Journal of Pharmacognosy and Phytochemistry

Available online at www.phytojournal.com

E-ISSN: 2278-4136
P-ISSN: 2349-8234
JPP 2019; 8(2): 155-162
Received: 21-01-2019
Accepted: 25-02-2019

Riyas CT
Department of Botany, University of Kerala, Kariavattom, Thiruvananthapuram, Kerala, India

Arun R Pillai
Department of Botany, University of Kerala, Kariavattom, Thiruvananthapuram, Kerala, India

Kamarudeenkunju M
Department of Botany, University of Kerala, Kariavattom, Thiruvananthapuram, Kerala, India

TS Swapna
Department of Botany, University of Kerala, Kariavattom, Thiruvananthapuram, Kerala, India

Correspondence
TS Swapna
Department of Botany, University of Kerala, Kariavattom, Thiruvananthapuram, Kerala, India

A review on phytochemical, ethnomedicinal and pharmacological studies of genus *Pittosporum* (Pittosporaceae), in India

Riyas CT, Arun R Pillai, Kamarudeenkunju M and TS Swapna

Abstract
Pittosporum is a genus of family Pittosporaceae, which includes approximately 200 species having world wide distribution and the richest concentration is in Australia and China. In India only 11 species were reported till date. Among these, 7 species have been explored for its phytochemical compounds. In this review phytochemical, pharmacological and ethnomedicinal properties of the genus *Pittosporum*, in India has been evaluated and documented with maximum available data from journals, thesis, and various books. So far 26 principle compounds were isolated from the four species of the genus *Pittosporum*. Most of them belongs to the class of essential oils followed by glycosides and diterpenes. A highly promising compound Isosteviol isolated from the *P. tetraspermum* has anti-microbial as well as anti-biofilm activity. Methanolic extract of different species of *Pittosporum* bark showed promising antimicrobial, anti-inflammatory, antioxidant and hepatoprotective activity. The different species have been used traditionally for ethnomedicinal purpose especially for eczema, arthritis, diabetic, diuretic, chest pain and antidote of snake bite etc. Hence, in this review an attempt was made to analyse and review the information generated through pharmacological studies of phytoconstituents from the genus *Pittosporum* distributed in different parts of India.

Keywords: phytochemistry, essential oils, pharmacology, isosteviol, *Pittosporum*

Introduction
Pittosporum is the genus of the family Pittosporaceae which consists of approximately 200 species in the world [1]. The family Pittosporaceae includes trees, shrubs, and lianas with nearly about 200 species that included in 9 genera. In India, the family is represented only by one genera, *Pittosporum* which contains eleven species such as *Pittosporum anamallayense*, *P. ceylanicum, P. dasycaulon, P. eriocarpum, P. ferrugineum, P. humile, P. neelgherrense, P.* podocarpum, *P. tetraspermum, P. viridulum* and *P. wightii* [2].
The history of the genus *Pittosporum* began from the specimen collected and defined by Joesph Banks from New Zealand. The generic name derived from the Greek word "*Pitta"*, pitch, and "*sporos"* defining the 'seeds' which are enveloped by resinous pulp. During his expedition to Japan, Kaempfer collected the first member of this genus which was scientifically studied by European botanists for the first time. The genus is mainly concentrated in Australia, but China has the richest concentrations of species in Asiatic continent. In India most of the species were known by the mid-19th century and a Scottish botanist William Roxburg recorded the species in Flora of Indica [3] as the genus *Celastrus*, for first time where the botanist Wight observed *Celastrus* as the genus *Pittosporum* [4]. It is commonly known as 'cheese woods'. Gondwana is probably considered as the origin of the genus *Pittosporum*. Now it is distributed in parts of Australia, Eastern Asia and some parts of Africa [5].
Different species of *Pittosporum* were widely used for medicinal purposes. Flower, root, bark and leaves were used traditionally against inflammations, arthritis, snake poison, rheumatic swelling, chronic bronchitis etc [6]. Phytochemical screening of several *Pittosporum* species had been started from the last decades. From this investigations, several physiologically potent chemical constituents such as triterpenoids, flavinoids, glycosides, sesquiterpenes, saponins, carotinoids and essential oils were reported [7, 8]. The different parts of the plants such as root, bark, leaves and flowers of the genus *Pittosporum* were used as anti-inflammatory as well as anti-septic drug and also used for rheumatic disorders as reported by Wetson [9, 10]. Several phytochemical studies emphasized the genus *Pitosporum* having wide range of pharmacological actions such as anti-oxidant, anti-inflammatory, anti-cancer, anti-microbial, etc. [11]. The different species of *Pittosporum*. (*P. dasycaulon and P. floribundum*) were used against inflammation and an anti-dote for snake poison etc [12, 13]. (Table; 1).

Among the eleven Species reported in India phytochemical investigations are confined to seven species. In the present review an effort is being made to retrieve maximum available data based on the phytochemical works of the seven species in genus *Pittosporum* from the available literature and assess its important potential phytochemical constituents with respect to their pharmacological actions.

Table 1: Ethnomedicinal values of selected species of the genus Pittosporum

Sl. No.	Binomial nomenclature	Local name	IUCN status	EthnomedIcinal Uses	References
1.	*P.floribundum*	Rakamuki	Not evaluated	Antidote of snake poison, arthritis and chest pain	[14, 15]
2.	*P. eriocarpum*	Agni	Endangered	Diabetes and bronchitis etc	[16,14]
3.	*P. tetraspermum*	Analivegam Kachapatta Suneri	Endangered	Chronic bronchitis, rheumatism, leprosy, snake poison, secondary syphilis, chest infections	[17, 18]
4.	*P. dasycaulon*	Kasumaram Boogri	Not evaluated	Anti-dote of snake poison, chronic bronchitis, Intestinal diseases etc.	[19]
5.	*P. neelgherrense*	Analivegam	Not evaluated	Anti dot of snake poison and bowel complaints	[20, 11]
6.	*P. ferrugineum*	Un known	not evaluated	Leaves and fruits used against fish poison	[11]

1.1 Distribution pattern in India

The members of *Pittosporum* are mainly found in rain forest, usually at altitudes between 500-2800 m which covers Western Ghats and Himalayan regions. *P. anamallayense, P. ceylanicum, P. dasycaulon, P. neelgherrense, P. tetraspermum, P. viridulum and P. wightii* were are commonly found in peninsular India and *P. anamallayense, P. dasycaulon, P. neelgherrense, P. viridulum* are are endemic to the Western Ghats [21]. *P. eriocarpum* and *P. humile* were recorded as endemic to Himalaya [4].

1.2 Systematic position of the genus Pittosporum

Kingdom : Plantae
Division : Magnoliophyta
Class : Magnoliopsida
Order : ApialesNakai.
Family : Pittosporaceae R. Br.
Genus : *Pittosporum* Banks ex Soland

1.3 List Pittosporum species in India

1. *P. anamallayense* M. P. Nayar & G. S. Giri
2. *P. ceylanicum* Wight
3. *P. dasycaulon* Miq.
4. *P. eriocarpum* Royle
5. *P. ferrrugineum* W. T. Aiton
6. *P. floribundum* Wight &Arn.
7. *P. humile* Hook. F. & Thomson
8. *P. neelgherrense* Wight &Arn.
9. *P. podocarpum* Gagnep
10. *P. tetraspermum* Wight &Arn.
11. *P. viridulum* M. P. Nayar, G. S. Giri & V. Chandradas

1.4 Discription

The members of the genus are tree or large shrub or climbers, growing 2- 30 m tall, commonly with lenticels or resin canals. Leaves are simple, entire, rarely lobed and spirally arranged around the stem. Flowers are hermaphrodite, complete, actinomorphic, and solitary and found in racemose as corymb or umbel inflorescence. Sepals and petals are five each, and flowers are sweetly scented. Fruit is a capsule with many seeds which are enveloped by resinous pulp. Several species of the genus is aromatic with fragrant flowers and hence are cultivated in gardens.

2. Materials and Methods

The information regarding the pharmacological, ethno medicinal and isolated phytoconstituents of selected plants are retrieved from the reported online data, thesis, websites, and other accessible journals. A comprehensive investigation was under taken for this work during the time 2018. The work reported from time period 1951- 2018 were collected for the review.

3. Phytochemical constituents

Phytoconstituents like terpenoids, flavonoids, lignans, coumarins, saponins, and carotenoids from traditional herbs are sources of many therapeutic drugs for different kinds of diseases [22, 23, 24].

The preliminary phytochemical screening of different species of *Pittosporum* were reported by many authors. Different types of phytoconstituents like flavonoids, phenols, alkaloids, lignins, antroquinones, steroids, tannins, saponins, fixed oils and glycosides were reported from *Pittosporum* [14,19]. Phenolic compounds are principle plant compounds with potential biological activities due to its redox potential, hence it exhibit diverse biological activities including anti-cancerous, anti-inflammatory [25] properties. Anticancerous potential of the plant could be due to its phenolic compounds having ability to neutralize the free radicals [26, 27]. In most of the selected species, it is observed that only preliminary phytochemical analysis were reported, where as in *P. neelgherrense* and *P. viridulum* detailed investigations on essential oil from leaves and fruits has been studied. Only in *P. dasycaulon* detailed studies on phytochemical constituent's hves been reported [5].

By analyzing the available data of the selected *Pittosporrum* species, details regarding the name of phytochemical constituents and it source of accumulation is represented in Table; 2.

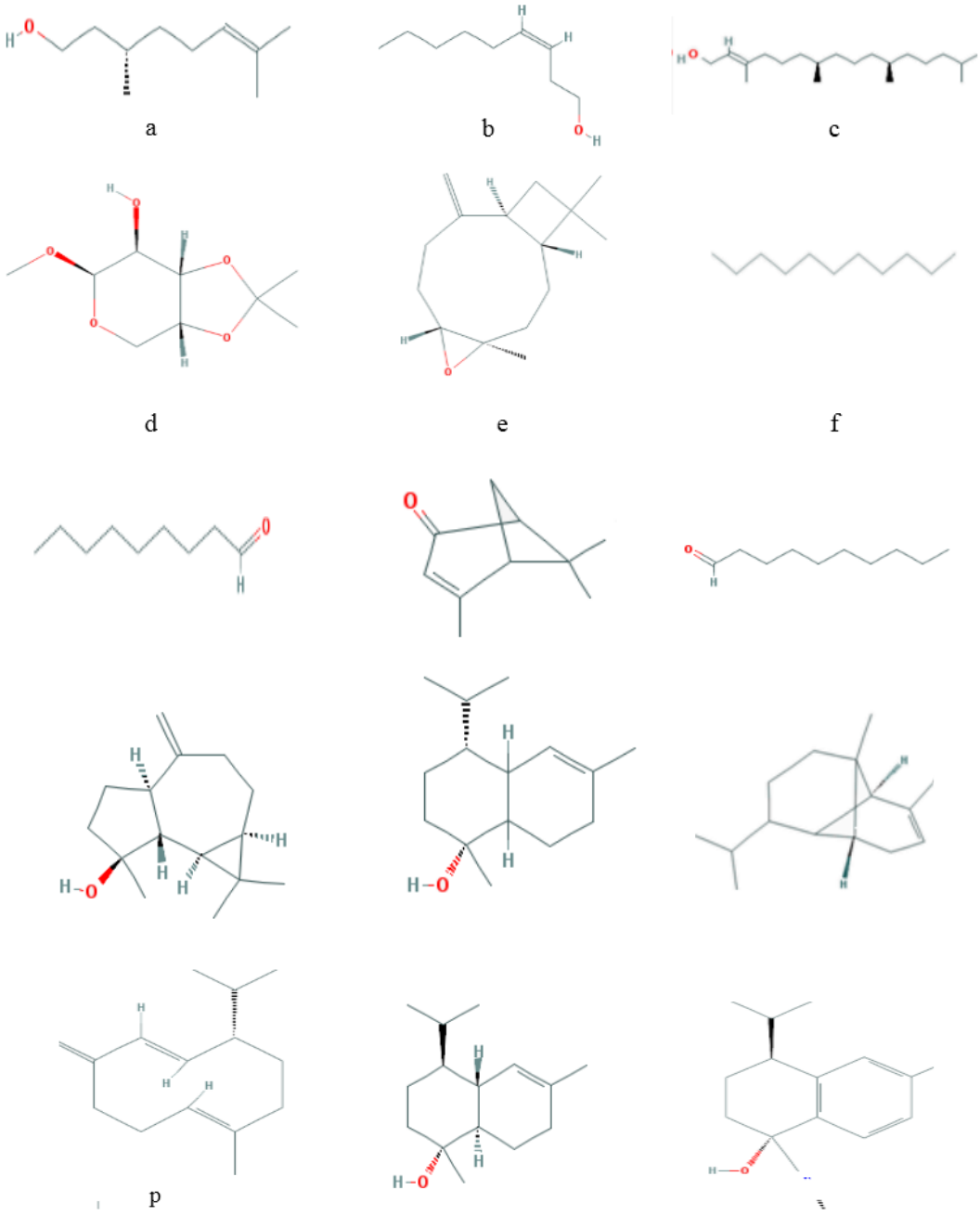
Table 2: phytochemical constituents of investigated species in Pittosporum

Sl no	Phytoconstituents	Class	Plant species	Source	References
1.	Cis-3- nonene -1-ol	Alkenes	*P. dasycaulon*	Stem bark	[28]
2.	Beta-citronellon	Monoterpenes	*P. dasycaulon*	Stem bark	[28]
3.	Phytol	Diterpene alcohol	*P. dasycaulon*	Stem bark	[28]
4.	β- 1 arabinopyranoside	Glycosides	*P. dasycaulon*	Stem bark	[28]
5.	1,2 bis benzene	Hydrocarbons	*P. dasycaulon*	Stem bark	[28]
6.	Isosteviol	Diterpene	*P. tetraspermum*	Stem bark	[18]

7.	Carophyllene oxide	Essential oils	*P. neelgherrense*	Leaves and fruits	[11]
8.	Undecane	Essential oils	*P. neelgherrense*	Leaves and fruits	[11]
9.	Nonanal	Essential oils	*P. neelgherrense*	Fruit	[11]
10.	Verbenon	Essential oils	*P. neelgherrense*	Fruit	[11]
11.	Decanal	Essential oils	*P. neelgherrense*	Fruit	[11]
12.	β- pinane	Essential oils	*P. neelgherrense*	Fruit	[11]
13.	β- selinene	Essential oils	*P. neelgherrense*	Fruit and leaves	[11]
14.	α- cardinal	Essential oils	*P. neelgherrense*	Fruit and leaves	[11]
15.	β- atlandol	Essential oils	*P. neelgherrense*	Fruit and leaves	[11]
16.	caryophyllene oxide	Essential oils	*P. viridulum*	Leaves	[29]
17.	Spathulenol	Essential oils	*P. viridulum*	Fruit and leaves	[29]
18.	Epi α muurolol	Essential oils	*P. viridulum*	Leaves	[29]
19.	Undecane	Essential oils	*P. viridulum*	Leaves	[29]
20.	α-copaene	Essential oils	*P. viridulum*	Fruit and leaves	[29]
21.	germacrene D	Essential oils	*P. viridulum*	Fruit	[29]
22.	α-cadinol	Essential oils	*P. viridulum*	Fruit and leaves	[29]
23.	*trans*-calamenen-10-ol	Essential oils	*P. viridulum*	Fruit	[29]
24.	δ−cadinene	Essential oils	*P. viridulum*	Fruit	[29]
25.	β- elemene	Essential oils	*P. viridulum*	Leaves	[29]
26.	Cyclocolorenone	Essential oils	*P. viridulum*	Fruit	[29]

4. Pharmacology of Isolated compounds

The reported pharmacological uses and structure of the phytoconstituents were shown below in Figure 1



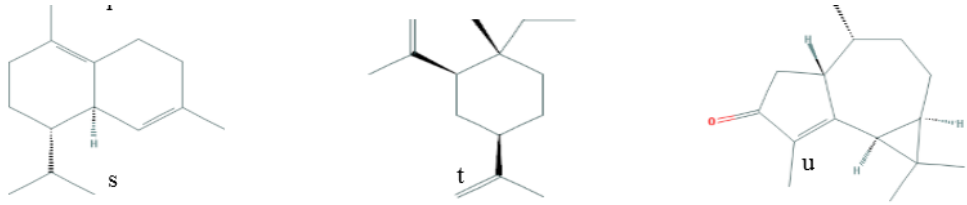


Fig 1: showed the structural elucidation of identified compounds; a- Beta- citronellon [30] b; Cis- 3- nonene- 1- ol [31].c. Phytol [32]. d. β- 1 arabinopyranoside [33].e; caryophyllene oxide [34]. f;Undecane [35]. g; Nonanal [36]. h; Verbenone [37]. i- Decanal [38]. j- betapinene [39]. k- betaselinene [40]. l- Isosteviol [41]. m- Spathulenol [42]. n- Epialfamuurolol [43]. o- α-copaene [44]. p- GermaceneD [45].q; α-cadinol [46]. r- Trans-calamenen- 10- ol [47]. s- deltacadinene [48]. t; βelemene [49]. u; cyclocolorenone [50].

4.1 Isosteviol
Acid hydroxylation of steviosides forms isosteviol [51]. It is keto sugar 200 times sweeter than the sugar naturally obtained from the leaves of *Stevia rebaudiana* [41]. Hence it is used as natural sweetener in Japan and Brazil [52]. Several studies reported that it inhibit Human DNA polymerase and topoisomerase 1[41], hence can be used as anti tumour agents and anti- inflammatory agent [53]. Anti- inflammatory effect of Isosteviol can reduce ischaemia/ reperfusion injury in rat brains and heart by inhibiting calcium uptake in membranes of heart cells [54]. Isosteviole showed anti hyperglycemic activity because it helps to reduces plasma glucose level in fatty liver cells of rat [55].

4.2 Caryophyllene oxide
Beta caryophyllene and its oxide obtained from the leaves of *Laurusnovo canariensis* showed significant repellent activities against *Anopheles gambier* [56]. It induces glutathione S transferase enzyme activity which helps for the detoxification in liver and intestine of mouse [57]. Caryophyllene oxide has been reported with anti-inflammatory activity by decreasing the level of nitric oxide suppression along with its analgesic activity [58].

4.3 α-copaene
It is the general name of oily liquid hydrocarbons with tricyclic sesquiterpenes. α-copaene was first isolated from the resin producing tropical tree *Copaiba*. The studies about alfacopaene revealed anti-genotoxicity (prevent damages of genes for protecting genetic information) effect and it significantly exhibited anti-oxidant capacity in human lymphocytes *in vitro* [59].

4.4 Germacrene D
It is a class of volatile sesquiterpenes which showed anti-fungal and insecticidal property [45] and play an important role as insect pheromones [60]. Antioxidant property of germacrene D by scavenging super oxide ions was established well by Dickson which may be due to the action of its cyclic moiety [61].

4.5 βelemene
Belemene is one of the predominant essential oil constituent found in *Curcuma zedoaria* with anti-microbial property [62]. It induces cell cycle arrest by inhibiting G2/ M phase and apoptosis hence, studies revealed that beta elemene showed anti tumour effect [63, 64]. Development of scar tissues in an organ or tissues in response to injury or repair is known as fibrosis [11]. In liver it mainly occur due to impairment in the repair system of hepatic tissue. Investigation revealed that beta elemene has been reported anti- fibrotic effect by interacting with Angiotensinogen 2 enzymes [65].

5. Pharmacogical Property of Pittosporum
5.1 Antioxidant activity (Free radical scavenging property)
Metabolic reaction in animal system usually end up with a highly reactive molecules such as super oxide anion, hydroxyl radicals and hydrogen peroxide which are called as free radicals or reactive oxygen species (ROS) [28]. They have several detrimental effects on other biomolecules which alters the normal physiological process. Anti-oxidants are compounds that are involved in scavenging these free radicals and thereby protecting other vital molecules of the living system [19]. The antioxidant molecules can helps directly or indirectly to scavenging free radicals by inducing the activity of scavenging enzymes or induce non-enzymatic compounds like vitamin E, and C [61]. Anti-oxidant property were reported in *Pittosporum* species like *P. eriocarpum* [16]. *P. dasycaulon* and *P. floribundum* [15]. Free radicle scavenging property was determined in the methanolic and ethanolic leaf extract of *P. eriocarpum* by using DPPH assay, using ascorbic acid as standard by Semwal [8, 16]. In the assay maximum radicle scavenging property was observed in methanolic extract followed by ethanolic extract [8]. Antioxidant activity of methanolic and aqueous extract of stem bark of *P. dasycaulon* were assessed and was proportionally effective with its concentration. Nitric oxide scavenging property was also reported in *P. dasycaulon*, which indicated higher nitric acid scavenging potential of aqueous extract than methanolic extract [19].

5.2 Anti-inflammatory activity
Inflammation is the series of tissue responses of living body against pathogens, injuries or diseased conditions. These mechanisms consisting of extravagations of fluids, plasma and affected inflammatory cells in to the affected tissues. During the inflammation different types of chemicals are produced primarily by phagocytic cells, such as histamine, free radicals, prostaglandins and serotonin. Dilation of blood vessels is another sign of inflammatory responses. Some chemical compound (Aspirin) used against these kind of inflammations are said to be antiinflammatory drugs [15]. Different plant species having potential anti-inflammatory activity were investigated and reported. Phyto constituent can be considered as valid drugs only after passing through rigorous evaluation processes for its efficacy and safety. For this purpose methanolic extracts of plant parts such as bark of stem, root and leaf of *Pittosporum tetraspermum* were evaluated using, Phenylbutazone as standard. Plant extract exhibited high suppressant activity against carrageenan induced edema in albino rat. The methanolic extract of bark of *P. teraspermum*i induced significant reduction in the edema level with increasing dosage [17]. The methanolic bark extract of *P. floribundum* showed significant dose dependent antiinflammatory action against carrageenan induced odema in rat. In these investigations methanolic bark extracts showed

57% of inhibition compared to standard drug diclofenac sodium which showed 53% of inhibition against carrageenan induced *in vitro* inflammation [15].

5.3 Anti-microbial activity

According to World Health Organization, current classes of antibiotics are insufficient to resist growing threats of microbial resistance. Number of newly discovered antibiotics are modified versions of existing class of antibiotics. Due to this reason some kind of pathogens can withstand those kinds of antibiotics. Hence, scientific world focus on urgent need of identification of new anti-microbial products especially against gram negative bacteria, multi drug resistant strains and many antibiotic resistant infections including Tuberculosis [66]. In everyday life, plants have been used worldwide to treat several diseases due to its viable options [67]. The use of natural compounds as anti-biotic was started at the time of 2nd World War. Microbial derived Penicillin and Streptomycine were commonly used in those days. Now a day's plant derived compounds were also used as anti-microbial agents. Many scientific studies pointed out therapeutic potential of secondary metabolites in plants [68]. Among the *Pittosporum* spp. in India 7 species such as *P. floribundum, P. dasycaulon, P. neelgherense, P. ferrugeneum, P. tetraspermum, P. eriocarpum and P. viridulum* were reported to have anti- microbial compounds. Methanolic extracts of all parts of *P. floribundum* exhibited better effect against the bacterial strains such as *Bacillus subtilis and E. coli* compared to Ampicillin which was used as control. The methanolic extract of leaf and bark extract *of P. floribudum* showed effective inhibition against two fungal strains such as *Candida albicus and Aspergillus niger* [14].The leaf methanolic and ethanolic extracts of *P. eriocarpum* was also effective against the fungal strains *C. glabrata, C. tropicalis* and *C. albicus.* The aqueous extract of leafs of this species also showed anti-bacterial activity against the strains *Pseudomonas aureus* and *P. Aeruginosa* [16]. By using the disc diffusion methods the anti-bacterial property of *P. neelgherrense and P. viridulum* leaves and fruit oils were analyzed against strains of gram positive bacteria namely *Staphylococcus aureus, Bacillus subtilis, B. Cereus, Salmonella typhi*, and gram negative bacteria like *Pseudomonas fluorescence, P. aerugenosa, Klebsialla pneumonia and E. coli.* From these above investigations on antibacterial activity, leaf oil showed high potential due to the chemical constituents such as undecane and carophyllene oxide [29, 11]. The antibacterial property of *P. ferrugineum* was repeated with Amphicillin as reference drug using Disc diffusion method. The chloroform extract from the plants effectively inhibit the bacterial strains such as *Salmonella typhii*, *Pseudomonas aeruginosa* and *E. coli* [68]. The GC/MS evaluation of *P. dasycaulon* showed the presence of effective phytoconstituents such as Cis- 3 Nonene-1-ol; beta-citronellol, methyl; phytol; urosilic acid; 1,4,2,5, Cyclohexanetetrol and beta- 1- Arabinopyranoside having action against both gram positive and gram negative bacteria namely, *Bacillus cerus* and *Pseudomonas aeruginosa* respectively [28]. Hence, the species can be considered as a good source antibacterial compounds [5]. Isosteviol obtained from the *Pittosporum tetraspermum* showed anti-bacterial activity along with antibiofilm activity [69].

5.4 Ant biofilm activity

Some strains of bacteria is now recognized to have ability to withstand and survive the stress from various sources as including antibiotics, nutrient limitation, heat shock and immune responses of host body. Biofilms forming capacity is one of the main reason behind resistance which, refers to structural aggregation of microbial mass which enveloped in an extra cellular matrix of host cell. Osteomyelitis and Endocarditis are some of the important life threatening infections caused by *Staphylococcus aureus* because of the biofilm formation. So many studies emphasized the significance and repeated the development of therapeutic drugs against biofilm formations [69]. Isosteviol isolated from the plant *Pittosporum tetraspermum* showed *in vitro* anti-biofilm activity against the strains of bacteria such as *E. coli*, *Salmonella*. *typhi*, *Pseudomonas aeruginosa* etc. which was concentration dependent. In this investigation maximum reductions of cell attachment were observed in *P. aeroginosa* at 100 mg/ml concentration [18].

5.5 Hepato protective activity

Liver is the major organ in human body which execute diverse functions including storage of glycogens, fats etc, synthesis, detoxification and secretion, hence its protection must be prioritized [70]. The quest of scientific community for an effective and nontoxic hepatoprotective drug had been mainly focused on plant derived products [71]**.** Silymarin is a previously investigated phyto constituent obtained from *Silybum marianum* (Asteraceae) which was used to treat acute and chronic hepatic diseases [72, 73]. Sylimarin is the combination of lignin and flavanoids [74]. Stem bark of *Pittosporum neelgherrense* showed significant hepato protective effect against the liver damage induced by toxins such as CCl_4, D- GalN, and APAP in rat cells which was confirmed by SGOT and SGPT assay. Histopathological studies indicated that the toxin induced liver damage seems to be reverted in rat group treated with the stem bark extracts and was comparable to group treated with the standard hepato protective compound Silymarin [26].

6. Conclusion

The genus *Pittosporum* includes 300 species which are distributed all over the world. India is reported to have 11 species of the genus with traditional ethanomedicinal values. Among these only 7 species were subjected to preliminary phytochemical and pharmacological analysis by the scientific community. By keeping the available literature from the few species of the genus *Pittosporum,* the investigated studies emphasized that, the so far discovered phytoconstituents have potent biological activities. About 26 predominant compounds were reported in different species of *Pittosporum* in India which includes essential oils, glycosides, alkaloids, flavenoids, alcohols, and phenols. From these compounds essential oils were mostly reported in fruits and leaves of the genus *Pittosporum* which has high potent values. The crude methanolic extract of stem bark showed more biological potent activities. There for, the remaining species of the genus *Pittosporum* should be given more attention for research studies especially focusing on the analysis of phytochemicals along with its pharmacological properties. So far *in vivo* and *in vitro* studies have been conducted using the phytochemical compounds derived from different species of this highly potential genus. Clinical trials should be done ahead which can pave the way to drug development from the bioactive compounds discovered so far.

7. References

1. Mabberley DJ. Mabberley's plant-book: aportable dictionary of plants, their classifications and uses 3 rd ed. Cambridge University Press, 2008.
2. Nayar MP, Giri GS. Fascicles of Flora of India: fascicle 6. Pittosporaceae. Howrah: Botanical Survey of India 15p. Illus., key. Icones. Geog, 1980, 6.
3. Nathaniel Wallich. Flora of indica (William Gary edt.). 1824; 2:39.
4. Gowda M. The genus *Pittosporum* in the Sino-Indian region. Journal of the Arnold Arboretum. 1951; 32:263-301.
5. Bince mani. Bioactivities genetic analysis and conservation of *Pittosporum dasycaulon* Miq Pittosporaceae from the Western Ghats. Thesis, MG University kottayam, chapter. 2015a; 1:1-13.
6. Sharma BD, Balakrishnan NP. Flora of India, Botanical Survey of India. Culcutta. 1993; 2:442- 443.
7. Feng C, Li BG, Gao XP, Qi HY, Zhang GL. A new triterpene and an antiarrhythmic liriodendrin from *Pittosporum brevicalyx*. Archives of pharmacal research 2010; 33: 927-1932.
8. Semwal P, Anthwal P, Kapoor T, Thapliyal A. Preliminary investigation of phytochemicals of *Saussurea obvallata* (brahmkamal) and *Pittosporum eriocarpum* (agni): two endangered medicinal plant species of Uttarakhand. International Journal of Pharmacognosy. 2014; 1; 266-269.
9. Weston RJ. Aromatic components of the leaves of the New Zealand lemonwood tree *Pittosporum eugenioides*. Zeitschriftfür Naturforschung. 2004; 59:32-34.
10. Weston RJ. Composition of essential oil from the leaves of seven New Zealand species of *Pittosporum* (Pittosporaceae). Journal of Essential Oil Res. 2004b; 16: 453-458.
11. John AJ, GeorgeV, Pradeep NS, Sethuraman MG. Composition and Antibacterial Activity of the Leaf and Fruit Oils of *Pittosporum neelgherrense* Wight etArn. Journal of Essential Oil Research. 2008; 20:380-382.
12. Binu S, Nayar TS. *Pittosporum neelgherrense* (Wight &Arnott [Pittosporaceae]) in Treatment of Snake-bite. Economic botany. 2005; 59:295-295.
13. Khare CP. Indian medicinal plants: an illustrated dictionary. Springer – Verlag, Berlin, Germany, 2007, 496.
14. Nagamalleswari K, Yasodamma N, Binny AJR. Phytochemical screening, antibacterial and antifungal studies of *Pittosporum floribundum* wight & Arn. leaf, bark, fruit and seed extracts. Journalof pharma & biosciences. 2013; 4:464-474.
15. Yasodamma N, Malleswari KN, Chaithra D. Anti-inflammatory activity of *Pittosporum floribundum* Wt. & Arn. World Journal of Pharmacy and Pharmaceutical Sciences. 2015; 4:351-362.
16. Semwal P. Evaluation of phytochemical, radical scavenging and antimicrobial profile of *Pittosporum eriocarpum* royal (Agni) from Uttarakhand Region, India. International Journal of Green Pharmacy (IJGP). 2018; 12:1-4.
17. Rosakutty PJ, Roslin AS, Ignacimuthu S. Anti-inflammatory and acute toxicity effects of *Pittosporum tetraspermum* Wight and Arn. on rats. Journal of Phytology. 2010; 6:14-20.
18. Abdullah Al Dhabi N, Valan Arasu M, Rejiniemon T S. *In vitro* antibacterial, antifungal, antibiofilm, antioxidant, and anticancer properties of isosteviol isolated from endangered medicinal plant *Pittosporum tetraspermum.* Evidence-Based Complementary and Alternative Medicine. 2015; 8:1-11
19. Mani B, Dennis T. Evaluation of the antioxidant potential of *Pittosporum dasycaulon* Miq. stem bark. Food Science and Biotechnology. 2014; 23:539-545.
20. Shyamal S, Latha PG, Shine VJ, Suja SR, Rajasekharan S, Devi TG. Hepatoprotective effects of *Pittosporum neelgherrense* Wight & Arn, a popular Indian ethnomedicine. Journal of ethno pharmacology. 2006; 107:151-155.
21. Bhatnagar SS, Santapau H, Desa JDH, Maniar AC, Ghadially NC, Solomon MJ, Rao TNS. Biological Activity of Indian Medicinal Plants. Part I. Antibacterial, Anti-tubercular and Antifungal Action. Indian Journal of Medical Research. 1961; 49:799-813.
22. Parkin DM, Bray F, Ferlay J, Pisani P. Estimating the World Cancer burden; Globocan. International Journl of Cancer. 2001; 94:153-156.
23. Perestelo NR, Jimnez IA, Tokuda H, Hayashish H, Bazzocihi IL. Sesquiterpenes from *Maytenu sjelskii*as potential cancer chemopreventive agents. Journal of Natural products. 2010; 7:127-132.
24. Pehlican Karakas F, Yildirin A, Turker A. Biological screening of various medicinal Plant extracts for antibacterial and anti-tumor activities. Turkish Journal of Biology. 2012; 36:127-132.
25. Ke Xue Z, Kai Xia L, Xiao Na G, Wei P, Hui Ming Z. Antioxidant activities and total poly phenolic content of various extracts from defatted wheat germ. Food chem. 2011; 126:1122-1126.
26. Petti S, Scully C. Poly phenols and oral health and disease; A review. J Dent. 2009; 37:413- 423.
27. Mishra SL, Sinhamahapatra, PK, Nayak A, Das R, Sannigrahi S. *In vitro* antioxidant potential of different parts of *Oroxylum indicum*: A comparative study. Indian Journal of Pharmaceutical Science. 2010; 72:267-269.
28. Bince mani. Bioactivities genetic analysis and conservation of *Pittosporum dasycaulon* Miq Pittosporaceae from the Western Ghats. Thesis, MG University kottayam, chapter. 2015b; 2:56-91.
29. John AJ, Karunakaran VP, George V, Pradeep NS, Sethuraman MG. Constituents and antibacterial activity of the essential oils from the leaves and fruits of *Pittosporum viridulum*. Journal of Essential Oil Research. 2007; 19:591-593.
30. Lee C H, Lee S G, Lee HS. Acaricidal effects of *Thymus vulgaris* leaf-derived materials and monoterpene alcohols against *Dermatophagoides* spp. Journal of the Korean Society for Applied Biological Chemistry. 2010; 53:170-174.
31. National Center for Biotechnology Information. PubChem Compound Database, 2018. CID=5352807, https://pubchem. ncbi.nlm.nih.b gov /compound /5352807.
32. Rajab MS, Cantrell CL, Franzblau SG, Fischer NH. Antimycobacterial activity of (E)-phytol and derivatives: a preliminary structure-activity study. Plantamedica. 1998; 64:2-4.
33. Gela J, Horton D, Wander JD. 7 (S)-Acetoxy-2 (S)-methoxy-1 (S)-3, 6, 8-trioxabicyclo [3.2. 1] octane. Characterization of the product from periodic acid

oxidation methyl. Beta.-L-arabinopyranoside in methyl sulfoxide. The Journal of Organic Chemistry. 1974; 39:1946-1947
34. Yang D, Michel L, Chaumont JP, Millet Clerc J. Use of caryophyllene oxide as an antifungal agent in an in vitro experimental model of onycho mycosis. Mycopathologia, 2000; 148; 79-82.
35. Shen Q, Hilderbrandt RL. The structure of methyl silatrane (1-methyl-2, 8, 9-trioxa-5-aza-1-silabicyclo (3.3. 3) undecane) as determined by gas phase electron diffraction. Journal of Molecular Structure. 1980; 64:257-262.
36. Parola M, Pinzani M, Casini A, Leonarduzzi G, Marra F, Caligiuri A *et al*. Induction of procollagen type I gene expression and synthesis in human hepatic stellate cells by 4-hydroxy-2, 3-nonenal and other 4-hydroxy-2, 3-alkenals is related to their molecular structure. Biochemical and biophysical research communications. 1996; 222:261-264.
37. Hurst JJ, Whitham GH. The photochemistry of verbenone. Journal of the Chemical Society (Resumed). 1960; 579:2864-2869.
38. Shareef HK, Muhammed HJ, Hussein HM, Hameed IH. Antibacterial effect of ginger (*Zingiber officinale*) roscoe and bioactive chemical analysis using gas chromatography mass spectrum. Oriental Journal of Chemistry. 2016; 32:20-40.
39. Hill RK, Morgan JW, Shetty RV, Synerholm ME. Stereochemistry of the thermal addition of. Beta.-pinene to maleic anhydride. Journal of the American Chemical Society. 1974; 96:4201-4206.
40. Harirchian B, Bauld NL. Cation radical Diels-Alder cycloadditions in organic synthesis. A formal total synthesis of (-)-. Beta.-selinene. Journal of the American Chemical Society. 1989; 111:1826-1828.
41. Mizushina Y, Akihisa T, Ukiya M, Hamasaki Y, Murakami Nakai C, Kuriyama I *et al*. Structural analysis of isosteviol and related compounds as DNA polymerase and DNA topoisomerase inhibitors. Life sciences. 2005; 77:2127-2140.
42. Jakupovic J, Schuster A, Bohlmann F, King RM, Haegit L. Labdane derivatives and other constituents from Waitzia acuminate. Phytochemistry. 1989; 28:1943-1948.
43. Lopes Lutz D, Alviano DS, Alviano CS, Kolodziejczyk P P. Screening of chemical composition, antimicrobial and antioxidant activities of *Artemisia* essential oils. Phytochemistry. 2008; 69:1732-1738.
44. Hameed IH, Salman HD, Mohammed GJ. Evaluation of antifungal and antibacterial activity and analysis of bioactive phytochemical compounds of *Cinnamomum zeylanicum* (Cinnamon bark) using gas chromatography-mass spectrometry. Oriental Journal of Chemistry. 2016; 32:16-25.
45. Schmidt CO, Bouwmeester HJ, Frankeand König WA. Mechanisms of the biosynthesis of sesquiterpene enantiomers (+) -and (−) -germacrene D in Solidagocanadensis. Chirality: The Pharmacological, Biological.
46. Machado ATP, Iulek J, Silva M, Besten MA, Nunes DS. Isolation, Bioactivity and Structural Studies of 6-acetyl-7-hydroxy-2, 2-dimethylchoromene from Caleahispida. De Química Revista Virtual. 2016; 8:122-124.
47. National Center for Biotechnology Information. PubChem Compound Database; CID=10798883, 2018. https://pubchem.ncbi.nlm.nih.gov/compound/10798883.
48. National Center for Biotechnology Information. Pub Chem Compound Database; CID=441005, 2018. https://pubchem.ncbi.nlm.nih.gov/compound/441005.
49. Chen W, Lu Y, Wu J, Gao M, Wang A, Xu B. Beta-elemene inhibits melanoma growth and metastasis via suppressing vascular endothelial growth factor-mediated angiogenesis. Cancer Chemotherapy and Pharmacology. 2011; 67:799-808.
50. Gijsen HJM, Wijnberg JBPA, De Groot A. Structure, occurrence, biosynthesis, biological activity, synthesis, and chemistry of aromaden drain sesquiterpenoids. In Fortschritte der Chemieorganischer Naturstoffe/Progress in the Chemistry of Organic Natural Products. Springer, Vienna, 1995, 149-193.
51. Kinghorn A. *Stevia*: The genus *Stevia*. In Medicinal and Aromatic Plants—Industrial Profiles; Hardman, R., Ed.; Taylor and Francis: London, UK. 2002; 19:195.
52. Akihisa T, Hamasaki Y, Tokuda H, Ukiya M, Kimura Y, Nishino H. Microbial Transformation of Isosteviol and Inhibitory Effects on Epstein− Barr Virus Activation of the Transformation Products. Journal of natural products. 2004; 67:407-410.
53. Ferrazzano GF, Cantile T, Alcidi B, Coda M, Ingenito A, Zarrelli A *et al*. Is Stevia rebaudiana Bertoni a non-cariogenic sweetener? A review. Molecules 2015; 21:38.
54. Xu D, Zhang S, Foster DJ, Wang J. The effects of isosteviol against myocardium injury induced by ischaemia-reperfusion in the isolated guinea pig heart. Clin. Exp. Pharmacol. Physiol. 2007; 34:488-493.
55. Ma J, Ma Z, Wang J, Milne RW, Xu D, Davey AK, *et al*. Isosteviol reduces plasma glucose levels in the intravenous glucose tolerance test in Zucker diabetic fatty rats. Diabetes Obes. Metab. 2007; 9:597-599.
56. Omolo MO, Okinyo D, Ndiege IO, Lwande WL, Hassanali A. Repellency of essential oils of some Kenyan plants against Anopheles gambiae. Phytochemistry. 2004; 65:2797-2802.
57. Kubo I, Chaudhuri SK, Kubo Y, Sanchez Y, Ogura T, Saito T *et al*. Cytotoxic and antioxidative sesquiterpenoids from *Heterotheca inuloides*. Planta Med. 1996; 62:42-430
58. Chavan MJ, Wakte PS, Shinde DB. Analgesic and anti-inflammatory activity of caryophyllene oxide from *Annona squamosa* L. Bark. Phytomedicine 2010; 17:149-151.
59. Türkez H, Çelik K, Toğar B. Effects of copaene, a tricyclic sesquiterpene, on human lymphocytes cells in vitro. Cytotechnology. 2014; 66:597-603.
60. Flamini G, Ciom PL, Morelli I. Compositions of essential oils *in vivo* emission of volatiles of four *Lamium* species from Italy; *L. purpuream, L. hybridium, L. bifidum and L. amplexicaule.* Food chemistry. 2005; 91(1):63-68.
61. Dickson RA. Antibacterial and antioxidant property of terpenoids from *Caesal piniabenthamiana*. Phytochemistry. 2007; 68:1436-1441.
62. Lai EY, Chyau CC, Mau JL, Chen CC, Lai YJ. Antimicrobial activity and cytotoxicity of the essential oil of *Curcuma zedoaria*. Am J Chin Med. 2004; 32:281-290.
63. Wang G, Li X, Huang F, Zhao J, Ding H. Antitumor effect of beta-elemene in non-small-cell lung cancer cells is mediated via induction of cell cycle arrest and apoptotic cell death. Cell Mol Life Sci. 2005; 62:881-893.

64. Yao YQ, Ding X, Jia YC, Huang CX, Wang YZ. Anti-tumor effect of beta-elemene in glioblastoma cells depends on p38 MAPK activation. Cancer Lett. 2008; 264:127-134.
65. Zhu R, Yang L, Shen L, Ye J, Liu J. ANG II-AT1 receptor pathway is involved in the anti-fibrotic effect of beta-elemene. J Huazhong Univ Sci Technol Med Sci. 2009; 29:177-181.
66. World Healh Organisation. Antibacterial agents in clinical developments: an analysis of the anti-bacterial clinical development pipeline, including tuberculosis. The pharmaceutical Journal. 2017; 299:34-36.
67. Mukherjee PK, Wahile A. Integrated approaches towards drug developments from Ayurveda and other Indian system of Medicines. Journal of Ethnopharmacology. 2006; 103:25-30.
68. Anil Farhan MU, Lee PC, How SE, Julang AG. Antibacterial activity of *Agave Angustifolia* and *Pittosporum ferrugineum.* Journal of Environmental Microbiology and Toxicology. 2013; 1:15-17.
69. Pooi Y, Chung Yien S Toh. Anti-biofilm agents: recent breakthrough against multi- drug resistant *Staphylococcus aureus*. Pathogense and diseases. 2014; 70:231-239.https://doi.org/10.1111/2049-632X.12141
70. Subramoniam A, Pushpangadan P. Development of phyto medicine for liver diseases. Indian J Pharmacol.1999; 31:166-175.
71. Liu GT. Pharmacological actions and clinical use of *Fructus schisandrae.* Journl of chineese medicine 1989; 102:740-749.
72. Hikino H, Kiso Y, Wagner H, Fiebig M. Antihepatotoxic actions of flavonolignans from *Silybum marianum* fruits. Planta Med. 1984; 50:248-250
73. Flora K, Hahn M, Rosen H, Benner K. Milk thistle (*Silybum marianum*) for the therapy of liver disease. Am J Gastroenterol. 1998; 93:139-143.
74. Madrigal Santillán E, Madrigal Bujaidar E, Cruz Jaime S, Valadez Vega MC, Sumaya Martínez MT, Pérez Ávila KG *et al*. The Chemoprevention of Chronic Degenerative Disease through Dietary Antioxidants: Progress, Promise and Evidences. In: Morales-González JA, editor. Oxidative stress and chronic degenerative diseases-a role for antioxidants. Rijeka: Croatia in Tech, 2013, 155-185.