urinaria* and *Solanum nigrum*	CCl_4 induced liver damage in rats; feeding of 1 mL/kg daily for 7 days.	At 120 g/kg; ↓ALT (60%) ↓ALP (58%) ↓Total Bilirubin (71%) ↓Albumin (01%)	NA	In vivo; India
Yadav and Kumar, 2014	Sarvakalp kwath		Ethanol induced hepatotoxicity in rats; feeding of 3.7 gm/kg for 45 days.	At 100 g/kg; ↓SGOT (36%) ↓SGPT (44%) ↓ALP (35%) ↓Bilirubin (32%)	Silymarin (50 g/kg) ↓SGOT (48%) ↓SGPT (54%) ↓ALP (46%) ↓Bilirubin (44%)	In vivo; India
Shah *et al.*, 2011	Punar-navashtak kwath	*Boerhaavia diffusa, Picrorhiza Kurroa, Tinospora cordifolia, Zingiber officinalis, Berberis aristata, Terminalia chebula, Azadirachta indica* and *Tricosanthes dioica*	CCl_4 induced liver damage in rats; injecting of 1 mL/kg for two days.	At 150 g/kg; ↓AST (60%) ↓ALT (66%) ↓ALP (52%) ↓Bilirubin (43%)	Silymarin (50 g/kg) ↓AST (66%) ↓ALT (66%) ↓ALP (56%) ↓Bilirubin (47%)	*In vivo*; India
Shah *et al.*, 2011	Punar-navashtak kwath	*Boerhaavia diffusa, Picrorhiza Kurroa, Tinospora cordifolia, Zingiber officinalis, Berberis aristata, Terminalia chebula, Azadirachta indica* and *Tricosanthes dioica*	CCl_4 induced hepatotoxicity activity on HepG2 cell line	At 15 µg/mL; ↑viability of HepG2 cell (87.84%)	Silymarin (50 µg/mL) ↑ viability of HepG2 cell (84.48%)	*In vitro;* India

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Kareemulla *et al*., 2018	Ethanolic Polyherbal Extract	*Annona squamosa* , *Cassia fistula* and *Illicium verum*	Paracetamol induced liver toxicity in rats; feeding of 2 gm/kg for 21 days.	At 400 g/kg; ↓SGOT (46%) ↓SGPT (45%) ↓ALP (35%) ↓Bilirubin (74%)	Silymarin (100 g/kg) ↓SGOT (46%) ↓SGPT (52%) ↓ALP (42%) ↓Bilirubin (79%)	*In vivo*; India
Kareemulla *et al*., 2018	Ethanolic Polyherbal Extract	*Annona squamosa* , *Cassia fistula* and *Illicium verum*	Ethanol induced hepato-toxicity in rats; feeding of 2 mL gm/kg 40% ethanol 2 mL gm/kg for 14 days	At 400 g/kg; ↓SGOT (46%) ↓SGPT (45%) ↓ALP (32%) ↓Bilirubin (92%)	Silymarin (100 g/kg) ↓SGOT (50%) ↓SGPT (47%) ↓ALP (35%) ↓Bilirubin (93%)	*In vivo*; India
Rao and Satyanaraya-na, 2015	HEM	*Phyllanthus amarus, Terminalia chebu-la, Ricinus communis, Cichorium inty-bus, Vitex negundo* and *Aloe vera*	Ethanol-induced hepato-toxicity in rats; feeding of 40% ethanol 3.76 gm/ kg twice daily for 25 days.	At 600 g/kg; ↓SGOT (20%) ↓SGPT (22%) ↓ALP (35%) ↓Total Bilirubin (32%)	Silymarin (100 g/kg) ↓SGOT (21%) ↓SGPT (23%) ↓ALP (36%) ↓Total Bilirubin (32%)	*In vivo*; India
Goyal *et al*., 2012	Rohitaka ghrita	*Tecomella undulate, Ziziphus jujube, piper longum, Piper retrofractrum, Plumbago zeylanica* and *Zingiber offic-inalis*	Paracetamol induced liver toxicity in rats; feeding of 3 gm/kg on 3rd and 5th day.	At 3.6 gm/kg; ↓SGOT (36%) ↓SGPT (36%) ↓ALP (26%) ↓Bilirubin (33%)	Silymarin (25 g/kg) ↓SGOT (49%) ↓SGPT (41%) ↓ALP (45%) ↓Bilirubin (45%)	*In vivo*; India

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Yadav and Kumar, 2014	Sarvakalp kwath	*Boerhavia diffusa, Phyllanthus urinaria* and *Solanum nigrum*	CCl_4 induced liver damage in rats; feeding of 1 mL/kg daily for 7 days.	At 120 g/kg; ↓ALT (60%) ↓ALP (58%) ↓Total Bilirubin (71%) ↓Albumin (01%)	NA	*In vivo*; India
Ganapaty *et al*., 2013	Indian folklore medicine	*Begonia laciniata, Cuscuta epithymum* and *Dendrobium ovatum*	CCl_4 induced liver damage in rats; feeding of 1 mL/kg daily for 5 days.	At 150 g/kg; ↓SGOT (33%) ↓SGPT (50%) ↓ALP (32%) ↓Total Bilirubin (49%)	Silymarin (50 g/kg) ↓SGOT (13%) ↓SGPT (19%) ↓ALP (10%) ↓Total Bilirubin (27%)	*In vivo*; India
Lal *et al*., 2007	HM	*Glycyrrhiza glabra, Hemidesmus indicus, Phyllanthus amarus* (Syn *Phyllanthus niruri*), *Phyllanthus emblica, Picrorhiza scrophulariiflora, Ricinus communis* and *Tinospora cordifolia*	CCl_4 induced liver damage in mice; injecting of 2 mL/kg once every 48 h for 9 days.	At 1000 g/kg; Male mice ↓ALT (27%) ↓AST (80%)	Liv 52 (1000 g/kg) Male mice ↓ALT (35%) ↓AST (84%)	*In vivo*; India
Shakya *et al*., 2012	Sharbat-e-Deenar	*Cichorium intybus, Cuscuta reflexa, Rosa damascene, Rheum emodi, Borago officinalis and Nymphaea alba*	CCl_4 induced liver damage in mice; injecting of 1.5 mL/kg once.	At 4 g/kg; ↓ALT (81%) ↓AST (54%) ↓Urea (35%) ↓Albumin (16%)	Silymarin (50 g/kg) ↓ALT (87%) ↓AST (61%) ↓Urea (44%) ↓Albumin (16%)	*In vivo*; India

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Honwad *et al*., 2015	Somanathi Tamra Bhasma	Shudhatamra, Parada, Gandhaka, Haritala and Manashila	Paracetamol induced liver toxicity in rats; injecting of 1 gm/kg on 5th day.	At 13 g/kg; ↓SGOT (26%) ↓SGPT (26%) ↓ALP (38%) ↓Total Bilirubin (00%)	Silymarin (50 g/kg) ↓SGOT (42%) ↓SGPT (80%) ↓ALP (43%) ↓Total Bilirubin (76%)	*In vivo*; India
Kumar and Mishra, 2004	Trikatu Churna	*Piper longum, Piper nigrum* and *Zingiber officinale*	CCl_4 induced liver damage in mice; injecting of 1 mL/kg single dose.	At 150 g/kg; ↓SGOT (40%) ↓SGPT (36%) ↓ALP (18%) ↓Total Bilirubin (28%)	Liv 52 ↓SGOT (2%) ↓SGPT (42%) ↓ALP (29%) ↓Total Bilirubin (39%)	*In vivo*; India
Kotecha *et al*., 2015	Vasa-guduchyadi kwatha	*Adhatoda vasica, Terminalia chebula, Terminalia bellerica, Emblica officinalis, Swertia chirayita* and *Picrochiza kurroa.*	Isoniazid (27 g/kg), rifampicin (54 g/kg) and pyrazinamide (135 g/kg) twice a day for 60 days induced liver damage in rats.	At 5.04 mL/kg; ↓SGOT (23%) ↓SGPT (36%) ↓ALP (07%) ↓Total Bilirubin (30%)	Silymarin (50 g/kg) ↓SGOT (23%) ↓SGPT (31%) ↓ALP (22%) ↓Total Bilirubin (78%)	*In vivo*; India
Achliya *et al*., 2003	Amalkadi Ghrita	*Emblica officinalis, Glycyrrhiza glabra* and cow's ghee	CCl_4 induced liver damage in rats; feeding of 1 mL/kg 24 h before the start of treatment.	At 300 g/kg; ↓SGOT (41%) ↓SGPT (53%) ↓ALP (48%) ↓Total Bilirubin (58%)	Silymarin (100 g/kg) ↓SGOT (54%) ↓SGPT (70%) ↓ALP (48%) ↓Total Bilirubin (62%)	*In vivo*; India

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Dhuley and Naik, 1997	Rhinax	*Withania somnifera, Asparagus racemosus, Mucuna pruriens, Phyllanthus emblica, Glycyrrhiza glabra, Terminalia chebula* and *Myristica fragrans*	CCl_4 induced liver damage in rats; injecting of 2.5 mL/kg single dose.	At 80 g/kg; ↓AST (83%)	NA	*In vivo*; India
Gupta *et al*., 2004	New Livfit®	*Eclipta alba, Phyllanthus niruri, Rheum emodi, Tephrosea purpurea, Cichorium intybus, Tinospora cordifolia, Terminalia chebula, Boerrhaavia diffusa, Andrographis paniculata, Picorrhiza kurroa* and *Fumaria officinalis*	Pyrogallol induced liver damage in rats; injection of 100 g/kg.	At 50 g/kg; ↓AST (25%) ↓ALT (37%)	NA	*In vivo*; India
Kandasamy *et al*., 2010	PHF	NR.	CCl_4 induced liver damage in rats; injecting of 2 mL/kg single dose.	At 1 mL/kg; ↓SGOT (77%) ↓SGPT (79%) ↓ALP (74%) ↓Bilirubin (71%)	Liv 52 (1 mL/kg) ↓SGOT (76%) ↓SGPT (78%) ↓ALP (48%) ↓Bilirubin (62%)	*In vivo;* India
Patel *et al*., 2013	PHF	*Allium sativum, Rubus fruticosus, Curcuma longa* and *Viscum articulatum*	Paracetamol induced liver toxicity in rats; feeding of 2 gm/kg daily for 7 days.	At 500 g/kg; ↓ALT (20%) ↓AST (35%) ↓ALP (31%) ↓Total Bilirubin (56%)	Liv 52 (5.2 mL/kg) ↓ALT (23%) ↓AST (44%) ↓ALP (33%) ↓Total Bilirubin (63%)	*In vivo;* India

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Rajesh and Latha, 2004	Kamilari	*Berberis aristata, Cordia myxa, Curculigo orchioides, Elettaria cardamomum, Glycyrrhiza glabra, Piper longum, Thespesia populnea* and *Zingiber offcinale*	CCl_4 induced liver damage in rats; feeding of 0.1 mL/100 gm twice a week for 2 months.	At 750 g/kg; ↓ALT (60%) ↓AST (25%) ↓ALP (31%) ↓Total Bilirubin (79%)	NA	*In vivo;* India
Rastogi *et al*., 2015	Mentat	NR.	CCl_4 induced liver damage in rats; injecting of 1 mL/kg every 72 h.	At 2 mL/kg; ↓SGPT ↓SGOT ↓ALP ↓Total Bilirubin	Silymarin (0.5 mL/100 gm) ↓↓SGPT ↓↓SGOT ↓ALP	*In vivo;* India
Saroj *et al*., 2012	PHF	*Emblica officinalis, Terminalia chebula, Terminalia bellirica, Picrorhiza kurroa, Tinospora cordifolia, Swertia chirata, Azadirachta indica*, and *Adhatoda vasica.*	Paracetamol induced liver toxicity in rats; injecting of 300 g/kg on 8th day.	At 300g/kg; ↓ALT (26%) ↓AST (59%) ↓ALP (26%) ↓Total Bilirubin (34%)	Liv 52 (standard) ↓ALT (34%) ↓AST (26%) ↓ALP (06%) ↓Total Bilirubin (11%)	*In vivo;* India
Shah *et al*., 2019	PHF	*Eclipta alba, Andrographis paniculata,* Triphla churna (formulation), *Phyllanthus niruri, Boerhavia diffusa* and *Tinospora cordifolia*	Ethanol induced hepatotoxicity in rats; feeding of 20% ethanol 3.76 gm/kg daily for 18 days.	At 180 g/kg; ↓ALT (30%) ↓AST (29%) ↓ALP (26%) ↓Total Bilirubin (41%)	Silymarin (100 g/kg) ↓ALT (46%) ↓AST (42%) ↓ALP (58%) ↓Total Bilirubin (47%)	*In vivo;* India
Wai *et al*., 2021	Triphala	*Terminalia chebula* , *Terminalia bellerica* and *Emblica officinalis*	CCl_4 induced liver damage in rats	At dose 1.2 gm/kg; ↓AST decrease ↓ALT decrease	DDB (7.5 mg/kg) ↓AST decrease ↓ALT decrease	*In vivo;* China

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Venkateswaran *et al.*, 1997	Livex	*Tephrosia purpurea, Aconitum heterophyllum, Solanum nigrum, Cichorium intybus, Cassia occidentalis, Tamarix gallica, Embelia ribes, Andrographis paniculata* and *Piper longum*	Erythromycin estolate induced hepatotoxicity in rats; feeding of 800 g/kg daily for 10 days.	At 121.25 gm/kg; ↓ALT (25%) ↓AST (14%) ↓ALP (14%) ↓Bilirubin (48%)	NA	*In vivo;* India
Yang *et al.*, 2012	AEF	*Artemisia capillaris, Lonicera japonica* and *Silybum marianum*	CCl_4 induced liver damage in rats; feeding of 20% CCl4 dissolved in olive oil.	At 1.4 gm/kg; ↓AST (32%) ↓ALT (49%) ↓TG (10%)	Silymarin (200 g/kg) ↓AST (46%) ↓ALT (72%) ↓TG (6%)	In vivo; Taiwan
Bhatt *et al.*, 2018	LIVT	*Boerhavia diffusa, Tinospora cordifolia, Eclipta alba, Andrographis paniculata, Picrorhiza kurroa, Phyllanthus amarus, Embelia ribes, Cichorium intybus*, and *Tecomella Undulate*	D-Galactosamine induced HepG2 cell toxicity model. Treating with 20 mM of D-galactosamine for 24 h.	At 62.5 µg/mL ↑ Protection (37%)	Silymarin (12.5 µg/mL) Comparable to test drug	*In vitro;* India
Eswaran et al., 2021	Liv-Pro-08	*Nigella sativa* (Seed), *Entada pursaetha* (Seed) and *Ficus glomerata* (Fruit)	CCl_4 induced HePG2 cells	At 50, 250, 500, 750, and 1000 µg mL IC_{50} of AST, ALP, ALT were found as 141.51, 231.69, and 182.05 µg mL	Silymarin is comparable to test drug	*In vitro;* India

Author(s)	Polyherbal preparation name	Herbal constituents	Study design	Effects of polyherbal preparation (% of change)	Effects of reference drug (% of change)	Study design and Country
Rafi *et al*., 2021	Dawa-Ul-Kurkum	*Nardostachys jatamansi, Commiphora myrrha, Cinnamomum tamala, Saussurea lappa, Cymbopogon shoenanthus, Cinnamomum zylenicum, Crocus sativa, Saussurea costus* and *Saccharum officinarum*	Paracetamol induced liver toxicity in rats; feeding of 2 g/kg daily for 14 days.	At 500 gm/kg; ↓SGPT (43%) ↑SGOT (42%) ↓ALP (45%) ↓Total Bilirubin (62%)	Silymarin (50 mg/kg) ↓SGPT (44%) ↑SGOT (32%) ↓ALP (45%) ↓ Total Bilirubin (55%)	*In vivo;* India
Reshi *et al*., 2021	Dawa-Ul-Kurkum	*Nardostachys jatamansi, Commiphora myrrha, Cinnamomum tamala, Saussurea lappa, Cymbopogon shoenanthus, Cinnamomum zylenicum, Crocus sativa, Saussurea costus* and *Saccharum officinarum*	D-Galactosamine induced liver in rats; injecting of 500 mg/kg for 3 months	At 250gm/kg; ↑SGOT (48%) ↓SGPT (33%) ↓ALP (44%) ↓Total Bilirubin (54%)	Silymarin (50 mg/kg) ↑SGOT (44%) ↓SGPT (39%) ↓ALP (51%) ↓Total Bilirubin (59%)	*In vivo;* India
Husain *et al*., 2021	Sharbat-e-Deenar	*Cichorium intybus* (seed and root bark), *Cuscuta reflexa* (seed), *Rosa damascene* (flower bud), *Rheum emodi* (root), *Nymphaea alba* (flower), *Borago officinalis* (leaves), Aab (water) and Qand Safaid (sugar)	90-day repeated dose oral toxicity	At dose 10 mL/kg; ↓ALT (10%) ↑AST (20%) ↓ALP (26%) ↑Bilirubin (43%)	NA	*In vivo;* India

Eclipta alba, Andrographis paniculata, Picrorhiza kurroa, Phyllanthus amarus, Embelia ribes, Cichorium intybus, and *Tecomella undulata,* which exhibited significant cytoprotection against D-galactosamine-induced cytotoxicity of HepG2 cells, which were comparable to the standard silymarin tested in this model (Bhatt et al., 2018)

2.6.2 Pre-clinical trials

Forty-nine PHFs were tested for their therapeutic efficiency on the biochemical parameters of CCl_4-induced hepatotoxic rodent and chick models (Table 2.1). Twenty-two PHPs were tested against paracetamol-induced hepatotoxic rodents. The hepatoprotective activity of Livergen (Arsul et al., 2011), Heptoplus (Sarkar et al., 2015), Sharbat Chylosin (Huda and Mosaddik, 2018), Clearliv (Kumar et al., 2013), LINK LIVECARE™ (Karunarathn et al., 2017), CURNA (Golla 2018), Normeta (Patere 2009), Liv 100 (Saraswathy and Devi, 1999), PHF08 (Desai et al., 2010), AHPL/AYTAB/0613 (Nipanikar et al., 2017), Arogyavardhini Rasa (Sapkota et al., 2017), Bonjigar® (Khaliq et al., 2017), F1,F2 and F3 (Dandagi et al., 2008), Majoon -e-Dabeed-ul-ward (Shakya et al., 2012), Gluconorm-5 (Gengiah et al., 2014), LivPro (Bigoniya and Singh, 2014), Haridradighrita (Satturwar et al., 2003), F1 and F2 (Kamble et al., 2008), NPCF (Iqbal and Khan, 2018), PHE (Singh et al., 2015), HHF (Tatiya et al., 2012), PHF (Sreshta and Babu, 2018), HEPIN (Joseph et al., 2018), HP-1 (Tasaduq et al., 2003), Jawarish-e-Amla Sada (Shailajan et al., 2015), Jigrine (Ahmad et al., 2001), Kumaryasava (Khan et al., 2015), F1 and F2 (Chung et al., 2014), LIV-first (Lima et al., 2010), Livomyn (Kenjale et al., 2011), Livplus (Maheshwari et al., 2015), Herbal formulation (Fathima et al., 2015), PHF (Khan et al., 2018), Punarnavashtakkwath (Shah et al., 2010), Punarnavashtakkwath (Shah et al., 2011), Ethanolic Polyherbal Extract (Kareemulla et al., 2018), Rohitakaghrita (Goyal et al., 2012), HM (Lal et al., 2014), Sharbat-e-Deenar (Shakya et al., 2012), TrikatuChurna (Kumar and Mishra, 2004), Triphala (Rasool et al., 2007; Wei et al., 2021), AmalkadiGhrita **(**Achliya et al., 2003**),** PHF (Patel et al., 2013), Mentat (Rastogi et al., 2015), PHF (Shah et al., 2019), AEF **(**Yang et al., 2012**)** were less effective when compared to reference drug. Some PHFs used in these studies like Hepax, HP-4, AYUSH-LIV.04, Ginseng essence, Livobond, RVSPHF567, PoHF, Jawarish-e-Amla Sada, Jigrine, Khamira Gaozaban Ambri JadwarOod Saleeb Wala, Liv.52 and Livactine were found to be more effective than the standard drugs.

Dinesh et al., 2014 formulated three formulations where F-I consists of *Tinospora cordifolia, Boerhavia diffuse, Phyllanthus amarus*, sorbitol, sucrose, carboxy methyl

cellulose (CMC), olive oil and distilled water and F-II composed of *Boerhavia diffuse*, *Euphorbia hirta, Wedelia chinesis,* sorbitol, sucrose, CMC, olive oil and distilled water with differences in their ingredients, but F-III includes *Tinospora cordifolia, Euphorbia hirta, Boerhavia diffusa, Wedelia chinensis*, *Phyllanthus amarus, s*orbitol, sucrose, CMC, olive oil and distilled water all ingredients of both F-I and F-II preparations. F-I and F-II were reported to be more effective than F-III compared to the standard silymarin as in table 2.1. The same types of preparations found in this study were also reported in several other studies: Dandagi et al., 2008 with three formulations where F1, F2, and F3 show less effect when compared to the standard LIV-52; Gite et al., 2014 reported two formulations, F1 and F2, where F2 preparation has more effectiveness against hepatotoxicity induced in rats when compared to control; Chung et al., 2014 prepared two F1 and F2 formulations where both the preparations are comparable to the standard Hepakhan; and the two F1 and F2 formulations by Kamble et al., 2008 are comparable to the standard drug Silymarin.

On the other hand, no reference drug has been used for the following PHFs such as BV-7310 (Dey et al., 2020)`, DHC-1 (Bafna and Balaraman, 2013), Enliv® (Bhar et al., 2005), F1 and F2 (Gite et al., 2014), HD-03/ES (Anturlikar et al., 2012), HD-03 (Mitra et al., 2000), Superliv Liquid (Nehal and Belal, 2011), Jigrine (Kapur et al., 1994), Livomyn (Kenjale et al., 2011), Mandur Bhasma (Gawate et al., 2016), Prak-20 (Prakash and Mukherjee, 2010), Sarvakalpkwath (Yadav and Kumar, 2014), Rhinax (Dhuley and Naik, 1997), New Livfit® (Gupta et al., 2004), Kamilari (Rajesh and Latha, 2004) and Livex (Venkateswaran et al., 1997).

Fiaz et al., 2017 have formulated the PoHF, a polyherbal formulation comprising of four herbal constituents and tested it on rabbits with paracetamol-induced liver toxicity. In the animal model, paracetamol (2 g/kg) was injected, resulting in elevated blood levels of ALT, AST, ALP, and total bilirubin on the 9^{th} day. The pretreatment of the animal group with PoHF proved to be successful in controlling the hepatotoxicity at the dose of 500 g/kg; on the other hand, the reference drug was comparatively unable to decrease the concentration of ALT, AST, total bilirubin and ALP to a significant level. The efficacy of the polyherbal formulation Hepax was studied by Devaraj and his team (2011) on the hepatotoxic rats. Both the low (100 mg/kg) and high (200 mg/kg) doses of Hepax were able to normalize the elevation of serum biological parameters such as SGPT, SGOT, ALP and total bilirubin with better results when compared to the reference drug. The low doses were reported to

be more effective than the higher ones. Therefore, inhibited the histopathological abnormalities caused by CCl_4.

Sapkota et al., 2017 formulated Arogyavardhini Rasa, consisting of seven herbal constituents, which are mentioned in the table 2.1. The Arogyavardhini Rasa consists of *Terminalia chebula, Terminalia belerica, Phyllanthus emblica, Plumbago zeylanica, Picrorhiza kurroa, Azadirachta indica* and *Commiphora wightii.* In addition to this, they have included calcinated iron, mica, copper and processed product, i.e., processed black bitumen, processed mercury, and processed sulphur.

Dey et al., 2020 have evaluated the medicinal effects of the hepatoprotective BV-7310, which composed of *Tephrosia purpurea, Phyllanthus niruri, Andrographis paniculate,* and *Boerhavia diffusa*. The researchers deduced that it may be advantageous for the management of alcoholic liver disease and other illnesses that might induce liver damage.

Recently in 2021, Triphala (Wei et al., 2021), Liv-Pro-08 (Eswaran et al., 2021) and Arogyavardhini (Rouf et al., 2021) PHFs having the same constituents were re-evaluated and the result suggests that it can be used for the treatment of liver problems.

2.6.3 Clinical trials

This study focused on evaluating the safety and effectiveness of a specific drug called Livwin in patients with acute viral hepatitis. Livwin was tested in a randomised double-blind placebo-controlled clinical trial. The results showed that Livwin had significant effects in improving the recovery of weakness and hepatic markers (serum bilirubin, ALT, and AST) in patients who received Livwin compared to those who received a placebo on different days (Yang, 2020)

2.7 Plant used in polyherbal formulations for hepatoprotective activity

Since the desirable therapeutic effect of a single plant with its bioactive components is insufficient to treat a disease or disorder, the concept of polyherbalism has been developed (Parasuraman et al., 2014). Hundreds and hundreds of plants have been traditionally processed to treat liver disorders worldwide since the dawn of human civilization. In this review, 166 species of plants belonging to 74 families forming 95 PHFs which are used for hepatoprotective effects were documented (Table 2.1). Diversity-wise, Fabaceae is the most dominating family with 17 species. Of the 95 PHFs enlisted, *Picrorrhiza kurroa* (Plantaginaceae) with its roots as the primary ingredient was the most repeated plant species used as one of the ingredients for 26

formulations, followed by the aerial parts of *Andrographis paniculata* (Acanthaceae) and leaves of *Cichorium intybus* (Asteraceae) for 23 and 22 formulations, respectively. Similarly, several bioactive compounds have been isolated, purified and identified from numerous plants to treat liver disorders. The bioactive compounds with hepatoprotective properties obtained from 166 plant species studied so far are listed in the table 2.2.

For instance, Andrographolide (AG), being one of the active constituents of *Andrographis paniculate,* aid in the healing of liver during hepatic diseases. AG, a labdane diterpenoid, has been shown to provide substantial protection against hepatotoxic drugs like CCl_4. It does this by lowering the levels of serum transaminases (GOT and GPT), serum alkaline phosphatase, serum bilirubin, and hepatic triglycerides (Handa and Sharma, 1990). AG is also reported by Trivedi and his team (2007) to have effective cure against severe liver damages. Likewise, Chlorogenic acid (CGA) is a type of phenolic acid present in the seed and leaf of *Apium graveolens,* which possesses potential therapeutic effects in the management of liver problems. The antioxidative action of CGA is accountable for its liver protective activity and comparatively provides better therapeutic protection than silymarin, which is mostly used as a standard drug (Kapil et al., 1995). It has been reported that CGA could partially neutralize the toxicity caused by lipopolysaccharide in many metabolic pathways, which include energy metabolism, amino acid metabolism, and glutathione metabolism (Cheng et al., 2019).

Gallic acid (GA) is a bioactive compound most abundantly found in many plants under the study including *Ricinus communis* (leaf), *Butea monosperma* (leaf and bark) and *Macrotyloma uniflorum* (seed) which is one of the constituents of polyherbal formulations HM (Lal et al., 2007), PTF-1 and PTF-2 (Gupta et al., 2014) and Gluconorm-5 (Gengiah et al., 2014) respectively. GA have been reported to exhibit a free radical scavenging action, antiproliferate effect of cancer, and hepatoprotective activity, and through such properties, it contributes to protect liver damage (Rasool et al., 2010). Followed by GA, bioactive compounds such as rutin (Girish and Pradhan, 2012; Liu et al., 2017) kaempferol (Wang et al., 2015) quercitin (Truong et al., 2016), catechin (Venkatakrishnan et al., 2018) were found abundantly in PHFs used for hepatoprotection.

Berberine (BER), anisoquinoline alkaloid, is one of the major bioactive constituents of *Berberis chitria,* which exhibits hepatoprotective activities by diminishing the negative cause of superoxide dismutase and preventing an amplification of lipid

Table 2.2: List of plant parts and its compound with hepatoprotective activity

Family	Species	Parts used	Compounds with hepatoprotective activity
Acanthaceae	*Adhatoda vasica*	Leaf (Bhattacharyya et al., 2005; Vinothapooshan and Sundar 2010; Kumar et al., 2015)	Vasicine (Roja et al., 2011; Puri et al., 2016) Vasicinone (Roja et al., 2011; Sarkar et al., 2014)
	Andrographis paniculata	Whole plant (Handa and Sharma, 1990; Verma et al.,2013) Arial parts (Mishra et al., 2007)	Andrographolide (Handa and Sharma, 1990; Chander et al., 1995; Maiti et al., 2010; Valan et al., 2010; Shi et al., 2012; Verma et al., 2013; Dey et al 2020) Neoandrographolide (Chander et al., 1995)
	Asteracantha longifolia	Whole plant (Sunita and Abhishek, 2008) Arial parts (Lina et al., 2012; Nigam et al., 2015) Seed (Gupta et al., 2015)	Phytosterol, kurchicine (Gupta and Sharma, 2007; Girish and Pradhan, 2012)
Amaryllidaceae	*Allium sativum*	Bulb (Ajayi et al., 2009; Wu et al., 2011; Guan et al., 2018; Nasir et al., 2020) Oil (Nasir et al., 2020)	Allicin (Vimali and Devaki, 2004) Diallyl sulfide (DAS), Di-allyl disulfide (DADS) and S-methyl-l-cysteine (Shang et al., 2019; Oosthuizen et al., 2017; Azab and Albasha, 2018; Zaidi- et al., 2019)
Annonaceae	*Annona squamosa*	Fruit (TS et al., 2008) Leaf (Rajeshkumar et al., 2015; Sonkar et al., 2016) Seed (Zahid et al 2020)	β-caryophyllene (Cho et al., 2015; Kelany and Abdallah, 2016) Limonene (Amini et al., 2020)
Apiaceae	*Apium graveolens*	Seed (Singh and Handa, 1995; Ahmed et al., 2002; Asadi-Samani et al., 2015) Leaf (Popović et al., 2006; Shivashri et al., 2013)	Apiin, apigenin (Girish and Pradhan, 2012; Yue et al., 2020) Chlorogenic acid (Girish and Pradhan, 2012; Ali et al., 2016; Chen et al., 2019)
	Carum copticum	Seed (Gilani et al., 2005; Adewusi et al., 2010; Kumar et al., 2011)	Ajowan oil (thymol) (Palabiyik et al., 2016; Geyikoglu et al., 2019) Carvacrol (Palabiyik et al., 2016)
	Coriandrum sativum	Leaf (Pandey et al., 2011; Al-Snafi, 2016A) Seed and fruit (Al-Snafi, 2016B)	β-caryophyllene (Cho et al., 2015; Kelany and Abdallah, 2016) Eugenol (Prakash et al 2005; Lister et al., 2019) Linalo-ol (Altınok-Yipel et al., 2019)
	Foeniculum vulgare	Seed (Özbek et al., 2003; Adewusi et al., 2010; Rabeh et al., 2014; Nazir et al., 2020)	Essential oils (Özbek et al., 2003; Priya, 2010; Rather et al., 2016)
	Ferula asafoetida	Gum resin (Dandagi et al., 2008; Bagheri et al., 2018; Sharma et al., 2018)	Ferulic Acid (Rukkumani et al., 2004) Vanillin (Makni et al., 2011; Tiwari et al., 2020)
Apocynaceae	*Alstonia scholaris*	Stem bark (Kumar et al., 2012; Baliga, 2012; Kumar et al., 2014) Fruit (Shankar et al., 2012) Root (Pratyush et al., 2011)	Lupeol (Sunitha et al., 2001; Santiago et al., 2015; Gajapriya et al., 2019) Linalool (Altınok-Yipel et al., 2019) β-Sitosterol (Sujila et al., 2014; Abdou et al., 2019) Betulin (Buko et al., 2020) ursolic acid (Sukla et al., 1992; Gutiérrez-Rebolledo et al., 2016)
	Hemidesmus indicus	Root (Prabakn et al., 2000; Baheti et al., 2006; Ashaa et al., 2011; Murali et al 2012; Banerjee and Ganguly, 2014)	Hyperoside (Girish and Pradhan, 2012) Rutin (Janbaz et al., 2002; Girish and Pradhan, 2012; Domitrović et al., 2012; Liu et al., 2017)
	Holarrhena antidysenterica	Bark (Babar et al., 2009)	Conessine (Kumar and Ali, 2000)

Family	Species	Parts used	Compounds with hepatoprotective activity
Araliaceae	*Panax ginseng*	Rhizome (Kumarpal et al., 2002) Root (Hikino et al., 1985; Murthy et al., 2014)	Ginsenosides (Lee et al., 2005; Murthy et al., 2014; Ren et al., 2019)
	Panax quinquefolius	Root and Flower bud (Yoshikawa et al., 2003)	Dammarane-type triterpene saponins (Yoshikawa et al., 2003) Ginsenosides (Lee et al., 2005; Murthy et al., 2014; Ren et al., 2019)
Aristolochiaceae	*Aristolochia longa*	Rhizome (Samir et al., 2017) Root (Sana, 2020)	Aristolochic acid (Samir et al., 2017)
	Asarum europaeum	Rhizome (Sadati et al., 2016) Root (Bozorgi, 2017; Iqbal and Khan et al., 2019)	α asarone (Prakash, 2017) Quercetin (Gulati et al., 1995; Bhatt et al., 2010; Domitrović et al., 2012; Eftekhari et al., 2018)
Asparagaceae	*Asparagus racemosus*	Root (Kamat et al., 2000; Rahiman et al., 2011; Kumar, 2014; Selvaraj et al., 2019) Whole plant (Kumar et al., 2011)	Flavonoid (Acharya et al., 2012) Quercetin (Gulati et al., 1995; Bhatt et al., 2010; Domitrović et al., 2012; Eftekhari et al., 2018) Rutin (Janbaz et al., 2002; Liu et al., 2017)
Asphodelaceae	*Aloe barbadensis*	Arial parts (Chandan et al., 2007) Leaf (Madhav and Bairy, 2011)	Acemannan (Bhatt et al., 2014; Kumar and Kumar, 2019) Aloe -Emodin (Woo et al., 2002; Dong et al., 2020) Aloin (Cui et al., 2014; Jung and Kim, 2018)
Asteraceae	*Achillea millefolium*	Aerial parts (Yaeesh et al., 2006; Al-Ezzyet al., 2017)	Achilline (Satyavati et al., 1987) 1,8-Cineole (Santos et al., 2004; Murata et al., 2015) Linalool (Altınok-Yipel et al., 2019) β-caryophyllene (Cho et al., 2015; Kelany and Abdallah, 2016)
	Artemisia capillaris	Aerial parts (Zhao et al., 2014; Pereira et al., 2016)	Eupatolin, pilocarpine (Valan et al., 2010; Dey et al., 2013)
	Centaurea behen	Root (Chougule et al., 2012; Fatima et al., 2019)	Not available
	Cichorium intybus	Leaf (kumar et al., 2011; Kumar et al 2011; Jain et al., 2013; Okaiyeto et al., 2018) Seed (Adewusi and Afolayan, 2010) Plant (Kshirsagar et al., 2011)	Sesquiterpenelactones, coumarins (Atmaca et al., 2011; Girish and Pradhan, 2012; Shi et al., 2014), flavonoids (Atmaca et al., 2011; Girish and Pradhan, 2012; Shi et al., 2014)
	Eclipta alba	Leaf (Singh et al., 2001; Lal et al., 2010; Arun and Balasubramanian, 2011; Ramírez and Jiménez, 2019) Root (Lal et al., 2010) Plant juice (Kshirsagar et al., 2011)	Wedelolactone and desmethylwedelolactone (Singh et al., 2001; Dalal et al 2010; Luo et al., 2018)
	Saussurea lappa syn *saussurea costus*	Root (Yaeesh et al., 2010; Ansari et al., 2018; Kadhem, 2019)	Costunolide (Deo and Reddy, 2010; Mao et al., 2018; Ban et al., 2019) Dehydrocos- tus lactone (Deo and Reddy, 2010) Betulinic acid (Jain et al., 2012; Harwansh et al., 2017)
	Silybum marianum	Seed (Madani et al., 2008; Hermenean et al., 2015)	Silymarin (Madani et al., 2008; Girish et al., 2009; Valan et al., 2010; Vargas et al., 2014)
	Wedelia chinensis	Whole plant (Mishra et al., 2009) Leaf (Murugaian et al., 2008)	Isoflavonoids (Kushnerova et al., 2014; Grishchenko et al., 2016) Wedelolactones (Upadhyay et al., 2012; Luo et al., 2018) Nor-wedelolactone (Patel et al., 2009) Limonene (Amini et al., 2020) Apigenin (Zheng et al., 2005; Yue et al., 2020)

Family	Species	Parts used	Compounds with hepatoprotective activity
Begoniaceae	*Begonia laciniata*	Root (Ganapaty et al., 2013; Pushplata et al., 2014)	Not available
Berberidaceae	*Berberis aristata*	Root (Sharma et al., 2004; Singh and Kakkar, 2009; Dehar et al., 2013) Fruit (Gilani and Janbaz,1995) Root, Shoot and Fruit (Komal et al., 2011)	Berberine (Gulfraz et al., 2004; Srivastava et al., 2006; Gupta and Sharma, 2007; Gulfraz et al., 2008; Tripathi and Pushpangadan, 2010; Komal et al., 2011)
	Berberis chitria	Root (Khan et al., 2016; Srivastava et al., 2015) Stem bark (Bera et al., 2011)	Berberine (Gulfraz et al., 2004; Srivastava et al., 2006; Gupta and Sharma, 2007; Gulfraz et al., 2008; Tripathi and Pushpangadan, 2010; Komal et al., 2011)
	Berberis lyceum	Root (Ahmed et al., 2017; Sherani et al., 2019)	Berberine (Gulfraz et al., 2004; Srivastava et al., 2006; Gupta and Sharma, 2007; Gulfraz et al., 2008; Tripathi and Pushpangadan, 2010; Komal et al., 2011)
Bignoniaceae	*Tecomella undulata*	Stem (Rana et al., 2008; Kumar et al., 2011; Jain et al., 2012) Aerial parts (Okaiyeto et al., 2018) Leaf (Singh and Gupta, 2011)	Lapachol (Gupta and Sharma, 2007) Flavonoids (Rana et al., 2008) Betulinic acid (Jain et al., 2012; Harwansh et al., 2017)
Bombycidae	*Bombyx mori*	Fecal matter (Raghavendra et al., 2010) Silkworm excrement powder (Kim et al., 2008)	35 kDa protein (Raghavendra et al., 2010; Xia et al., 2013)
Boraginaceae	*Borago officinalis*	Aerial parts (Hamed and Wahid, 2015) Leaf (Mrudula et al., 2013)	Officinalioside and kaempferol 3-O-β-D-galactopyranoside (Hamed and Wahid, 2015)
	Cordia myxa	Fruit extracts (Al-Snafi, 2016) Leaf (Malik and Ahmad, 2015)	Rutin (Janbaz et al., 2002; Liu et al., 2017) Hesperidin (Ilankeswaran et al., 2011; Tabeshpour et al., 2020) Lutein (Oh et al., 2013)
Brassicaceae	*Cheiranthus cheiri syn Erysimum cheiri*		Not availabe
	Matthiola incana	Aerial parts (Mohammed et al., 2017)	Ferulic Acid (Rukkumani et al., 2004) Protocatechuic acid (El-Sonbaty et al., 2019) Naringenine (Yen et al., 2009; Kapoor and Kakkar, 2014; Den Hartogh and Tsiani, 2019) Vanillic acid (Itoh et al., 2010) Sinapic acid (Shin et al., 2013) Rutin (Janbaz et al., 2002; Domitrović et al., 2012; Liu et al., 2017) Vitexin (Peng et al., 2020; Duan et al., 2020)
	Raphanus sativus	Root (Ahn et al., 2018) Leaf (Syed et al., 2014)	Raphanusanin (Ahn et al., 2018)
Burseraceae	*Commiphora opobalsamum*	Aerial parts (Al-Howiriny et al., 2004; Abbas et al., 2007) Wood, gum and fruit (Shamsi et al., 2014)	Friedelin (Mann et al., 2011; Sunil et al., 2013) Syringic acid (Itoh et al., 2010; Srinivasulu et al., 2018; Sun et al., 2020) Quercetin (Gulati et al., 1995; Bhatt et al., 2010; Domitrović et al., 2012; Eftekhari et al., 2018)
	Commiphora wightii	Oleo gum resin (Singh et al., 2019; Morya et al., 2020)	Guggulsterone (Nafeer and Zalzala, 2019) Eugenol (Prakash et al 2005; Lister et al., 2019) Linalool (Altınok-Yipel et al., 2019) 1,8-Cineole (Santos et al., 2004; Murata et al., 2015) Geraniol (Canbek et al., 2017; Lei et al., 2019)
	Commiphora myrrha	Resin (Ahmad et al., 2015)	β-caryophyllene (Cho et al., 2015; Kelany and Abdallah, 2016) Germacrene D (Vinholes et al., 2014) Camphene (Hachlafi et al., 2021) Citronellal (Liu et al., 2021)

Family	Species	Parts used	Compounds with hepatoprotective activity
Caesalpiniaceae	*Cassia angustifolia*	Leaf and fruit (Shanmugasundram et al., 2010; Gupta et al., 2015; Bellassoued et al., 2019)	Stigmasta-5, 22-dien-3. beta. -ol, (3. beta.,22E)-/stigmasterol (Praveen et al., 2016)
Capparaceae	*Capparis spinosa*	Bark (Aghela et al., 2007) Leaf (Tlili et al., 2017)	p-methoxy benzoic acid (Gadgoli and Mishra, 1999; Tlili et al., 2017)
Caprifoliaceae	*Lonicera japonica*	Flower buds (Yang et al., 2013; Ge et al., 2018)	Japoflavone D (Ge et al., 2018) Caffeic acid (Janbaz et al., 2004; Yang et al., 2013)
	Nardostachys jatamansi	Rhizome (Ali et al., 2000; Dandagi et al., 2008; Purnima and Kothiyal, 2015) Root (Iqbal and Khan et al., 2019)	Not available
Coccidae	*Coccus lacca*	Secretion by leaves insect (Shakya and Shukla, 2011; Shakya et al., 2012)	Not available
Combretaceae	*Terminalia arjuna*	Bark (Manna et al., 2006; Adewusi et al., 2010; Doorika and Ananthi, 2012; Haidry and Malik, 2014)	Arjunin, arjunetin, tannins (Manna et al., 2006)
	Terminalia bellerica	Fuits (Anand et al., 1994) Aerial parts (Rashed et al., 2014)	3,4,5-trihydroxybenzoic acid (Satyavati et al., 1987; Anand et al., 1997; Jadon et al., 2007)
	Terminalia chebula	Fruit (Anand et al., 1994; Tasduq et al., 2006; Jain et al., 2008; Nishanth et al., 2014)	Glucoside, tannin, tannic acid (Gupta and Sharma, 2007; Haque et al., 2011)
Convolvulaceae	*Argyreia speciosa*	Root (Habbu et al., 2008; Galani et al., 2010)	Quercetin (Gulati et al., 1995; Bhatt et al., 2010; Domitrović et al., 2012; Eftekhari et al., 2018) Caffeic acid (Janbaz et al., 2004; Yang et al., 2013) Coumarin (Atmaca et al., 2011; Girish and Pradhan; Shi et al., 2014)
	Ipomoea turpethum	Root (Kohli et al., 2010; Gupta et al., 2015; Shah et al., 2017) Stem (Chumbhale, 2011) Aerial parts (Gupta and Ved, 2017)	Operculinosides A-D (Gupta and Ved, 2017)
	Operculina turpethum	Root (Ahmad et al., 2009; Arka et al., 2015; Ahmad et al., 2017)	Turpethein, a-turpethein and b-turpethein (Girish, 2009; Gupta and Ved, 2017)
Cucurbitaceae	*Coccinia indica*	Fruit (Rao et al., 2003 Vazir and Asdaq, 2005; Deokate and Khadabadi, 2011)	Rutin (Janbaz et al., 2002; Domitrović et al., 2012; Liu et al., 2017) Naringenine (Yen et al., 2009; Kapoor and Kakkar, 2014; Den Hartogh and Tsiani, 2019) Apigenin (Zeng et al., 2005; Yue et al., 2020) Kaempferol (Wang et al., 2015)
	Luffa echinata	Fruit (Ahmed et al., 2001; Kamble et al., 2008; Kumar et al., 2012; Modi and Kumar, 2014; Alam et al., 2016)	Cucurbitacin, elaterine-2-glycoside, chrysirol and β-chrysoeriol -7- aploglucosid (Modi, and Kumar, 2014)
	Momordica charantia	Fruit (Chumbhale, 2011; Hossain et al., 2011; Zahra et al., 2012) Leaf (Jain et al., 2008; BP et al., 2009; Mada et al., 2014))	Cucurbitane Triterpenoids (Haque et al., 2011; Hussain et al., 2014) Tannic acid (Gupta and Sharma, 2007; Haque et al., 2011)
	Trichosanthes dioica	Leaf (Kumar et al., 2009; Kumar et al., 2012; Awoal et al., 2018)	Cucurbitacin (Kumar et al., 2012)

Family	Species	Parts used	Compounds with hepatoprotective activity
Cuscutaceae	*Cuscuta epithymum*	Aerial parts (Jafarian et al., 2014; Ahmad et al., 2017) Whole plant (Ganapaty et al., 2013)	Quercetin (Gulati et al., 1995; Bhatt et al., 2010; Domitrović et al., 2012; Eftekhari et al., 2018; Eftekhari et al., 2018)
	Cuscuta reflexa	Seed (Ahmad et al., 2002; Najmi et al., 2005; Shakya et al., 2012) Whole plant (Amaresh et al., 2014)	Gallic acid (Siddiqui et al., 2017; Pujari et al., 2020) Vanillic acid (Itoh et al., 2010)
Cycadaceae	*Cycas circinalis*	Flower (Sankar et al., 2015; Ramírez and Jiménez, 2019)	Naringenine (Yen et al., 2009; Kapoor and Kakkar, 2014; Den Hartogh and Tsiani, 2019)
Cyperaceae	*Cyperus rotundus*	Rhizome (Kumar and Mishra, 2005; Arsul et al., 2011; Parvez et al., 2019) Aerial parts (Awaad et al., 2012)	Nootkatone (Kudi, 2016; Kurdi et al., 2018) Anthocyanidins (Hou et al., 2013; Wang et al., 2017) Isoflavones (Alipour and Karimi-Sales, 2020) Eugenol (Lister et al., 2019; Sharma et al., 2019) Limonene (Amini et al., 2020) α-Copaene (Turkez et al., 2014)
	Cyperus scariosus	Tuber (Gilani and Janbaz,1995; Kumar et al., 2017) Root (Chawda et al., 2014)	Limonene (Amini et al., 2020) β-caryophyllene (Cho et al., 2015; Kelany and Abdallah, 2016) Germacrene D (Vinholes et al., 2014) α-Copaene (Turkez et al., 2014) Myrtenal (Rathinam et al., 2014; Ayyasamy and Leelavinothan, 2016)
Euphorbiaceae	*Baliospermum montanum*	Root (Mali and Wadekar, 2008; Wadekar et al., 2008; Govind, 2011; Verma, 2018; Ahirwar and Ahirwar, 2019)	Not available
	Euphorbia hirta	Root (Anitha and Mythili, 2017) Whole plant (Tiwari et al., 2011) Whole plant (Dubay and Mehta, 2014)	Quercitrin (Rajeswary et al., 2011; Truong et al., 2016) Gallic acid (Siddiqui et al., 2017; Pujari et al., 2020) Myricitrin (Domitrović et al., 2015; Omidi et al., 2020) β-Amyrin (Oliveira et al., 2005; Nogueira et al., 2019) β-Sitosterol (Sujila et al., 2014; Abdou et al., 2019)
	Ricinus communis	Leaf (Visen et al., 1992; Chumbhale, 2011; Babu et al., 2017)	Ricinine (Xiao and Duan, 2006; Oriakhi et al., 2020) Kaempferol (Wang et al., 2015) Quercitrin (Rajeswary et al., 2011; Truong et al., 2016) 8-cineole/eucalyptol (Bhowal and Gopal, 2015; Patra et al., 2020) β-caryophyllene (Cho et al., 2015; Kelany and Abdallah, 2016) Gallic acid (Siddiqui et al., 2017; Pujari et al., 2020) Gentisic acid (Pujari et al., 2020) Rutin (Girish and Pradhan, 2012; Liu et al., 2017) Epicatechin (Singha et al., 2012; Shanmugam et al., 2017) Ellagic acid (Girish and Pradhan, 2012; Afifi et al., 2018)

Family	Species	Parts used	Compounds with hepatoprotective activity
Fabaceae	*Acacia catechu*	Hard wood (Jayasekhar et al., 1997) Powdered pale catechu (Hiraganahalli et al., 2012; Verma, 2018)	Catechin (Ryle et al., 1983; Venkatakrishnan et al., 2018) Epicatechin (Singha et al., 2012; Shanmugam et al., 2017) Protocatechuic acid (El-Sonbaty et al., 2019) Kaempferol (Wang et al., 2015) Quercitrin (Rajeswary et al., 2011; Truong et al., 2016)
	Butea monosperma	Flower (Ahmad et al., 2010; Sharma and Shukla, 2011) Bark (Tiwari et al., 2011; Kaur et al., 2017)	Butein (Semwal et al., 2005; Alshammari et al., 2018) Chalcones (Singh et al., 2016; Karimi-Sales et al., 2018) Gallic acid (Siddiqui et al., 2017; Pujari et al., 2020) Butrin (Wagner et al., 1986) Cyanidin-3-glucoside (Park et al., 2017; Yu et al., 2020)
	Bauhinia variegata	Bark (Bodakhe and Ram, 2007; Chaturvedi et al., 2011) Root (Bodakhe and Ram, 2007)	β-Sitosterol (Sujila et al., 2014; Abdou et al., 2019)
	Cassia fistula	Leaf (Bhakta et al., 1999; Bhakta et al., 2001; Jehangir et al., 2010) Seed (NB et al., 2009; Kumar et al., 2011)	Sennosides A and B, , barbaloin, aloin (Pradeep et al., 2005) Rhein (Pradeep et al., 2005; Bu et al., 2018)
	Cassia occidentalis	Leaf (Jafri et al., 1999; Najmi et al., 2005; Uzzi and Grillo, 2013)	Emodin, physcion, chrysophanol, sitosterol and xanthonecassiolin (Girish, 2009)
	Clitoria ternatea	Leaf (Shanmugasundram et al., 2010; Nithianantham et al., 2011; Jayachitra et al., 2012)	Kaempferol (Wang et al., 2015) Quercitrin (Rajeswary et al., 2011; Truong et al., 2016) Myricetin (Semwal et al., 2016; Lv et al., 2020) β-Sitosterol (Sujila et al., 2014; Abdou et al., 2019) Essential oil (Girish 2009)
	Glycyrrhiza glabra	Root (Kshirsagar et al., 2011, Verma, 2018; Maksoud et al., 2019)	Glycrrhizin and Glycyrrhetinic acid (Rossum and Man,1998; Valan et al., 2010)
	Indigofera tinctoria	Aerial parts (Singh et al., 2001; Chumbhale, 2011) Whole plant (Sreepriya and Devaki, et al., 2001)	Indigtone (Singh et al., 2001; Renganathan, 2009) Indirubin (Varela et al., 2010; Jai et al., 2017) Ferulic Acid (Rukkumani et al., 2004) Sinapic (Shin et al., 2013) Vanillic acid (Itoh et al., 2010) 4-hydroxyphenylacetic acids (Zhao et al., 2018) Vicenin-2 (Lee and Bae, 2020) Chlorogenic acid (Ali et al., 2016; Chen et al., 2019) Caffeic acid (Janbaz et al., 2004; Yang et al., 2013)
	Macrotyloma uniflorum	Seed (Das et al., 2014; Panda et al., 2015; Ramasamy et al., 2017)	Cyanidin 3-glucoside (Park et al., 2017; Zafra et al., 2020; Yu et al., 2020) Daidzein (Choi and Kim, 2009; wang et al., 2016) Genistein (Li et al., 2016; Ganai and Husain, 2017) Kaempferol (Wang et al., 2015) Quercitrin (Rajeswary et al., 2011; Truong et al., 2016) Myricetin (Semwal et al., 2016; Lv et al., 2020) Gallic acid (Siddiqui et al., 2017; Pujari et al., 2020) Protocatechuic acid (El-Sonbaty et al., 2019) Syringic acid (Itoh et al., 2010; Srinivasulu et al., 2018; Sun et al., 2020) Vanillic acid (Itoh et al., 2010) Caffeic acid (Janbaz et al., 2004; Yang et al., 2013) Chlorogenic acid (Ali et al., 2016; Chen et al., 2019) Ferulic Acid (Rukkumani et al., 2004) Sinapic acid (Shin et al., 2013)
	Mucuna pruriens	Leaf (Obogwu et al., 2014; Ibeh et al., 2020) Root (Mujeeb et al., 2010)	β-Sitosterol (Sujila et al., 2014; Abdou et al., 2019) Nicotine (Tupe et al., 2011)
	Pongamia pinnata	Root and seed (Govind, 2011) Flower (Chelvan et al., 2008; Anuradha, 2011) Leaf (Behera et al., 2012, Essa and Subramanian, 2008) Bark (Kaur et al., 2014)	Kaempferol (Wang et al., 2015) Quercitrin (Rajeswary et al., 2011; Truong et al., 2016) Isoquercitrin (Xie et al., 2016; Huang et al., 2017) Rutin (Janbaz et al., 2002; Girish and Pradhan, 2012; Domitrović et al., 2012; Liu et al., 2017) Vicenin-2 (Lee and Bae, 2020) α-cadinol (Tung et al., 2011; Sriramavaratharajan et al., 2016) Lupeol (Sunitha et al., 2001; Santiago et al., 2015; Gajapriya et al., 2019) Betulinic acid (Jain et al., 2012; Harwansh et al., 2017) β-Sitosterol (Sujila et al., 2014; Abdou et al., 2019)

Family	Species	Parts used	Compounds with hepatoprotective activity
Gentianaceae	*Gentiana olivieri*	Aerial parts (Aktay ey al, 2000; Orhan et al., 2003)	Gentiopicroside (Tang et al., 2016; Han et al., 2018) Isoorientin (Lin et al., 2015; Yuan et al., 2016; Fan et al., 2018)
	Swertia chirayita	Whole plant (Verma et al., 2013; Mahmood et al., 2014) Aerial parts (Nagalekshmi et al., 2011)	Isoorientin (Lin et al., 2015; Yuan et al., 2016; Fan et al., 2018) Mangiferin (Jain et al., 2013; Imran et al., 2017) Sweroside (Hase et al., 1997; Yang et al., 2016) Swertiamarin (Jaishree and Badami, 2010; Allum et al., 2015; Wu et al., 2017) Swerchirin (Sadegi et al., 2006; Zeng et al., 2014) Amarogentin (Zhang et al., 2017; Zhang et al., 2018) Oleanolic acid (Jeong, 1999; Gutiérrez-Rebolledo et al., 2016) Ursolic acid (Liang et al., 2008) β-amyrin (Oliveira et al., 2005; Nogueira et al., 2019)
Hypoxidaceae	*Curculigo orchioides*	Rhizome (Venukumar and Latha, 2002; Govind, 2011; Kumar and Shukla, 2019)	Curculigenin Syringic acid (Itoh et al., 2010; Srinivasulu et al., 2018; Sun et al., 2020)
Iridaceae	*Crocus sativus*	Petal (Omidi et al., 2014; Riaz et al., 2016) Stigma and style (Shamsi et al., 2014; Iqbal and Khan et al., 2019)	Crocin (Chen et al., 2016; Morya et al., 2020) Safranal (Ozkececi et al., 2016; Alayunt et al., 2019)
	Iris ensata	Root (Govind, 2011; Sharma et al., 2014; Khan et al., 2015; Iqbal and Khan et al., 2019)	Not available
Lamiaceae	*Lallemantia royleana*	Seed (Kazim et al., 2012; Al-Barram, and Al-Asady, 2017; Al-Snafi, 2019)	Not available
	Lavandula stoechas	Aerial parts (Selmi et al., 2015; Miraj et al., 2016)	Limonene (Amini et al., 2020) Essential oil (Miraj, 2016) Eucalyptol (Bhowal and Gopal, 2015; Patra et al., 2020) Thymol (Palabiyik et al., 2016; Geyikoglu et al., 2019)
	Leonurus cardiaca	Aerial parts (Pereira et al., 2019)	Ursolic acid (Liang et al., 2008; Sukla et al., 1992; Gutiérrez-Rebolledo et al., 2016) Oleanolic acid (Liang et al., 2008; Patil et al., 2010; Ibrahim et al., 2011; Lodh and Swamy, 2019) Corosolic acid (Al-Assaf, 2013; Balakrishnan and Al Assaf, 2016) Syringic acid (Itoh et al., 2010; Srinivasulu et al., 2018; Sun et al., 2020) Kaempferol (Wang et al., 2015) Quercitrin (Rajeswary et al., 2011; Truong et al., 2016) Isoquercitrin (Xie et al., 2016; Huang et al., 2017) Rutin (Janbaz et al., 2002; Girish and Pradhan, 2012; Domitrović et al., 2012; Liu et al., 2017)
	Melissa parviflora	Leaf (Adhikari, 2007; Chhetri et al., 2008; Sharma et al., 2014)	Caffeic acid (Janbaz et al., 2004; Yang et al., 2013) Rosmarinic acid (Yang et al., 2013; Lin et al., 2017; Elufioye and Habtemariam, 2019) Ferulic Acid (Rukkumani et al., 2004)
	Ocimum gratissimum	Leaf (Arhoghro et al 2009; Iweala, 2012; Gupta et al., 2013; Awogbindin et al.,2014)	Eugenol (Prakash et al 2005; Lister et al., 2019) Thymol (Palabiyik et al., 2016; Geyikoglu et al., 2019) Linalool (Altınok-Yipel et al., 2019) 1,8-Cineole (Santos et al., 2004; Murata et al., 2015) Oleanolic acid (Liang et al., 2008; Patil et al., 2010; Ibrahim et al., 2011; Lodh and Swamy, 2019) Citral (Uchida et al., 2017; Li et al., 2018)
	Salvia haematodes	Root (Akhtar et al., 2013; Hussain and Kadibagil, 2019))	Not available
	Vitex negundo	Seed (Avadhoot and Rana, 1991) Whole shrub (Najmi et al., 2005; Govind, 2011) Flower and leaf (Sharma et al., 2014)	β-caryophyllene (Cho et al., 2015; Kelany and Abdallah, 2016) 8-cineole/eucalyptol (Bhowal and Gopal, 2015; Patra et al., 2020) Linalool (Altınok-Yipel et al., 2019) Eugenol (Prakash et al 2005; Lister et al., 2019) Limonene (Amini et al., 2020) 1,8-Cineole (Santos et al., 2004; Murata et al., 2015) Dihydromyrcenol (Bayram et al., 2011)

Family	Species	Parts used	Compounds with hepatoprotective activity
Lauraceae	*Cinnamomum cassia*	Stembark (Bansode, 2012; Shamsi et al., 2014; Iqbal and Khan et al., 2019)	Cinnamaldehyde (Zahran et al., 2016; Kumar and Pandey, 2018)
	Cinnamomum zeylanicum	Stembark (Moselhy and Ali, 2009; Eidi et al., 2012; Shamsi et al., 2014)	Cinnamaldehyde (Zahran et al., 2016; Kumar and Pandey, 2018) α-Copaene (Turkez et al., 2014) α-cadinol (Tung et al., 2011; Sriramavaratharajan et al., 2016) Stigmasterol (Praveen et al., 2016)
	Cinnamomum tamala	Leaves (Qureshi, 2015; Dodda et al., 2020)	Copaene (Turkez et al., 2014)
Lecythidaceae	*Careya arborea*	Fruit (Najmi et al., 2005) Bark (Senthikumar et al., 2008; Islam et al., 2018)	Gallic acid (Siddiqui et al., 2017; Pujari et al., 2020) Kaempferol (Wang et al., 2015) Quercitrin (Rajeswary et al., 2011; Truong et al., 2016)
Liliaceae	*Lilium longiflorum*	Bulb (Tang et al., 2015, Lu et al., 2017)	Not available
Malvaceae	*Sida cordifolia*	Root (Rejitha et al., 2012; Khurana et al., 2016; Morya et al., 2020) Whole plant (Kotoky and Das, 2000)	Fumaric acid (Girish 2009; Valan et al., 2010) Vasicinone (Roja et al., 2011; Sarkar et al., 2014)
	Thespesia populnea	Heart wood and Leaf (Sharma et al., 2014) Leaf, flower and stem bark (Ilavarasan et al., 2003; Yuvaraj and Subramoniam, 2009)	Gallic acid (Siddiqui et al., 2017; Pujari et al., 2020) Catechin (Tsuchiya, 1999; Liu et al., 2015; Venkatakrishnan et al., 2018) Myricetin (Semwal et al., 2016; Lv et al., 2020) Protocatechuic acid (El-Sonbaty et al., 2019) Epigallocatechin galate (Gupta and Sharma, 2007; Bhatt et al., 2010) Rosmarinic acid (Yang et al., 2013; Lin et al., 2017; Elufioye and Habtemariam, 2019) Ellagic acid (Girish and Pradhan, 2012; Afifi et al., 2018) Rutin (Janbaz et al., 2002; Girish and Pradhan, 2012; Domitrović et al., 2012; Liu et al., 2017) Naringenine (Yen et al., 2009; Kapoor and Kakkar, 2014; Den Hartogh and Tsiani, 2019) Quercetin (Gulati et al., 1995; Bhatt et al., 2010; Domitrović et al., 2012; Eftekhari et al., 2018) Apigenin (Girish and Pradhan, 2012; Yue et al., 2020) Coumarin (Atmaca et al., 2011; Girish and Pradhan, 2012; Shi et al., 2014)
Marasmiaceae	*Lentinus edodes*	Fruiting bodies (Sasidharan et al., 2010; Bisen et al., 2010; Nisar et al., 2017)	Lentinan (Bisen et al., 2010)
Melastomataceae	*Artermesia absinthium*	Aerial parts (Amat et al., 2010; Mohammadian et al., 2016) Leaf (Gilani and Janbaz, 1995; Adewusi and Afolayan, 2010)	Guaiazulene (Kourounakis et al., 1997) Linalool (Altınok-Yipel et al., 2019) 1,8-Cineole (Santos et al., 2004; Murata et al., 2015) Eugenol (Lister et al., 2019; Sharma et al., 2019) Geraniol (Canbek et al., 2017; Lei et al., 2019) Cardamonin (Xu et al., 2020; Yu et al., 2011) Coumarin (Atmaca et al., 2011; Girish and Pradhan; Shi et al., 2014) Chlorogenic acid (Girish and Pradhan, 2012; Ali et al., 2016; Chen et al., 2019) Ferulic Acid (Rukkumani et al., 2004) Gallic acid (Siddiqui et al., 2017; Pujari et al., 2020) Caffeic acid (Janbaz et al., 2004; Yang et al., 2013) Rosmarinic acid (Yang et al., 2013; Lin et al., 2017; Elufioye and Habtemariam, 2019) Tannic acid (Gupta and Sharma, 2007; Haque et al., 2011) Syringic acid (Itoh et al., 2010; Srinivasulu et al., 2018; Sun et al., 2020) Vanillic acid (Itoh et al., 2010)
	Osbeckia octandra	Leaf (Thabrew et al., 1995a; Thabrew et al., 1995b)	Not available

Family	Species	Parts used	Compounds with hepatoprotective activity
Meliaceae	*Azadirachta indica*	Leaf (Chattopadhyay et al.,1992; Kale et al., 2003; Chattopadhyay, 2003; Chattopadhyay et al., 2005; Sani et al., 2020) Aerial parts (Morya et al., 2020) Bark (Gomase et al., 2011)	Quercitrin (Gulati et al., 1995; Bhatt et al., 2010; Rajeswary et al., 2011; Domitrović et al., 2012; Memariani et al., 2015; Eftekhari et al., 2018; Zafra et al., 2020) Rutin (Janbaz et al., 2002; Girish and Pradhan, 2012; Domitrović et al., 2012; Liu et al., 2017), nimbidin, neem oil (Rajeswary et al., 2011)
	Aphanamixis polystachya	Leaf (Mishra et al., 2014; Snigdha et al., 2016) Bark (Valan et al., 2014)	Stigmasterol (Praveen et al., 2016)
	Naregamia alata	Root (Saravanan, 2004; Sharma et al., 2014) Stem and leaf (Sharma et al., 2014) Aerial parts (Undarathi, 2017)	β-Sitosterol (Sujila et al., 2014; Abdou et al., 2019)
Menispermaceae	*Cissampelos pereira*	Roots (Surendran et al., 2011)	Nuciferine (Guo et al., 2013; Shu et al., 2019) Berberine (Gulfraz et al., 2004; Srivastava et al., 2006; Gupta and Sharma, 2007; Gulfraz et al., 2008; Tripathi and Pushpangadan, 2010; Komal et al., 2011) Thymol (Palabiyik et al., 2016; Geyikoglu et al., 2019) Quercitrin (Gulati et al., 1995; Bhatt et al., 2010; Rajeswary et al., 2011; Domitrović et al., 2012; Memariani et al., 2015; Eftekhari et al., 2018; Zafra et al., 2020)
	Tinospora cordifolia	Leaf, stem and root (Kavitha et al., 2011; Singh et al., 2019) Stem (Kshirsagar et al., 2011, Singh et al., 2015)	Giloin, gilenin, gilosterol (Bishayi et al., 2002)
Moraceae	*Ficus bengalensis*	Bark (Baheti and Goyal, 2011) Leaf (Shinde et al., 2012; Parameswari et al., 2013) Latex (Kumar et al., 2019)	Rutin (Janbaz et al., 2002; Girish and Pradhan, 2012; Domitrović et al., 2012; Liu et al., 2017) Friedelin (Mann et al., 2011; Sunil et al., 2013) Syringic acid (Itoh et al., 2010; Srinivasulu et al., 2018; Sun et al., 2020) Lupeol (Sunitha et al., 2001; Santiago et al., 2015; Gajapriya et al., 2019) Coumarins (Atmaca et al., 2011; Girish and Pradhan, 2012; Shi et al., 2014)
	Ficus glomerata synonym *Ficus racemosa*	Fruit (Eswaran et al., 2021)	Taraxasterol (Xu et al., 2018) Friedelin (Mann et al., 2011; Sunil et al., 2013)
Myrsinaceae	*Embelia ribes*	Leaf and Root (Jain et al., 2013; Gupta et al., 2015) Fruit (Tabassum and Agrawal, 2003; Govind, 2011; Mahendran et al., 2011)	Embelin (Girish ,2009; Mahendran et al., 2011; Li et al., 2019) Caffeic acid (Janbaz et al., 2004; Yang et al., 2013) Vanillic acid (Itoh et al., 2010)
Myrtaceae	*Eugenia caryophyllus*	Cloves buds (Khalaf et al., 2008)	Eugenol (Prakash et al 2005; Lister et al., 2019) β-caryophyllene (Cho et al., 2015; Kelany and Abdallah, 2016) Vanillin (Makni et al., 2011; Tiwari et al., 2020) Kaempferol (Wang et al., 2015) Oleanolic acid (Liang et al., 2008; Patil et al., 2010; Ibrahim et al., 2011; Lodh and Swamy, 2019) Stigmasterol (Praveen et al., 2016)
	Syzygium aromaticum	Bud (Abdel-Rahman and El-Megeid, 2006; Prasad et al., 2010; Kazi et al., 2016; Hadary and Hassanien, 2016; Morya et al., 2020)	Eugenol (Prakash et al 2005; Lister et al., 2019) β-caryophyllene (Cho et al., 2015; Kelany and Abdallah, 2016) Vanillin (Makni et al., 2011; Tiwari et al., 2020) Kaempferol (Wang et al., 2015) Oleanolic acid (Liang et al., 2008; Patil et al., 2010; Ibrahim et al., 2011; Lodh and Swamy, 2019) Stigmasterol (Praveen et al., 2016) α-Copaene (Turkez et al., 2014)

Family	Species	Parts used	Compounds with hepatoprotective activity
Nitrariaceae	*Peganum harmala*	Whole plant (Sharma et al., 2014) Seed (Mankani et al., 2005; Sharma et al., 2014; Bourogaa et al., 2015)	Vasicine (Roja et al., 2011; Puri et al., 2016) Vasicinone (Roja et al., 2011; Sarkar et al., 2014)
Nyctaginaceae	*Boerhaavia diffusa*	Root (Rawat et al., 1997; Kumar et al., 2011; Kshirsagar et al., 2011; Iqbal and Khan et al., 2019)	Punarnavine (Gupta and Sharma, 2007; Kumar et al., 2012) Ursolic acid (Liang et al., 2008; Sukla et al., 1992; Gutiérrez-Rebolledo et al., 2016)
Nymphaeaceae	*Nymphaea alba*	Flower (Paharia and Pandurangan, 2013; Bakr et al., 2017; Nasiruddin et al., 2018) Rhizome and leaf (Bakr et al., 2017)	Apigenin (Zheng et al., 2005; Yue et al., 2020) Kaempferol (Wang et al., 2015) Quercitrin (Gulati et al., 1995; Bhatt et al., 2010; Rajeswary et al., 2011; Domitrović et al., 2012; Memariani et al., 2015; Eftekhari et al., 2018; Zafra et al., 2020) Naringenine (Yen et al., 2009; Kapoor and Kakkar, 2014; Den Hartogh and Tsiani, 2019) Caffeic acid (Janbaz et al., 2004; Yang et al., 2013) Catechin (Ryle et al., 1983; Venkatakrishnan et al., 2018) Epicatechin (Singha et al., 2012; Shanmugam et al., 2017) Vanillic acid (Itoh et al., 2010) Tannic acid (Gupta and Sharma, 2007; Haque et al., 2011) Gallic acid (Siddiqui et al., 2017; Pujari et al., 2020) Ferulic Acid (Rukkumani et al., 2004) Ellagic acid (Girish and Pradhan, 2012; Afifi et al., 2018) Rutin (Janbaz et al., 2002; Girish and Pradhan, 2012; Domitrović et al., 2012; Liu et al., 2017)
Orchidaceae	*Dendrobium ovatum*	Whole plant (Ganapaty et al., 2013)	Not available
	Orchis mascula	Seed (Sankar et al., 2015; Mangwani et al., 2019)	Gallic acid (Siddiqui et al., 2017; Pujari et al., 2020) Catechin (Ryle et al., 1983; Venkatakrishnan et al., 2018) Syringic acid (Itoh et al., 2010; Srinivasulu et al., 2018; Sun et al., 2020)
Paeoniaceae	*Paeonia emodi*	Tuber (Kshirsagar et al., 2011) Rhizome (Ilahi et al., 2016; Zeb, 2018)	Paeonol (Gong et al., 2017; Jing et al., 2019; Adki and Kulkarni, 2020) Eugenol (Prakash et al 2005; Lister et al., 2019) Carvacrol (Palabiyik et al., 2016) Thymol (Palabiyik et al., 2016; Geyikoglu et al., 2019) Gallic acid (Siddiqui et al., 2017; Pujari et al., 2020) 1,8-Cineole (Santos et al., 2004; Murata et al., 2015) Syringic acid (Itoh et al., 2010; Srinivasulu et al., 2018; Sun et al., 2020) Lupeol (Sunitha et al., 2001; Santiago et al., 2015; Gajapriya et al., 2019) β-Amyrin (Oliveira et al., 2005; Nogueira et al., 2019)
Papaveraceae	*Fumaria officinalis*	Aerial parts (Udya Raj 2012; Morya et al., 2020) Whole plant (Sharma et al., 2014)	Fumarine (Girish, 2009) Chlorogenic acid (Girish and Pradhan, 2012; Ali et al., 2016; Chen et al., 2019) Caffeic acid (Janbaz et al., 2004; Yang et al., 2013) Fumaric acid (Girish 2009; Valan et al., 2010) Myricetin (Semwal et al., 2016; Lv et al., 2020) Kaempferol (Wang et al., 2015) Quercitrin (Gulati et al., 1995; Bhatt et al., 2010; Rajeswary et al., 2011; Domitrović et al., 2012; Memariani et al., 2015; Eftekhari et al., 2018; Zafra et al., 2020) Apigenin (Zheng et al., 2005; Yue et al., 2020) Ferulic Acid (Rukkumani et al., 2004) Sinapic acid (Shin et al., 2013)
	Fumaria parviflora	Whole plant (Tripathi et al., 2010) Aerial parts (Alqasoumi et al., 2009; Kshirsagar et al., 2011) Leaf (Khan and Iqbal, 2017)	Caffeic acid (Janbaz et al., 2004; Yang et al., 2013) Protocatechuic acid (El-Sonbaty et al., 2019) Stigmasterol (Praveen et al., 2016) β-Sitosterol (Sujila et al., 2014; Abdou et al., 2019) Berberine (Gulfraz et al., 2004; Srivastava et al., 2006; Gupta and Sharma, 2007; Gulfraz et al., 2008; Tripathi and Pushpangadan, 2010; Komal et al., 2011)

Family	Species	Parts used	Compounds with hepatoprotective activity
Phyllanthaceae	*Emblica officinalis*	Fruits (Jose and Kuttan, 2000; Achliya et al., 2004; Govind, 2011; Thilakchand et al., 2013)	Gallic acid (Siddiqui et al., 2017; Pujari et al., 2020) Apigenin (Zheng et al., 2005; Yue et al., 2020) Ellagic acid (Girish and Pradhan, 2012; Afifi et al., 2018) Quercitrin (Gulati et al., 1995; Bhatt et al., 2010; Rajeswary et al., 2011; Domitrović et al., 2012; Memariani et al., 2015; Eftekhari et al., 2018; Zafra et al., 2020) Corilagin (Liu et al., 2017; Li et al., 2018)
	Phyllanthus amarus	Aerial parts (Krithika et al., 2009) Whole plants (Sankar et al., 2015; Ramírez and Jiménez, 2019)	Geraniin (Aayadi et al., 2017; Moorthy et al., 2019) Corilagin (Liu et al., 2017; Li et al., 2018) Rutin (Janbaz et al., 2002; Girish and Pradhan, 2012; Domitrović et al., 2012; Liu et al., 2017) Gallic acid (Siddiqui et al., 2017; Pujari et al., 2020) Ellagic acid (Girish and Pradhan, 2012; Afifi et al., 2018) Phyllanthin and Hypophyllanthin (Ravikumar et al., 2011; Sethiya et al., 2015) Catechin (Ryle et al., 1983; Venkatakrishnan et al., 2018) Epigallocatechin galate (Gupta and Sharma, 2007; Bhatt et al., 2010)
	Phyllanthus emblica	Fruit (Shamsi et al., 2014; Huang et al., 2017; Abbas et al., 2017; Morya et al., 2020) Bark (Chaphalkar et al., 2017)	Tannin (Girish, 2009) Sesamin (Ma et al., 2014; Lv et al., 2015) Quercetin (Gulati et al., 1995; Bhatt et al., 2010; Domitrović et al., 2012; Memariani et al., 2015; Eftekhari et al., 2018; Zafra et al., 2020) Ellagic acid (Girish and Pradhan, 2012; Afifi et al., 2018) Kaempferol (Wang et al., 2015) β-Amyrin (Oliveira et al., 2005; Nogueira et al., 2019) β-Sitosterol (Sujila et al., 2014; Abdou et al., 2019)
	Phyllanthus niruri	Leaf (Harish and Shivanandappa, 2006; Kumar et al., 2011; Verma, 2018) Fruit (Harish and Shivanandappa, 2006)	Phyllanthin and Hypophyllanthin (Ravikumar et al., 2011; Sethiya et al., 2015) Hypophyllanthin Nirtetralin and Phyltetralin (Ravikumar et al., 2011) Coumarins (Atmaca et al., 2011; Girish and Pradhan, 2012; Shi et al., 2014) Cyanidin-3-glucoside (Park et al., 2017; Yu et al., 2020) Chlorogenic acid (Ali et al., 2016; Chen et al., 2019) Myricetin (Semwal et al., 2016; Lv et al., 2020)
Pinaceae	*Pinius succinifera*	Amber (Sankar et al., 2015; Ramírez and Jiménez, 2019)	Not available
Piperaceae	*Piper longum*	Fruits (Patel, 2009; Joseph et al., 2014; Verma, 2018; Morya et al., 2020) Root (Patel, 2009: Sharma et al., 2014)	Piperine (Sabina et al., 2010; Gorgani et al., 2017) Piplartine (Rajeswary et al., 2011) Sesamin (Ma et al., 2014; Lv et al., 2015) β-Sitosterol (Sujila et al., 2014; Abdou et al., 2019)
	Piper nigrum	Fruiting stalk (Sharma etal, 2014) Root (Bai et al., 2011) Fruit (Nirwane and Bapat, 2012)	Piperine (Sabina et al., 2010; Gorgani et al., 2017) Vanillic acid (Itoh et al., 2010) Chlorogenic acid (Ali et al., 2016; Chen et al., 2019)
	Piper retrofractum	Root and Stem (Mahaldar et al., 2019) Fruit (Kim et al., 2011)	Piperine (Sabina et al., 2010; Gorgani et al., 2017) Pipernonaline, dehydropipernonaline (Morikawa et al., 2004; Matsuda et al., 2009; Kim et al., 2011) Linalool (Altınok-Yipel et al., 2019)

Family	Species	Parts used	Compounds with hepatoprotective activity
Plantaginaceae	*Bacopa monnieri*	Leaf and shoot (Sharma et al., 2014) Aerial parts (Ghosh et al., 2007; Gudipati et al., 2012) Whole plant (Menon et al., 2010)	Bacoside-A (Sumathi and Nongbri, 2008) Apigenin (Zheng et al., 2005; Yue et al., 2020) Quercetin (Gulati et al., 1995; Bhatt et al., 2010; Domitrović et al., 2012; Memariani et al., 2015; Eftekhari et al., 2018; Zafra et al., 2020)
	Picrorrhiza kurroa	Root and rhizome (Lee et al., 2006; Negi et al., 2007; Kumar et al., 2011; Sankar et al., 2015; Ramírez and Jiménez, 2019)	Picroliv (Visen et al., 1991; Girish and Pradhan, 2012) Picroside I (Girish et al., 2009; Valan et al., 2010) Picroside II (Girish et al., 2009; Valan et al., 2010; Li et al., 2020) Kutkoside (Girish et al., 2009; Valan et al., 2010)
	Plantago major	Leaf (Najmi et al., 2005) Seed (Türel et al., 2009) Aerial parts (Eldesoky et al., 2018)	Acteoside (Eldesoky et al., 2018) Arabinogalactan (Singha et al., 2007; Sun et al., 2018) Caffeic acid (Janbaz et al., 2004; Yang et al., 2013) Chlorogenic acid (Girish and Pradhan, 2012; Ali et al., 2016; Chen et al., 2019)
	Picrorhiza scrophulariiflora	Root (Smit, 2000; Wang et al., 2004; Wang et al., 2006; Lal et al., 2007)	Iridoids (Wang et al., 2006; Huang et al., 2006)
	Scoparia dulcis	Whole plant (Praveen et al., 2009; Verma, 2018; Govind, 2011)	β-Sitosterol (Sujila et al., 2014; Abdou et al., 2019) Apigenin (Girish and Pradhan, 2012; Yue et al., 2020) Acacetin (Cho et al., 2014; Choi et al., 2014) α-Amyrin (Oliveira et al., 2005) Betulinic acid (Jain et al., 2012; Harwansh et al., 2017) Friedelin (Mann et al., 2011; Sunil et al., 2013) Syringic acid (Itoh et al., 2010; Srinivasulu et al., 2018; Sun et al., 2020) Gentisic acid (Pujari et al., 2020) β-Sitosterol (Sujila et al., 2014; Abdou et al., 2019) Stigmasterol (Praveen et al., 2016) Vitexin (Peng et al., 2020; Duan et al., 2020)
Plumbaginaceae	*Plumbago zeylanica*	Root (Kanchana and Sadiq, 2011; Sharma et al., 2014)	Plumbagin (Girish and Pradhan, 2011; Wei et al., 2015; Zaki et al., 2018) β-Sitosterol (Sujila et al., 2014; Abdou et al., 2019) Vanillic acid (Itoh et al., 2010)
Poaceae	*Bambusa bambos*	Shoot (Patil et al., 2018)	Not available
	Cymbopogon jwarancusa	Whole plant (Shakya and Shukla, 2011; Shakya et al., 2012)	Citral (Uchida et al., 2017; Li et al., 2018) Geraniol (Canbek et al., 2017; Lei et al., 2019)
	Hordeum vulgare	Grains (Sharma et al., 2014) Seed (Shah et al., 2009a; Shah et al., 2009b)	Flavonoids and saponarin (Girish and Pradhan, 2012) Caffeic acid (Janbaz et al., 2004; Yang et al., 2013) Chlorogenic acid (Girish and Pradhan, 2012; Ali et al., 2016; Chen et al., 2019) Ferulic Acid (Rukkumani et al., 2004) Protocatechuic acid (El-Sonbaty et al., 2019) Syringic acid (Itoh et al., 2010; Srinivasulu et al., 2018; Sun et al., 2020) Vanillic acid (Itoh et al., 2010) Catechin (Ryle et al., 1983; Venkatakrishnan et al., 2018)
	Oryza sativa	Seed (Sinthorn et al., 2016; Morya et al., 2020)	γ-Oryzanol (Wang et al., 2015; Shu et al., 2019; Huang et al., 2020) γ-aminobutyric acid (Park et al., 2020)
	Cymbopogon schoenanthus	Aerial part (Kadri et al., 2017)	Eucalyptol (Bhowal and Gopal, 2015; Patra et al., 2020)
	Saccharum officinarum	Leaf (Dewi et al., 2021), Sugarcane juice (Khan et al., 2015)	Apigenin (Girish and Pradhan, 2012; Yue et al., 2020) Caffeic acid (Janbaz et al., 2004; Yang et al., 2013), Sinapic acid (Shin et al., 2013) Vitexin (Peng et al., 2020; Duan et al., 2020) Schaftoside (Liu et al., 2020)

Family	Species	Parts used	Compounds with hepatoprotective activity
Polygonaceae	*Rheum emodi*	Rhizome (Najmi et al., 2005; Iqbal and Khan et al., 2019)	Emodin (Girish, 2009; Tu et al., 2015; Dong et al., 2016) Aloe -Emodin (Woo et al., 2002; Dong et al., 2020) Physcion, Chrysophanol (Girish, 2009) Rhein (Pradeep et al., 2005; Bu et al., 2018) Rutin (Janbaz et al., 2002; Liu et al., 2017) Epicatechin (Singha et al., 2012; Shanmugam et al., 2017)
Ranunculaceae	*Aconitum heterophyllum*	Root (Konda et al., 2016; Paramanick et al., 2017; Sinha and Ojha, 2020)	Freidelin (Konda et al., 2016)
	Delphinium denudatum	Root (Zafar et al., 2002; Nizami and Jafri, 2006; Hussain et al., 2012)	Quercetin (Gulati et al., 1995; Bhatt et al., 2010; Domitrović et al., 2012; Memariani et al., 2015; Eftekhari et al., 2018; Zafra et al., 2020) Stigmasterol (Praveen et al., 2016)
	Nigella sativa	Seed (Adam et al., 2016; Al-Seeni et al., 2016)	Myristic (Liu et al., 2019; Prasath et al., 2019) Palmitic (Saxena et al., 2007; Daoudi et al., 2021) Stearic (Pan et al., 2010; Daoudi et al., 2021) Oleic (Zhang et al., 2014) Linoleic (De Carvalho et al., 2014) β-Sitosterol (Sujila et al., 2014; Abdou et al., 2019)
Rhamnaceae	*Ziziphus jujube*	Fruit (Gao et al., 2013; Rajopadhye and Upadhye, 2016) Leaf (Bai et al., 2017)	Maslinic acid (Gao et al., 2013; Rajopadhye and Upadhye2016) Oleanolic acid (Liang et al., 2008; Patil et al., 2010; Ibrahim et al., 2011; Lodh and Swamy, 2019) Betulinic acid (Jain et al., 2012; Harwansh et al., 2017) Ursolic acid (Liang et al., 2008; Sukla et al., 1992; Gutiérrez-Rebolledo et al., 2016)
	Hovenia dulcis	Fruit (Hase et al.,1997; Hyun et al., 2010) Seed and fruit (Yoshikawa et al., 1997)	Hovenitin I (Yoshikawa et al., 1997) Myricetin (Semwal et al., 2016; Lv et al., 2020) Quercetin (Gulati et al., 1995; Bhatt et al., 2010; Domitrović et al., 2012; Memariani et al., 2015; Eftekhari et al., 2018; Zafra et al., 2020)
Rosaceae	*Rosa damascena*	Flower (Achuthan et al., 2003; Najmi et al., 2005; Alam et al., 2008; Iqbal and Khan et al., 2019) Petal (Shamsi et al., 2014)	Quercetin (Gulati et al., 1995; Bhatt et al., 2010; Domitrović et al., 2012; Memariani et al., 2015; Eftekhari et al., 2018; Zafra et al., 2020) Essential oil (Fatemi et al., 2020)
	Rubus fruticosus	Fruit (Čanadanović et al., 2019; Zafra et al., 2020)	Quercetin (Gulati et al., 1995; Bhatt et al., 2010; Domitrović et al., 2012; Eftekhari et al., 2018; Zafra et al., 2020) Cyanidin-3-glucoside (Park et al., 2017; Yu et al., 2020) Daidzein (Choi and Kim, 2009; wang et al., 2016) Genistein (Li et al., 2016; Ganai and Husain, 2017) Ellagic acid (Girish and Pradhan, 2012; Afifi et al., 2018) Gallic acid (Bhatt et al., 2010) Caffeic acid (Janbaz et al., 2004; Yang et al., 2013) Catechin (Ryle et al., 1983; Venkatakrishnan et al., 2018) Epicatechin (Singha et al., 2012; Shanmugam et al., 2017)
Rubiaceae	*Oldenlandia corymbosa*	Whole plant (Sadasivan et al., 2006; Das et al., 2019)	Geniposide (Ma et al., 2011; Chen et al., 2016; Zhang et al., 2017) Auricularine, Oleanolic acid (Liang et al., 2008; Patil et al., 2010; Ibrahim et al., 2011; Lodh and Swamy, 2019) Ursolic acid (Liang et al., 2008; Sukla et al., 1992; Gutiérrez-Rebolledo et al., 2016) Rutin (Janbaz et al., 2002; Girish and Pradhan, 2012; Domitrović et al., 2012; Liu et al., 2017)
	Rubia cordifolia	Root (Najmi et al., 2005; Rao et al., 2006)	Rubiadin (Luper,1999; Rao et al., 2006) Purpurin, munjistin (Luper,1999) Gallic acid (Bhatt et al., 2010)

Family	Species	Parts used	Compounds with hepatoprotective activity
Salvadoraceae	*Salvadora persica*	Bark (Ibrahim et al., 2011) Fruit (Gupta et al., 2010)	Salvadorine (Khan et al., 2010) Oleanolic acid (Liang et al., 2008; Patil et al., 2010; Ibrahim et al., 2011; Lodh and Swamy, 2019) β-Sitosterol (Sujila et al., 2014; Abdou et al., 2019) Linalool (Altınok-Yipel et al., 2019)
Santalaceae	*Santalum album*	Leaf (Hegde et al., 2014) Stem (Vengal et al., 2014)	Not available
	Viscum articulatum	Whole plants (Patil et al., 2010; Balaji et al., 2016)	Oleanolic acid (Patil et al., 2010; Lodh and Swamy, 2019) Vanillin (Makni et al., 2011; Tiwari et al., 2020) Protocatechuic acid (El-Sonbaty et al., 2019) Oleanolic acid (Jeong, 1999; Gutiérrez-Rebolledo et al., 2016) Betulinic acid (Jain et al., 2012; Harwansh et al., 2017) Naringenine (Yen et al., 2009; Kapoor and Kakkar, 2014; Den Hartogh and Tsiani, 2019)
Schisandraceae	*Illicium verum*	Fruit (Kareemulla et al., 2018; Patra et al., 2020)	8-cineole/eucalyptol (Bhowal and Gopal, 2015; Patra et al., 2020) Anethole (Cho et al., 2013; da Rocha et al., 2017) Limonene (Amini et al., 2020)
Solanaceae	*Solanum nigrum*	Aerial parts (Bhawna and Kumar, 2009) Fruit (Raju et al., 2003; Najmi et al., 2005; Subash et al., 2011)	Steroid glycoalkaloids (Luper, 1999) Rutin (Janbaz et al., 2002; Girish and Pradhan, 2012; Domitrović et al., 2012; Liu et al., 2017) Catechin (Ryle et al., 1983; Venkatakrishnan et al., 2018) Gallic acid (Bhatt et al., 2010)
	Withania somnifera	Root (Ahmad and Sharafatullah, 2008; Mir et al., 2012; Kumar et al., 2015; Sankar et al., 2015; Ramírez and Jiménez, 2019)	Withaferin 'A' (Bhattacharya et al., 2000; Mir et al., 2012; Vedi and Sabina, 2016)
Tamaricaceae	*Tamarix dioica*	Leaf (Ahmad et al., 2002; Najmi et al., 2005)	Rutin (Janbaz et al., 2002; Girish and Pradhan, 2012; Domitrović et al., 2012; Liu et al., 2017) Catechin (Ryle et al., 1983; Venkatakrishnan et al., 2018) Gallic acid (Bhatt et al., 2010) Myricetin (Semwal et al., 2016; Lv et al., 2020) Quercetin (Bhatt et al., 2010; Domitrović et al., 2012; Eftekhari et al., 2018) Kaempferol (Wang et al., 2015)
	Tamarix gallica	Leaf (Kalam et al., 2016; Urfi et al., 2018) Flower (Kalam et al., 2016)	Tamarix (Kalam et al., 2016) Tannin (Gupta and Sharma, 2007) Catechin (Ryle et al., 1983; Venkatakrishnan et al., 2018) Quercetin (Gulati et al., 1995; Bhatt et al., 2010; Domitrović et al., 2012; Eftekhari et al., 2018) Gallic acid (Bhatt et al., 2010)

Family	Species	Parts used	Compounds with hepatoprotective activity
Theaceae	*Camellia sinensis*	Leaf (Sengottuvelu et al., 2008; Jwied, 2009; Kumar et al., 2010; Hiraganahalli et al., 2012)	Epigallocatechin galate (Gupta and Sharma, 2007; Bhatt et al., 2010) Quercetin (Bhatt et al., 2010; Domitrović et al., 2012; Eftekhari et al., 2018) Gallic acid (Bhatt et al., 2010) Catechin (Ryle et al., 1983; Venkatakrishnan et al., 2018) Epicatechin (Singha et al., 2012; Shanmugam et al., 2017)
Thymelaeaceae	*Aquilaria agallocha*	Stem (Shamsi et al., 2014) Leaf (Alam et al., 2015; Alam et al., 2017)	Apigenin (Girish and Pradhan, 2012; Yue et al., 2020) Vanillin (Makni et al., 2011; Tiwari et al., 2020) Ferulic Acid (Rukkumani et al., 2004)
Vitaceae	*Vitis venifera*	Seed (Hassan, 2012; Almajwal and Elsadek, 2015; Akaberi and Hosseinzadeh, 2016) Leaf (Orhan et al., 2007; Orhan et al., 2009)	Caffeic acid (Janbaz et al., 2004; Yang et al., 2013) Catechin (Ryle et al., 1983; Venkatakrishnan et al., 2018) Kaempferol (Wang et al., 2015) Quercetin (Gulati et al., 1995; Bhatt et al., 2010; Domitrović et al., 2012; Eftekhari et al., 2018)
Zingiberaceae	*Alpinia galangal*	Rizhome (Narayanasamy and Selvi, 2005; Hemabarathy et al., 2009; Devi et al., 2019)	1,8-Cineole (Santos et al., 2004; Murata et al., 2015) Galangin (Zhu et al., 2018; Patil et al., 2019; Aladaileh et al., 2019)
	Curcuma longa	Rhizome (Luper, 1999; Kumar et al., 2012; Salama et al., 2013; Sankar et al., 2015; Ramírez and Jiménez, 2019)	Curcumin (Shapiro et al., 2006; Girish ,2009; Valan et al., 2010; Kumar et al., 2012; Salama et al., 2013) Dihydrocholic acid (Valan et al., 2010; Dey et al., 2013) Volatile oils (Kumar et al., 2012)
	Elettaria cardamomum	Seed (Darwish and Azime, 2013; Aboubakr and Abdelazem, 2016; Khattab et al., 2020) Fruit (Shamsi et al., 2014)	Stigmasterol (Praveen et al., 2016) 1,8-Cineole (Santos et al., 2004; Murata et al., 2015) Linalool (Altınok-Yipel et al., 2019) β-caryophyllene (Cho et al., 2015; Kelany and Abdallah, 2016)
	Zingiber officinale	Rhizome (Ajith et al., 2007; Atta et al., 2010; Akinloye et al., 2014; Ezeasuka et al., 2015)	Oil of ginger, oleoresin (Gupta and Sharma, 2007) 1,8-Cineole (Santos et al., 2004; Murata et al., 2015) Linalool (Altınok-Yipel et al., 2019) Geraniol (Canbek et al., 2017; Lei et al., 2019) α-Copaene (Turkez et al., 2014)
Zygophyllaceae	*Tribulus terrestris*	Fruit (Li et al., 1998; Manikandaselvi et al., 2013) Aerial parts (Harraz et al., 2015) Seed (Almasi et al., 2017)	Tribulusamide A, Tribulusamide B, N-trans-Feruloyl tyramine, Terrestriamide and N-trans-Coumar-oyltyramine (Li et al., 1998) Kaempferol (Wang et al., 2015) Rutin (Janbaz et al., 2002; Girish and Pradhan, 2012; Domitrović et al., 2012; Liu et al., 2017) Quercetin (Gulati et al., 1995; Bhatt et al., 2010; Domitrović et al., 2012; Eftekhari et al., 2018) Ferulic Acid (Rukkumani et al., 2004) Vanillin (Makni et al., 2011; Tiwari et al., 2020) β-Sitosterol (Sujila et al., 2014; Abdou et al., 2019)

peroxidation. BER has been shown to decrease histopathological alterations and suppress the production of tumour necrosis factor-alpha (TNF-alpha) and cyclooxygenase-2 (COX-2), while also stimulating the activity of nitric oxide synthase (iNOS). (Domitrović et al., 2011).

Khamira Gaozaban Ambri JadwarOod Saleeb Wala is a PHF standardized by Akhtar and his team (2013) consists of *Centaurea behen* (root), Santalum album (leaf), *Lallemantiaroyleana* (seed), *Cheiranthus cheiri* (Syn *Erysimum cheiri*), *Borago officinalis* (aerial parts), *Coriandrum sativum* (Seed and fruit), *Bombyx mori* (feacal matter), *Salvia haematodes* (root), *Mellisa parviflora* (leaf), *Ocimum gratissimum* (leaf), *Lavendula stoechas* (aerial parts), *Mathiola incana* (aerial parts), *Delphinium denudatum* (root), *Paeonia emodi* (rhizome) and *Pandanus tectorius,* which is reported to be effective in reducing the hepatotoxicity induced in rodents. Although the parts of the plants used to develop the formulation were known, the bioactive compounds contributing to the hepatoprotective activity have not been explored for some plants of the formulation, such as *Centaurea behen* (root), *Santalum album*, *Lallemantia royleana* (seed), *Cheiranthus cheiri* and *Salvia haematodes* (root). In this study, 15 plants, including the previously five mentioned plants, need an exploration for bioactive compounds concerning the hepatoprotective activity, such as *Begonia laciniata, Nardostachys jatamansi*, *Coccus lacca*, *Baliospermum montanum*, *Iris ensata*, *Laccifer lacca*, *Lilium longiflorum*, *Osbekia octandra*, *Pinius succinifera*, and *Bambusa bambos*, which are the constituents of the following PHFs, viz., Indian folklore medicine (Ganapaty et al., 2013), F1, F2 and F3 (Dandagi et al., 2008), Majoon-e-Dabeed-ul-ward (Shakya et al., 2012), Prak-20 (Prakash and Mukherjee, 2010), NPCF (Iqbal and Khan, 2018), Ginseng essence (Lu et al., 2016), LINK LIVECARE™ (Karunarathn et al., 2017), Heptoplus (Sarkar et al., 2015) and Majoon-e-Dabeed-ul-ward (Shakya et al., 2012) respectively.

2.8 Additional ingredients of PHFs other than plant.

***2.8.1 Sodii carbonas impura*:** It is used in Siddha medicine for the treatment of rheumatism (anti-inflammation) and kidney disorders. It possesses pharmacological actions, which include anti-inflammatory, analgesic, anti-spasmodic and antacid that help in treatment of Vatha dieases, Gunman and Soolai (Pasupathy, 2019). Sodii carbonas impura is included as one of the ingredients of Hepax PHF for the management of hepatotoxicity in rats (Aslam et al., 2016).

***2.8.2. Calcii oxidum or Calcium oxide*:** It is a basic oxide of calcium obtained from

calcium carbonate by means of heating. It is a caustic irritant with basic properties requiring precautionary measures such as wearing protective goggles, protective clothing, and gloves. It is popularly used as a food additive and as a base for chemical experiments and calcium hydroxide production (Retrieved on March 23, 2021 from https://pubchem.ncbi.nlm.nih.gov/compound/Calcium-oxide).

***2.8.3. Potassii carbonas or Potassium bicarbonate*:** It is found in crystalline form and slightly alkaline. The Food and Drug Administration (FDA) has granted approval for its usage as a medicinal substance (antacid) and as an ingredient that is Generally Recognised As Safe (GRAS). It has the property to help conduct nerve impulses and maintain healthy renal function, acid-base balance and cellular function.CO2 produced by this bicarbonate compound has been the issue of potassium bicarbonate, which can cause eructation. (Available from: https:// pubchem.ncbi.nlm.nih.gov/compound/Potassium-bicarbonate).

***2.8.4. Lauha Bhasma* or *Calcinated Iron*:** Lauha Bhasma (LB) is a combination of herbs and minerals that forms a complex ayurvedic formulation and commonly used as a hematinic agent. The different levels of dose, such as therapeutic dose, intermediate dose and higher dose of LB can be used as an effective drug with minimum side effect. LB is used to manage chronic fever, phthisis, and breathlessness, and is known to possess vital energy-enhancing, strength-promoting and anti-aging properties (Joshi et al., 2016). It might be plausible that due to such properties, it is included in the formulation Arogyavardhini Rasa (Sapkota et al., 2017).

***2.8.5. Abhrak Bhasma* or *Calcinated Mica*:** It is anamorphous powdery ayurvedic drug preparation from frequent incineration of mica mineral with a decoction of various medicinal herbs. It mainly constitutes silicates of iron, magnesium and aluminum. Buwa et al., 2001 suggest that the hepatoprotective activity of Abhrak Bhasma may be due to the reduction of endoplasmic reticulum damage and free radical scavenging activity. Teli et al., 2014 reported that Abhrak Bhasma can be used as a potential drug in the management of liver disorders and for oxidative stress -related diseases. Sapkota *et al*., 2017 included Abhrak Bhasma in their formulation Arogyavardhini Rasa which was found to be effective in treating liver toxicity in rats.

***2.8.6. Tamra Bhasma or Calcinated Copper*:** Tamra Bhasma (TB) is a herbo-metallic ayurvedic formulation mentioned in the ayurvedic literature, and it is

advisable to use in a minute concentration for the management of liver-related problems. Copper, being part of an enzyme, helps in controlling metabolic pathways; therefore, lack of it causes different problems such as anemia and nervous weakness (Tripathi et al., 2003). Clinically, pretreatment with TB provides protection against paracetamol-induced hepatotoxicity (Honwad et al., 2015). Similarly, its potent antioxidant property acts effectively in the management of lipid peroxidation with minimum or no side effects (Tripathi and Singh, 1996). It has been used in the formulation of Arogyavardhini Rasa, where it is found to be effective against liver toxicity (Sapkota et al., 2017).

***2.8.7. Shuddha Gandhaka or Processed Sulphur*:** Shuddha Gandhakain association with other plant ingredients and minerals have been created an ayurvedic formulation which found to be effective in the handling of jaundice, liver related problems and various skin diseases (Zanwar et al., 2019). Similarly, Arogyavardhini is an ayurvedic preparation where processed sulphur is a part of the formulation and is helpful in the cure of various liver diseases including toxic liver injury (Rouf et al., 2021). Its efficacy and effectiveness may be the reason for using in the preparation of many ayurvedic formations including Avogyavardhini rasa PHF (Sapkota et al., 2017).

***2.8.8. Shuddha Parada* or *Processed Mercury*):** Shuddha Parada is a part of the Arogyavardhini formulation, an ayurvedic preparation which is helpful in the cure of various liver diseases, including toxic liver injury (Rouf et al., 2021). Furthermore, it is an integral component of the Chaturmukha Rasa ayurvedic concoction, necessitating a larger dosage for the management of kidney and liver ailments. Moreover, it has been used in the production of several Ayurvedic concoctions, such as Avogyavardhini rasa PHF, maybe owing to its efficacy in mitigating liver impairment (Sapkota et al., 2017).

2.8.9. Processed black bitumen (Copper containing stone).

***2.8.10. Coccus lacca*:** It is mainly secreted by a leaf insect called *Tachardia lacca (Laccifer lacca)*. The secretion of lac is for its defense mechanism.

***2.8.11. Qand Safed* or *Granular sugar*:** A product made from sugar cane.

***2.8.12. Asal* or *Honey*:** Honey is used as a base for herbal cough syrup preparation (Patil et al., 2020). A type of honey known as Apis cerana honey shows hepatoprotection against liver damage in mice (Zhao et al., 2018). Furthermore, Zhao and his team (2018) concluded that the presence of polyphenols in A. cerana

honey could be attributed to its antioxidant properties and intervention of oxidative stress, which might be responsible for its hepatoprotective activities. Similarly, vitex honey was also demonstrated to have protection against liver damage through its anti and pro-oxidative property (Wang et al., 2015). Since honey offers many properties, it was also used as one of the ingredients in the formulation of Jawarish-e-AmLa Sada PHF that that was reported to provide hepatoprotection against liver damage in rats (Shailajan et al., 2015).

***2.8.13. Sorbitol*:** It is a sugar alcohol found in fruits and some plants. It is a replacement for sugar in food, beverages, and medications. Moreover, it is used as an indicator and reagent for chemical, biological or pathological processes or conditions. It helps in cathartic activity. Sorbitol is widely reported to be used as an excipient, plasticizer, stabilizer, and diluent in herbal formulations. It also may be used as a marker for analytically assessing liver blood flow. Sorbiline solution composed of sorbitol and tricholine citrate is used to prevent or treat fatty liver disease. Dandagiet al., 2008 used it in their F I, F II, and F III formulations to treat liver damage in experimental rats. (Retrieved on March 17, 2021 from https:// pubchem.ncbi.nlm.nih.gov/compound/Sorbitol). Probably due to these reasons, it is included in the polyherbal formulation prepared by Fathima et al., 2015.

2.8.14. Sucrose (Fathima et al., 2015): Sucrose appears as a white, odorless crystalline material which is denser than water. It is known for its diverse uses, such as flavor mixer, sweetening agent, accentuator, modifier and dispersing agent, texture and bodying agent for food and beverages, and lubricant in foods. It also slows down the gelatinization process or increases the gelatinization temperature in starch-containing solutions. (Retrieved on March 17, 2021 from https:// pubchem.ncbi.nlm.nih.gov/compound/Sucrose).

2.8.15. Carboxy methyl cellulose (CMC) (Fathima et al., 2015): CMC is labeled as safe and used as a thickener in food preparation.

***2.8.16. Olive oil*:** Olive oil, particularly virgin olive oil, constitutes the predominant dietary lipid consumed by inhabitants of the Mediterranean region. It is reported to reduce blood pressure, obesity pandemic and possesses anti-atherosclerotic, anti-inflammatory, and antioxidant potential, and maintains homeostasis by modulating gene expression (Gaforio et al., 2019). Olive oil also shows hepatoprotective activity against liver damage (Al-Seeni et al., 2016). Fatima et al., 2015 used olive oil in their ayurvedic formulation to treat hepatotoxicity which shows effective results.

2.8.17. Mandoor Bhasma* or *Ferric Oxide (Prakash and Mukherjee, 2010): Mandoorbhasma, an ayurvedic preparation, comprises old iron rust as the main ingredient. In addition to that, it also consists of Triphala decoction, urine of cow and juice of Aloe vera. Chemically, it comprises either ferric oxide or red iron oxide (Fe_2O_3). The raw form of Mandoor Bhasma shows several side effects, whereas the well-prepared part shows no side effects. The efficacy of Mandoor Bhasma in protecting the liver from injury has been shown (Gawate et al., 2016).

***2.8.18. Cow's ghee*:** Ghee is a type of clarified butter fat which has been known to be used in India since ancient times. In Ayurveda, it has significant usage as a therapeutic agent and in religious rituals. Its contribution to characteristic flavor and aroma, nutritional qualities and pure nature (sacred) makes it popular among the Indians. It can be obtained from milk, cream, or butter of several animal species (Kumar et al., 2018). Achliya et al., 2004 used ghee in their PHF named AmalkadiGhrita, and it was reported to be a rejuvenator, stimulant and help to gain memory loss and maintain CNS disorders. However, no beneficial effect of cow ghee on cognition was seen by Karandilar et al., 2016.

***2.8.19. Bombyx mori*:** The fecal matter of Bombyx mori was used in the Khamira Gaozaban Ambri JadwarOod Saleeb Wala PHF formulated by Akhtar and his team (2013). Its partially purified 35 kDa protein from the fecal matter has been reported to have beneficial properties against various diseased conditions such as liver damage and oxidative stress, but is unable to inhibit the viral multiplication at maximum non-toxic concentration (MNTC) (Raghavendra et al., 2010).

2.9 Limitations of herbal drugs

The use of plant-based remedies for liver problems has been a longstanding tradition, seen not just in Ayurveda but also in Chinese, European, and other mainstream therapeutic approaches. Most of the folklore medical prescriptions are restricted to particular ethnic groups and are transmitted from generation to generation through verbal communication; thus, there are very few documentaries (Mordeniz, 2019). Though the traditional claim is very high, only hand full formulations are pharmacologically authenticated for their safety, efficiency, quality control and are commercialized till date (Girish *et al*., 2009) (Table 2.2).

Though an increase in the usage of PHFs without cautions just for the reason that it promises to cure leads to negligence towards safety and side effects, the approval of nutraceuticals based on pre-clinical and unreliable clinical trials with improper experimental designs can lead to sacrificing the high-quality outcomes and may

probably lead to severe consequences to peer-reviewed publications supporting the efficacy of herbal drugs based on clinical trials (Yang, 2020). Apart from this, the other setback that appears is the bioavailability, bioaccessibility, and bioefficiency of bioactive components, which influence the therapeutic actions of herbal drugs. It is the bioavailability, which, in turn, is responsible for bioefficiency of herbal preparations. The bioavailability of herbal drugs is affected by molecular size and structure, metabolizing enzymes, and bioaccessibility. The process involves an intricate sequence of steps, including liberation, absorption, distribution, metabolism, and elimination stages (LADME) (Rein et al., 2013).

Keche and his team 2010 reported that Livwin PHF has significant clinical recovery of fever, weakness, icterus and tender and enlarge liver at two weeks compared to placebo with few setbacks where two patients were affected with epigastric pain and a single person with diarrhea.

Though Processed black bitumen, Milk tuttam (Copper containing stone), Coccus lacca (secreted by leaf insect), and Qand Safed (Granular sugar) have been used by the researchers as ingredients for various PHFs, there is no scientific evidence to prove the efficacy of the individual ingredients of the PHF till date; however, there is a possibility that their ingredient may act in synergy with other components of the PHF

Based on our extensive review, only one PHF has been investigated for its hepatoprotective effect in a clinical study. This indicates that additional attention must be given to clinical studies of PHFs to explore the benefits of other PHFs on the market, which would help in successfully utilizing these PHFs for treating liver disorders.

2.10 Future prospects

Herbal medicine has gained significant popularity in many countries because to its simplicity and effectiveness in treating a broad variety of illnesses, both in developed and developing nations. These polyherbal treatments are breaking down barriers and gaining traction in today's culture (Ekor, 2014). Polyherbal medications are becoming increasingly scientifically focused and widely recognized in the market, with the potential to treat specific ailments. The bioactive substances contained in food components have a good impact on health in general (Usha et al., 2017). Though scientific and technological advancements aid in the characterization and structural elucidation of active substances, their abundance varies unexpectedly

in nature, resulting in the failure to produce the desired therapeutic effects. As a result, the concept of PHFs arose from the belief that numerous components operating on multiple sites are more helpful for illness treatment than a single chemical constituent working on a single site. The treatment of liver problems is based on the synergistic action of the numerous constituent components of PHFs. Despite the fact that plant-based treatments have been shown to be beneficial with few adverse effects, numerous obstacles remain, including bioavailability, bioefficiency, appropriate dose, lack of characterization, uncertain mechanism of action, and clinical efficacy. Nonetheless, developing a novel herbal lead is encouraged because they have a long and illustrious history for future indications.