Br J Med Health Res. 2022;9(09)

ISSN: 2394-2967



BJMHR

British Journal of Medical and Health Research Journal home page: www.bjmhr.com

A Review of Hepatoprotective Potential of Siddha Herbo mineral formulation - Saman Chooranam

Nalina Saraswathi Kolappan^{*1}, Ramani Mani ², Kabilan Natarajan ³, Velpandian Venkatachalapathy ⁴

 Lecturer, Post Graduate Department of Gunapadam, Government Siddha Medical College, Arumbakkam, Chennai - 600106, India.
 Research Scholar, Department of Siddha, The TamilNadu Dr. M. G. R. Medical University, Guindy, Chennai - 600032, India.
 Professor & Head, Department of Siddha, The TamilNadu Dr. M. G. R. Medical University, Guindy, Chennai - 600032, India.
 Professor, Post Graduate Department of Gunapadam, Government Siddha Medical College, Arumbakkam, Chennai - 600106, India.

ABSTRACT

Liver is a vital organ for metabolism and it is affected due to various diseases and toxic products. It also plays an important role as bio Transformer of xenobiotic which are more toxic and more reactive substances. Though there are some liver tonics in modern medicine, Siddha medicine has innumerable formulations to protect the liver. Jaundice is an important sign of liver disorder. Hepatocellular carcinoma is the commonest cause of liver cancers which leads to 5th common cause of cancers affecting mankind. Liver cirrhosis is the common cause of liver disease in India. There is a need of safe hepatoprotective drug from Siddha system of medicine. The available information was collected from various Siddha and modern literature, scientific databases such as PubMed, Science Direct, Scopus, Web of Science and Google Scholar etc. One such hepatoprotective drug is Saman Chooranam. But there is no sufficient collective literature report and scientific validation of this formulation. The significance of this review is aimed to provide a brief and collective scientific evaluation of the key active phytochemical components and its pharmacological actions for the possible development of this formulation Saman Chooranam in future perspective. This review reveals that the traditional use, phytochemistry and pharmacological profile of Siddha herbomineral formulation of Saman Chooranam thereby identifying the research lacuna and future steps regarding this drug.

Keywords: Siddha medicine, Saman Chooranam, Hepato protective, Herbomineral.

*Corresponding Author Email: <u>knalina.s@gmail.com</u> Received 05 July 2022, Accepted 22 August 2022

Please cite this article as: Kolappan NS *et al.*, A Review of Hepatoprotective Potential of Siddha Herbo mineral formulation - Saman Chooranam. British Journal of Medical and Health Research 2022.

INTRODUCTION

Liver is one of the most vital organs responsible for many important functions including metabolism, conjugation, and excretion of various endogenous substances and exogenous substances. Apart from these, liver also plays an important role as bio Transformer of xenobiotic which are toxic and more reactive substances. Jaundice is an important sign of liver disorder. Liver is a prime target for damage, which can lead to various types of hepatic diseases that can be classified into acute or chronic hepatitis, cirrhosis and hepatocellular carcinoma.

In the absence of reliable hepatoprotective medicines, liver diseases will be the next major lifestyle disorder of India after diabetes and hypertension. The worldwide annual incidence of drug-induced hepatotoxicity is increased day by day.¹

There has been a paradigm shift in the dynamics of liver cirrhosis and about 10 lakh new patients are diagnosed with it every year in India. Around 10 lakh patients of liver cirrhosis are newly diagnosed every year in India. Liver disease is the tenth most common cause of death in India as per the World Health Organization. Liver disease may affect one in 5 Indians. Liver Cirrhosis is the 14th leading cause of deaths in the world and could be the 12th leading cause of deaths in the world by 2020.²

Hepatocellular carcinoma (HCC) is the most frequent cause of all liver cancers and constitutes 90% of cancers of liver globally. Approximately 7.5 Lakhs of new cases of HCC per year occurs globally which makes HCC as the 5th common cause of cancers affecting human. ³ Hepatocellular carcinoma (HCC), or a cancer in the liver, is the second most common cause of death due to malignancy in the world.

The main symptom is jaundice, vomiting, dyspepsia, anorexia, enlargement or shrinking of liver, ascites, loss of function etc.

Herbal based preparations play a vital role in the treatment of various liver disorders. There are numerous medicinal plants and their formulations used for liver disorders in Siddha system of medicine. However, we do not have satisfactory scientific documentation for these herbal drugs. Few herbal drugs speed up the natural healing process of liver and evaluated for its hepatoprotective effects. Hence, the world is looking at the traditional Indian Siddha system of medicine for remedies to treat the hepatic disorders. Still the search for effective hepatoprotective drug continues. One such promising Siddha formulation '*SAMAN CHOORANAM*' mentioned in Siddha classical literature '*Agasthiyar Vaithya Chinthamani Venba* – 4000', ⁴ indicated for various liver disorders. This medicine is used by the Siddhars and Siddha medical practitioners to treat the liver disorders from *Sangam* era. However there are no reports regarding the pharmacological activities of this formulation.

Hence, the present review is aimed at compiling the data based on '*SAMAN CHOORANAM*' consisting herbs and minerals reported works on promising phytochemicals from medicinal plants and geological perspective of the mineral.

MATERIALS NEEDED FOR SAMAN CHOORANAM

The formulation of *Saman Chooranam* has been selected from the Classical Siddha Literature. '*Agasthiyar Vaithya Chinthamani Venba* – *4000*', Page No.178^{4.}

Table 1: Ingredients of Saman chooranam⁴

S.No	Ingredients	English Name	Scientific Name	Quantity
1	Indhuppu	Rock salt	Impure Sodium chloride	5gms
2	Perungayam	Asafoetida	Ferula asafoetida	5gms
3	Evatcharam	Wood salt	Impure Potassium	5gms
			Carbonate	
4	Kalluppu	Common salt	Sodium chloride	5gms
5	Kadukkai	Yellow myrobalan	Terminalia chebula	5gms
6	Chukku	Dried ginger	Zingiber officinale	5gms
7	Vaividangam	Embelia	Embelia ribes	5gms
8	Sathicharam	Mixture of fullers earth, Lime	Yet to be validated	5gms
		stone and Soil falling from the wall		-
9	Kodiveli	Leadwort	Plumbago zeylanica	5gms
10	Thippili	Long pepper	Piper longum	5gms
11	Kurosani Omam	Henbane seeds	Hyoscyamus niger	5gms

Method of preparation:

Purification process

All the above ingredients purified as per Siddha literature. After purification, the herbal ingredients are collected in equal parts and fried separately in a fry pan until golden brown.⁵ Then they are powdered separately. Rock salt, wood salt, common salt and *Sathicharam* are powdered and all the powders are mixed together in a stone mortar and finally stored in an air tight glass jar.

Adjuvant: It is consumed with rice and ghee.

Indications: Jaundice, Liver disorders, Anemia, Peptic ulcer and indigestion.

Pharmacognostic Aspect of each ingredient

1. Ferula asafoetida (Umbelliferae)

Common name: Asafoetida

Vernacular Name: Perungayam

Part used: Gum resin

Phytochemical constituents: It consists of three main fractions resin, gum and essential oil.⁶ The resin fraction contains ferulic acid and its esters, coumarins, sesquiterpene coumarins and other terpenoids.⁷ The gum includes monoterpenes and volatile terpenoids. Sulfur compounds in *Ferula asafoetida* resin shows various biological activities valuable in medicine.⁸

Actions: Stimulant, Carminative, Antispasmodic, Laxative, Anthelmintic and Diuretic.

Indications: It is used for flatulence, belching, gastric ulcer, ascites, worm infestation etc., ⁹ **Pharmacological activities:**

Hepatoprotective effect: Methanol-insoluble fraction has anti hepato toxic activity.¹⁰

Antihypertensive activity: Intravenous administration to dogs at variable doses showed antihypertensive activity.

Antitumor: The aqueous extract isolated from the dried oleoresin of *Ferula asafoetida* given to mice on CA-Ehrlich ascites and 53% increase in life span was observed. ¹¹

Anti-carcinogenic: *Ferula asafoetida* given to rats showed a remarkable reduction in the multiplicity and size of palpable N- methyl -N-Nitrosourea induced mammary tumours and there was delay in mean latency period of tumour appearance.

Antioxidant activity: *Ferula asafoetida* in rats significantly restored the level of antioxidant system. ¹²

2. Terminalia chebula (Combretaceae)

Common name: Yellow myrobalan

Vernacular Name: Kadukkai

Part used: Fruit rind

Phytochemical constituents: It contains high phenolic content, especially hydrolysable tannins, anthraquinone and flavonol. Other constituents contain chebulic acid, chebulinic acid, tannic acid, ellagic acid, gallic acid, flavonoids like luteolin, rutins and quercetin etc. ¹³ **Actions:** Stimulant, Stomachic, Tonic, Rejuvenator, Laxative

Indications: It digests the food materials which is hard to digest. It induces the peristaltic movement and defecation. It has an Anti-ageing property. It cures cheek, cervical, tongue, penile diseases, cancerous growth in the soles, ascites, ulcers, jaundice, poison due to plants, mineral and metals.⁹

Pharmacological activities:

Hepatoprotective effects: *Terminalia chebula* (fruit) prevents liver toxicity caused by subchronic administration of rifampicin, isoniazid and pyrazinamide in combination. The antioxidant potential associated with hepatoprotective effects was evidenced by the reduction in biochemical parameters along with the histopathological studies. ¹⁴

Cytoprotective effect: A 70% methanol extract of *Terminalia chebula* fruit, was studied for its effects on growth in several malignant cell lines including a hum4n (MCF-7) and mouse (S115) breast cancer cell line, a human osteosarcoma cell line (HOS-1), a human prostate cancer cell line (PC-3) and a non-tumorigenic, immortalized human prostate cell line (PNT1A) using assays for proliferation, cell viability and cell death). In all cell lines studied, the extract decreased cell viability, inhibited cell proliferation, and induced cell death in a

dose dependent manner. Chebulinic acid, tannic acid and ellagic acid were found to be the most growth inhibitory phenolics of *Terminalia chebula* fruit extract. ¹⁵

Antidiabetic and Renoprotective effects: Oral administration of the extracts reduced the blood sugar level in normal and in alloxan diabetic rats. Continued, daily administration of the drug produced a sustained effect.¹⁶

Antioxidant Activity: *Terminalia chebula* possess potent antioxidant properties due to the presence of the phenolic compounds in adult male Sprague-Dawley rats. ^{17, 18}

Antibacterial effect: *Terminalia chebula* extract reduces the colony formation of the bacteria confirming its antibacterial potential. ¹⁹ *Terminalia chebula* showed stimulatory effects on gastric emptying, due to its potent prokinetic properties. ²⁰

3. Zingiber officinale (Zingiberaceae)

Common name: Dried ginger

Vernacular Name: Chukku

Part used: Rhizome

Phytochemical constituents: The volatile oils and pungent phenol compounds found in ginger rhizome, such as shogaols, zingerone, and gingerols contribute to its taste and odour. Sesquiterpene and monoterpenoid hydrocarbons, gives ginger its distinct aroma and flavour. ²¹

Actions: Stimulant, Stomachic, Carminative

Indications: It cures indigestion, heart burn, alimentary tract diseases, diarrhoea, gastric ulcer, flatulence, pain in the flanks, anaemia, pain abdomen etc., ⁹

Pharmacological activities:

Hepatoprotective effect: *Zingiber officinale* is useful in preventing acute liver injury caused by CCl₄ and acetaminophen-induced liver damage and *Zingiber officinale* could be useful in preventing acute liver injury. ²²

Nephroprotective effect: Ethanol extract of *Zingiber officinale* is effective against Cisplatin induced nephrotoxicity. This protection is mediated by renal antioxidant defence system. ²³

Effect of Liver cancer: Gingerol can inhibit both proliferation and invasion of hepatoma cells and apoptosis.²⁴

Anti-diabetic effects: Ginger significantly lowered blood glucose, serum total cholesterol, LDL, VLDL, triglycerides and raised HDL in hyperglycemic rats.²⁵

4. Embelia ribes (Myrsinaceae)

Common name: Embelia

Vernacular Name: Vaividangam

Part used: Fruit

Phytochemical constituents:

The vilangin compound found in the dry ripe berries. ¹³ The other constituents isolated are volatile oils, fixed oil, resin, tannin, christembine, phenolic acids such as caffeic acid, vanillic acid, cinnamic acid, o-cumaric acid from the berries of *Embelia ribes*.²⁶ The new compounds detected from the seeds are embelinol, embeliaribyl ester and embeliol. The embelin is found in the fruit part.²⁷ It also contains components like potassium embelate, quercitol etc.,^{28, 29} It also contains Chromium, Potassium, Calcium, Copper, Zinc and Manganese along with steroids, cardiac glycosides, alkaloids, anthraquinones, tannins and phenolics.^{30, 31}

Actions: Anthelmintic, Carminative, Stomachic, Stimulant

Indications: It cures anaemia, gastric ulcer, ascites, flatulence, worm infestation and ulcer in anus. It prevents abdomen disorders.⁹

Pharmacological activities:

Hepatoprotective: The ethanolic extract of the *Embelia ribes* showed hepatoprotective activity on paracetamol-induced liver cell damage using a mice model. It decreases serum glutamate pyruvate transaminase in a dose-dependent manner. ³²

Antitumor: Embelin component of the *Embelia ribes* exhibits significant antitumor activity in methylcholan-threne-induced fibrosarcoma in albino rats. ³³

Antioxidant: The aqueous extract of the *Embelia ribes* showed antioxidant activity in the streptozotocin-induced diabetic rats. ³⁴

5. Sathicharam

Common name: Suvarsigai

Synthetic preparation:

Ingredients:

1.	Fuller's earth	: 130 ml
2.	Lime stone	: 65 ml
3.	Soil falling from the wall	: 130 ml
4.	Water	: 1300 ml

Preparation:

The fuller's earth and the limestone are mixed and kept in a holed straw barrel. Then the above said soil is dissolved in water and filtered. The filtrate is boiled till it attains the wax consistency and made into flat cakes and spread over a mat and allowed to cool. A salt is obtained which is called as *Sathicharam*.

Purification:

This is dissolved in goat's urine for 3 days and filtered. The filtrate is insolated. ³⁵

Chemical constituents:

Sodium carbonate, sulphate of soda, potash (fuller's earth), Na₂Co₃.NaHCo₃.2H₂O, Calcium oxide, Silicon dioxide, Calcium and Iron. ³⁶

Actions: Laxative, Diuretic

Indications:

Indigestion, constipation, splenomegaly, abdominal pain, ascites and diarrhoea.³⁵

Pharmacological activities:

Yet to be validated.

6. Plumbago zeylanica (Plumbaginaceae)

Common name: Indian Leadwort

Vernacular Name: Kodiveli

Part used: Root

Phytochemical constituents: It contains plumbagin, 3- chloroplumbagin, 3, 3- biplumbagin, binaphthoquinone, isozeylanone, zeylanone, elliptinone and droserone.^{37, 38}

Actions: Anti periodic and Diaphoretic

Indications: It cures dropsy, diarrhoea, worm infestation, anaemia, pricking pain, flatulence, fever due to indigestion, etc., ⁹

Pharmacological activities:

Hepatoproptective activity: Methanolic extract of *Plumbago zeylanica* significantly reversed hepato toxic changes dose dependently, as compared to hepatotoxicant control through its ant oxidative, anti-inflammatory and anti-fibrotic effects against experimentally induced liver toxicity. ^{39, 40, 41}

Anticarcinogenic Activity: Plumbagin is a potent inhibitor of the NF- κ B activation pathway that leads to suppression of NF- κ B-regulated gene products. This explained its cell growth modulatory, anti-carcinogenic and radio-sensitizing effects. ⁴²

7. *Piper longum* (Piperaceae)

Common name: Long pepper

Vernacular Name: Thippili

Part used: Fruit

Phytochemical constituents: Methyl piperine, pipernonaline, piperettine, pellitorine, piperundecalidine, piperlongumine, piperlonguminine, pergumidiene, pipercide, piperderidine, longamide, tetrahydropiperine. Piperine and piperlonguminine. ^{43, 44, 45}

Actions: Stimulant, Carminative

Indications: It cures gastric ulcer, anaemia, fatigue, dyspepsia, abdominal discomfort, worms, etc.⁹

Pharmacological activities:

Hepatoprotective activity: The fruit extract had hepatoprotective action against carbon tetrachloride induced liver damage. Piperine is effective against carbon tetrachloride-induced hepatotoxicity by reducing lipid peroxidation in vitro and in vivo. ^{46, 47}

Anticancer activity: The alcohol extract of *Piper longum* inhibits solid tumour development in mice. ⁴⁸

Antioxidant activity: *Piper longum* exhibits promising antioxidant potential against free radical-induced oxidative damage. Decrease lipid peroxide levels and maintain glutathione content, demonstrating antioxidant activity. ⁴⁹

Anti-inflammatory activity: A marked anti-inflammatory activity of *Piper longum* fruit decoction has been reported using carrageenan induced rat oedema. ^{50, 51}

Antihyperlipidemic activity: The ethanol extract of the *Piper longum* fruit exhibits appreciable antihyperlipidemic activity in vivo. ⁵²

8. Hyoscyamus niger (Solanaceae)

Common name: Henbane seeds

Vernacular Name: Kurosani Omam

Part used: Seed

Phytochemical constituents: It contains alkaloid hyoscyamine, hyoscine, scopolamine, atropine, etc., ^{53, 54, 55} volatile oil, glycoside, albumin, steroidal glycosides (atroposide A, atroposide C, atroposide E), phenolics, (vanillic acid, vanillin, pinoresinol, and N transferuloyltyramine) and phytosterols (daucosterol and beta-sitosterol), etc. ^{56, 57}

Actions: Hypnotic, Sedative, Anodyne, Antispasmodic, Mild diuretic

Indications: It cures dental diseases, mental disorders, tremor, memory impairment, insomnia, cardiomegaly, etc., ⁹

Pharmacological activities:

Cardioprotective activity: *Hyoscyamus niger* proved to protect from the cardiac damage by activation of antioxidant enzymes. ⁵⁸

Anticancer activity: Alkaloidal extract shows anticancer activity.⁵⁹

Antihypertensive: *Hyoscyamus niger* crude extract lowers blood pressure in animal models.

9. Impure Sodium chloride

Common name: Rock salt

Vernacular Name: Indhuppu

This is taken out from earth especially in the North West regions of Punjab and Sind (Pakistan). The out surface is greyish yellow which its inner core is white in colour; saline taste.

Purification: Rock salt is kept soaked in vinegar (leftover rice fermented water) for three days and insolated to get purified and detoxified form.

Chemical constituents: It consists of 95-98% sodium chloride, 2-4% polyhalite (potassium, calcium, magnesium, sulphur, oxygen, and hydrogen), 0.01% fluoride, 0.01% iodine and small amounts of numerous trace minerals.⁶¹

General properties:

Rock salt cures, eight types of gastric ulcer (*Gunmam*), indigestion, blood diseases, constipation, polydipsia, haemorrhoids, abscess, throbbing pain etc.,

Actions: Laxative, Purgative, Carminative, Diuretic, Stomachic

Indications: Hot fomentation of rock salt reduces painful swelling. It is an ingredient of *Indhuppu Chooranam* which cures indigestion, vomiting and ascites.³⁵

Pharmacological activities:

Antioxidant effect: It helps in getting rid of toxic minerals and refined salt deposits by stimulating blood circulation and mineral balance.⁶¹

10. Impure Potassium Carbonate

Common name: Wood salt

Vernacular Name: Evatcharam (Mara uppu)

It is available in the market as white solid chips. It is prepared by reducing to ashes the green spikes of barley, dissolving the ashes in water straining the solution and evaporating it over fire. The resulting salt is a clear amorphous powder with the saline taste.

Synthetic preparation of Impure Potassium carbonate:

Bogar one of the 18 Siddhars who was a pioneer in alchemy and various synthetic preparation of minerals has mentioned about the preparation of *Evatcharam* from ashes of *Hordeum decorticatum* (Barley corn-*Eva gothumai*).³⁵

Chemical constituents: Carbonate of potash ³⁶

Actions: Appetite, Stimulant, Laxative, Diuretics, Anti-inflammatory, Convalescence.

Indications: This is effective in diseases of the anasarca, gastric ulcer, throbbing pain, obesity, indigestion, urinary retention and splenomegaly etc.³⁵

Pharmacological activities:

Anti-microbial activity: It has very high activity against Escherichia coli.⁶²

11. Sodium chloride

Common name: Common salt

Vernacular Name: Kariuppu,

Purification:

It is dissolved in water or vinegar, filtered with a cloth and dried in sunshade.

Chemical constituents: Sodium chloride consists of sodium and chloride ions are in the ratio of 1:1. It is commonly called *table salt or common salt*. Seawater is a major source of this salt. The chemical formula of Sodium chloride is NaCl. It is an ionic compound which consists of a chloride anion (Cl⁻) and a Sodium cation (Na⁺). 63

Actions: Stomachic, Laxative, Anthelmintic, Febrifuge

Indications: It is effective in the treatment of liver disorders, flatulence, pricking pain, loss of taste, gastric ulcer, dryness of tongue, constipation etc. ³⁵

Antibacterial agent: It is a good antibacterial agent which prevents bacteria from developing and multiplying. ⁶⁴

Anti - Microbial activity:

The antimicrobial properties were proved against *Escherichia coli*, *Salmonella typhimurium*, *Listeria monocytogenes*, *Staphylococcus aureus and Clostridium perfringens*.⁶⁵

CONCLUSION AND FUTURE DIRECTIONS:

The entire world is in search of a potent liver treatment. There are very few safe and efficacious hepatoprotective drugs available in modern medicine. Though there are a lot of Siddha herbal and poly herbal formulations to treat liver disease effectively, many drugs are not scientifically validated so for. Hence, a need for scientifically validated potent herbal liver tonic at the same time safe and cost effective. The existing literature information about the Siddha herbomineral formulation Saman Chooranam is said to be hepatoprotective, hepato curative and anti-oxidant activities. Each ingredient of Saman Chooranam showed hepato protective effect confirmed by various scientific evidence. The detailed research on Saman chooranam includes phytochemical, physicochemical, biochemical and pharmacological studies is under process. Based on the results the clinical trial will be initiated.

ACKNOWLEDGEMENT:

Authors are thankful to all the faculties, Department of pharmacology, Govt. Siddha medical college, Chennai – 106 and The Tamil Nadu Dr.M.G.R. Medical University, Guindy, Chennai, for their guidance and encouragement provided for conducting this review article.

CONFLICTS OF INTEREST:

The authors have no conflicts of interest to share.

REFERENCES:

- Suk KT, Kim DJ. Drug-induced liver injury: present and future. ClinMolHepatol. 2012; 18(3): 249e57. PMID: 23091804.
- Intelligent Data Communication Technologies and Internet of Things. Proceedings of ICICI 2020. Germany: Springer Nature Singapore. 2021; p. 66.

- EASL–EORTC Clinical Practice Guideline Management of hepatocellular carcinoma. J Hepatol. 2012; 56: 908–943.
- Prema S. Agasthiyar Vaithya Chinthamani Venba 4000' Ennum Mani 4000, Part –1. Pari printers, Thamarai Nooolagam. Edition I. 1996 March; p.178.
- Deva Asirvatham Samuel. Marunthu Sei Ilyalum Kalaiyum. Department of Indian Medicine & Homeopathy, Chennai -106. Reprinted 2014; p.110
- Takeoka G. Volatile constituents of Asafoetida. In: Takeoka G.R., Guntert M., Engel K.-H., editors. Aroma Active Compounds in Foods. American Chemical Society; Washington, DC: 2001. p. 33–44.
- Iranshahy M., Iranshahi M. Traditional uses, phytochemistry and pharmacology of asafoetida (*Ferula asafoetida* oleo-gum-resin) – a review. JEthnopharmacol. 2011; 134: 1–10. [PubMed] [Google Scholar]
- Iranshahi M., Amin G., Salehi Sourmaghi M., Shafiee A., Hadjiakhoondi A. Sulphurcontaining compounds in the essential oil of the root of *Ferula persica* willd. var. *persica*. Flavour Frag J. 2006; 21: 260–261. [Google Scholar]
- Murugesa Mudhaliyar K.S. *Gunapadam Mooligai Vaguppu*. Dept. of Indian Medicine and Homeopathy, Reprinted Edition 6th 2003: 710, 206, 470, 806, 424, 383, 514, 176.
- 14. Soni KB, Rajan A, Kuttan R. Inhibition of aflatoxin-induced liver damage in ducklings by food additives. Mycotoxin Res 1993; 9: 22-7.
- 15. Sarkisyan RG. Effect of *Ferula* on arterial pressure. Meditsinskii Zhurnal Uzbekistana 1969; 9: 23-4.
- 16. Mallikarjuna GU, Dhanalakshmi S, Raisuddin S, Rao AR. Chemomodulatory influence of *Ferula asafoetida* on mammary epithelial differentiation, hepatic drug metabolizing enzymes, antioxidant profiles and N-methyl-Nnitrosourea induced mammary carcinogenesis in rats. Breast cancer research and treatment. 2003 Sep; 81 (1): 1-10.
- 17. Khan M U, Khalilullah H, Akhtar J, Osman Elhasan G, *Terminalia chebula*. An Ephemeral Glance. Int J Pharm Sci. 2014; Vol 7 (2): 40-43.
- Tasduq SA, Singh K, Satti NK, Gupta DK. *Terminalia chebula* (fruit) prevents liver toxicity caused by sub-chronic administration of rifampicin, isoniazid and pyrazinamide in combination. Hum Exp Toxicol. 2006; 25: 111-8.
- 19. Saleem A, Husheem M, Harkonen P, Pihlaja K. Inhibition of cancer cell growth by crude extract and the phenolics of *Terminalia chebula retz* fruit. J Ethnopharmacol 2002; 81: 327-36.
- 20. Sabu MC, Kuttan R. Anti-diabetic activity of medicinal plants and its relationship with their antioxidant property. J Ethnopharmacol 2002; 81: 155-60.

- Saleem MA, Pihlaja K. Total phenolics concentration and antioxidant potential of extracts of medicinal plants of Pakistan. Z Naturforsch 2007; 56: 973-8.
- 22. Naik GH, Priyadarsini KI, Bhagirathi RG. Banavalikar. In vitro antioxidant studies and free radical reactions of Triphala, an Ayurvedic formulation and its constituents. Phytother Res 2009; 19: 582-6.
- 23. Malekzadeh F, Ehsanifar H, Shahamat M, Levin M. Antibacterial activity of black myrobalan (*Terminalia chebula Retz*) against Helicobacter pylori. Int J Antimicrob Agents 2010; 18: 85-8.
- 24. Tamhane MD, Thorat SP, Rege NN, Dahanukar SA. Effect of oral administration of *Terminalia chebula* on gastric emptying: An Experimental Study. J Postgrad Med 2007; 43: 93-5.
- Tahreem K, Sadaf A, Entesar H, MiffthaY, Shimaa M H. Aboelnaga Z R. and Azaz Ahmad A, Therapeutic Role of Ginger (*Zingiber officinale*) – A Review. JPRI. 2021; 33(29B): 9-16. Article no. JPRI.67538.
- 26. Yemitan OK, Izegbu MC. Protective effects of *Zingiber officinale (Zingiberaceae)* against carbon tetrachloride and acetaminophen induced hepatotoxicity in rats. Phytother Res 2006; 20: 997-1002.
- 27. Ajith TA, Nivitha V, Usha S. Zingiber officinale Roscoe alone and in combination with alpha-tocopherol protect the kidney against cisplatin-induced acute renal failure. Food Chem Toxicol 2007; 45: 921-7.
- 28. Yagihashi S, Miura Y, Yagasaki K. Inhibitory effect of gingerol on the proliferation and invasion of hepatoma cells in culture. Cytotechnology. 2008; 57: 129-36.
- 29. Fuhrman B, Rosenblat M, Hayek T, Coleman R, Aviram M. Ginger extract consumption reduces plasma cholesterol, inhibits LDL oxidation and attenuates development of atherosclerosis in atherosclerotic, apolipoprotein E-deficient mice. J Nutr 2000; 130: 1124-231.
- Rao CB, Venkateswarlu V. Chemical Examination of *Embelia ribes*. I. Isolation of a New Constituent,-Vilangin || Its Constitution and Synthesis. The Journal of Organic Chemistry. 1961 Nov; 26 (11): 4529-32.
- 31. Haq K, Ali M, Siddiqui AW. New compounds from the seeds of *Embelia ribes* Burm.
 Die Pharmazie-An International Journal of Pharmaceutical Sciences. 2005 Jan 1; 60 (1): 69-71.
- 32. Indrayan AK, Sharma S, Durgapal D, Kumar N, Kumar M. Determination of nutritive value and analysis of mineral elements for some medicinally valued plants from Uttaranchal. Current science. 2005 Oct 10: 1252-5.

- 33. Lin P, Li S, Wang S, Yang Y, Shi J. A nitrogen-containing 3-alkyl-1, 4-benzoquinone and a gomphilactone derivative from *Embelia ribes*. Journal of natural products. 2006 Nov 27; 69(11): 1629-32.
- Latha C. Microwave-assisted extraction of embelin from *Embelia ribes*. Biotechnology letters. 2007 Feb; 29(2): 319-22.
- 35. Haq K, Ali M, Siddiqui AW. New compounds from the seeds of *Embelia ribes* Burm. Die Pharmazie-An International Journal of Pharmaceutical Sciences. 2005 Jan 1; 60(1): 69-71.
- 36. Nazam Ansari M, Bhandari U, Islam F, Tripathi CD. Evaluation of antioxidant and neuroprotective effect of ethanolic extract of *Embelia ribes Burm* in focal cerebral ischemia/reperfusion-induced oxidative stress in rats. Fundamental & clinical pharmacology. 2008 Jun; 22 (3): 305-14.
- 37. Chitra M, Sukumar E, Suja V, Devi S. Antitumor, anti-inflammatory and analgesic property of embelin, a plant product. Chemotherapy. 1994; 40(2): 109-13.
- 38. Bhandari U, Jain N, Pillai KK. Further studies on antioxidant potential and protection of pancreatic β-cells by *Embelia ribes* in experimental diabetes. Experimental Diabetes Research. 2007 Jan 1; 2007.
- Anaivaari Anandan R, Thulasimani M. Siddha Materia Medica (Mineral and animal section). Department of Indian Medicine & Homoeopathy, Chennai 106. Edition 1. 2008. p. 317.
- 40. Nadkarni K M. Indian Materia Medica. With Ayurvedic, Unani, Tibbi, Siddha, Allopathic, Homeopathic, Naturopathic and Home Remedies, Appendices and indexes. Printed in India. Tarun Enterprises, Delhi. Reprinted 2002; Vol -2. p.101, 89.
- 41. Satyavati GV, Gupta AK and Tondon N: Medicinal plants of India. Indian Council of Medical Research, New Delhi, 1st ed. (vol.2), 1987.
- 42. Kapoor LD: Handbook of Ayurvedic Medicinal plants. CRC Press, London, 1990
- 43. Rohit Goyal and Pyare Lal Sharma. Possible Mechanism of *Plumbago zeylanica* in Prevention of Hepatic Damage in Wistar Rat. American Journal of Pharmacology and Toxicology. 2012; 7 (3): 101-108.
- 44. Chen YC, Tsai WJ, Wu MH, Lin LC and Kuo YC. Suberosinn inhibit proliferation of human peripheral blood mononuclear cells through the modulation of the transcription factor NF/AT and NF/Kappa. British Journal of Pharmacology. 2007 Feb; 150 (3): 298-312.
- 45. Tilak JC, Adhikari S, Devasagayam TP. Antioxidant properties of *Plumbago zeylanica*, An Indian Medicinal Plant and Its Active Ingredient, Plumbagin. PMID: 15479566 [PubMed indexed for MEDLINE].

- 46. Sandur SK, Ichikawa H, Sethi G, Ahn KS and Agrawal BB. Plumbagin (5-hydroxy- 2methyle-1, 4-naphthoquinone Suppress NF-κB Activation and NF–κB-regulated gene product through modulation of p65 and Ικβα kinase activation, leading to potention of apoptosis induced by cytokine & chemotherapeutic agent. Journal of Biology and Chemistry. 2006 Jun; 281(25): 17023-17033.
- 47. Kirtikar KR, Basu BD. Indian Medicinal Plants. Mumbai, India: Orients Longman. 1980: 21–8.
- 48. Rastogi RP, Malhotra BN. Compendium of Indian Medicinal Plants. CDRI. Luckhnow and New Delhi, India. Nisc 1993; 504–857.
- 49. Suresh Kumar, Jitpal Kamboj, Suman, Sunil Sharma, Overview for Various Aspects of the Health Benefits of *Piper Longum Linn*. Fruit. J Acupunct Meridian Stud. 2011; 4(2): 134 140.
- 50. Koul IB, Kapil A. Evaluation of the liver protective potential of piperine. An active principle of black and long peppers. Planta Med 1993; 59: 413–7.
- Christina AJ, Saraswathy GR, Robert SJ, Kothai R, Chidambaranathan N, Nalini G, et al. Inhibition of CCl4 induced liver fibrosis by *Piper longum Linn*. Phytomedicine 2006; 13: 196–18.
- 52. Anuradha V, Srinivas PV, Rao JM. Isolation and synthesis of isodihydropiperlonguminine. Nat Prod Res 2004; 18: 247–51.
- 53. Natarajan KS, Narasimhan M, Shanmuga sundaram KR, Shanmuga sundaram ER. Antioxidant activity of a salt/ spice/herbal mixture against free radical induction. J Ethnopharmacol 2006; 105: 76–83.
- 54. Kumar S, Arya P, Mukherjee C, Singh BK, Singh N, Parmar VS, et al. Novel aromatic ester from *Piper longum* and its analogues inhibit expression of cell adhesion molecules on endothelial cells. Biochemistry 2005; 6; 44: 15944–52.
- 55. Choudhary GP. Mast cell stabilizing activity of *Piper longum Linn*. Indian J Allergy Asthma Immunol. 2006; 20: 112–6.
- 56. Jin Z, Borjihan G, Zhao R, Sun Z, Hammond GB, Uryu T. Antihyperlipidemic compounds from the fruit of *Piper longum L*. Phytother Res 2009; 23: 1194–6.
- 57. Paulsen BP. Highlights through the history of plant medicine. In: Bernhoft A, editor. Bioactive Compounds in Plants-Benefits and Risks for Man and Animals. Oslo: Proceeding from a Symposium Held at the Norwegian Academy of Science and Letters; 2010.
- 58. Li R, Reed DW, Liu E, Nowak J, Pelcher LE, Page JE, et al. Functional genomic analysis of alkaloid biosynthesis in *Hyoscyamus niger* reveals a cytochrome P450 involved in littorine rearrangement. Chem Biol 2006; 13: 513-20.

- 59. Bernhoft A. A brief review on bioactive compounds in plants. In: Bioactive Compounds in Plants-Benefits and Risks for Man and Animals. Oslo: Proceedings from a Symposium Held at the Norwegian Academy of Science and Letters; 2010.
- 60. Begum S, Sahai M, Sussmuth R, Asai T, Hara N, Fujimoto Y. Hyosgerin (I), a new optically active coumarinolignan, from the seeds of *Hyoscyamus niger*. Chem Pharm Bull 2006; 54: 538-41.
- 61. Ma CY, Liu WK, Che CT. The flowering hormones. BerDtsch Bot Ges. 2002; 57: 29-48.
- 62. Vallabi DE, Elango V. Preliminary studies on cardio protective effect of *Hyoscyamus niger Linn* in male albino rats. J Chem Pharm Res 2016; 8: 860-4.
- 63. Ma CY, Liu WK, Che CT. Lignanamides and non-alkaloidal components of *Hyoscyamus niger* seeds. J Nat Prod 2002; 65: 206-9.
- 64. Khan AU, Gilani AH. Cardiovascular inhibitory effects of *Hyoscyamus niger*. Methods Find Exp Clin Pharmacol 2008; 30: 295-300.
- 65. Apurbo S, Arittra G, Kinsuk S, Debojyoti B and Prof. Dr. Dhrubo Jyoti Sen, Halite; The Rock salt. Enormous Health Benefits. WJPR. 2016; 5 (12): P.407-416.
- 66. Şahin Ö, MelihaBurcu G, Hayreddin G, Mustafa C and Yakup B, Potassium carbonate mediated one-pot synthesis and antimicrobial activities of 2-alkoxy-4-(aryl)-5Hindeno [1,2- b]pyridine-3-carbonitriles, ACG Publications. Org. Commun. 2016; 4; 9: 125-132.
- 67. Sodium-chloride, chemistry, preparation, properties and uses, https://byjus.com/chemistry/preparation-properties-and-uses-of-sodium-chloride/
- 68. What is Sodium Chloride? Definition, Preparation, Properties, Uses, https://www.geeksforgeeks.org/what-is-sodium-chloride-definition-preparationproperties-uses/Last Updated: 17 Mar, 2022.
- Winker JJ, Koop G, Lipman LJ. Antimicrobial properties of salt (NaCl) used for the preservation of natural casings. Food Microbiol. 2006 Oct; 23(7): 657-62. doi: 10.1016/j.fm.2005.11.004. Epub 2006 Jan 10. PMID: 16943065.

