International Journal of Herbal Medicine
Available online at www.florajournal.com

E-ISSN: 2321-2187
P-ISSN: 2394-0514
www.florajournal.com
IJHM 2023; 11(5): 01-13
Received: 01-06-2023
Accepted: 06-07-2023

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Phyto-pharmacological review of genus manilkara

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DOI: https://doi.org/10.22271/flora.2023.v11.i5a.882

Abstract
Manilkra is a pantropical genus in the family Sapotaceae. Many species from this genus are economically important and yield quality timber, edible fruits and useful latex. The plants from Manilkara species are extensively distributed all over tropical and semitropical areas like Africa, Australia, Asia, Madagascar and Latin America, as well as islands such as Pacific and in the Caribbean. Phytochemical studies of different species showed the presence of triterpenoids, phenolic compounds and saponins as major phytoconstituents which were correlated with various pharmacological activities. Because of high diversity in chemical constituents and their biological activities, genus Manilkara can serve as a potential medicinal resource for drug discovery. The present review includes traditional use, phytopharmacological studies carried out on few medicinal plants from genus Manilkara. As a promising source of new bioactive compounds. The present review can provide baseline for future research studies.

Keywords: Manilkara, traditional use, phytochemicals, pharmacological potentials

1. Introduction
Medicinal plants and their derivatives play major role in treatment of diseases in spite of advances in chemical technology. Recently, there has been tremendous evolution in plant derived drugs in the world due to the realization of toxicity associated with synthetic drugs. People around the world are increasingly aware of the fact that drug from natural sources are safer. Therefore, there has been a tremendous increase in demand for drugs derived from plants.

The Genus Manilkara Adans. (Sapotaceae) is consisting of around 79 species, widely spread over major tropical regions of the world (30 South and Central American, 35 African and 14 Southeast Asian). It is mainly found in wet tropical forest, but most of the African species exist in dry forest, while many Asian species are present in coastal areas and on limestone. According to Pennington's (1991) classification, Sapotaceae consists of five tribes, Manilkara belongs to one of the three subtribes of Manilkarinae of the tribe Mimusopeae and is characterised by having perianth parts in multiples of three; a calyx of two whorls of three sepals, six petals, six stamens and six staminodes or absent; fruit indehiscent; seed scar usually elongate; basiventral [1].

The various parts of the plants of genus Manilkara have been used in folklore medicine and ethnomedicine for therapy of many human ailments [2]. These bioactivities are mainly due to the existence of certain classes of secondary metabolites like triterpenoids, flavonoids, saponins and so on [3].

Some plants from the genus Manilkara have received considerable interest due to their extremely high economical, medicinal and nutritional values. Only seven species such as *M. zapota*, *M. hexandra*, *M. kauki*, *M. obovata (synonym - M. argentea)*, *M. subseria*, *M. bidentata*, *M. pellegriniana* from Manilkara genus have been scientifically investigated for their pharmacological activity and phytochemical constituents. The most popular, widely utilized and highly investigated species in this genus are *M. zapota* and *M. hexandra and* other species in the genus are less unexplored [4, 5].

Present review includes list of traditional uses, isolated phytochemicals and pharmacological activities carried out on crude extracts, fractions and isolated compounds from different species of genus Manilkara. We aim to provide a way forward for future research studies mainly on unknown species from Manilkara.

2. Traditional uses and geographical distribution
Details of traditional uses and distribution of plants from genus Manilkara and related references are given in Table 1.

Table 1: Geographical Distribution and Traditional Uses

Species	Distribution	Traditional use	References
M. Hexandrum	Upper Gangetic plain, central and south India, Gujarat and Rajasthan, Vidarbha region of Maharashtra, and Madhya Pradesh	Fruit-aphrodisiac, useful in leprosy, extract of the leaves is given for vaginal discharges (Ayurveda), cures biliousness, good for the heart Bark-aphrodisiac, tonic to the body and heart, cures vomiting, bronchitis, appetiser Seeds-cure ulcers, opacities in the cornea (Yunani)	[2, 69, 70]
M. Kauki	A native of Malay peninsula, occasionally planted in Indian gardens	Root and bark-astringent, given in infantile diarrhoea. Leaves--treatment of Beri-Beri, tumour, Milk (latex)-used in inflammation of the ear and in conjunctivitis. Seeds-used in ophthalmia, employed internally as a tonic, febrifuge. Treatment of leprosy, thirst, delirium and disorder of the many secretions, used as anthelmintic	[2]
M. zapota	Widely seen in India, Southern Mexico, Caribbean and Central America as well as in South East Asia. *M. zapota* fruit is very popular in Malaysia, Thailand, Singapore, Cambodia and Indonesia	Fruit -reduces inflammation and pain in gastritis, anti-spasmodic agent Fruits and crushed seeds – have diuretic property helps in preventing oedema, prevent kidney and bladder stones formation. Latex -useful as a material for filling tooth cavities. Bark -- tea made from bark to treat dysentery, constipation and piles, Bark and fruit decoction is used for fevers and diarrhoea.	[5,65]
M. obovata Synonym- *M. argentea*	Widely distributed in Africa	Useful for treatment of cardiovascular ailments. Bark-African countries bark preparations are used for treatment of stomach troubles, skin and mucosal problems, Root-preparation from roots can be used as laxative	[15, 50, 71]
M. subseria	Widely found on the sand bank of eastern Brazil.	Used medicinally in Brazil also as food and timber	[2, 33]
M. bidentata	Widely found in northern South America, Central America and the Caribbean	Used to treat many diseases. Stem - to cure dysentery and nausea; Fruits - to treat constipation Leaves- treatment of paralysis of limbs	[3, 72]

3. Pharmacological activity

Various crude extracts and few isolated compounds from different parts of plants from genus Manilkara have been widely screened for their biological activity. According to the literature, plants of the genus Manilkara are potential sources of antibacterial, antioxidant, hepatoprotective, anticancer, hypolipidemic, hypoglycemic and antiarthritic activity.

3.1 Antioxidant activity

Kaneria *et al* reported the strong antioxidant activity of methanol and acetone extract of leaves with high phenolic content from 2 different studies supports the idea of direct correlation between phenolic content and strong antioxidant activity of zapota leaves [6, 7]. The cold ethanolic extract of leaves and Isolated compound myricetin-3-o-α-L-rhamnoside from crude methanolic extract of leaves were found to be having good antioxidant activity [8, 9]. Methanolic extract flowers showed higher dose dependent percentage inhibition in 2, 2-dipheny-l-1-picrylhydryzyl scavenging assay than aqueous extract with IC_{50} values 1.97 µg/ml and 4.22 µg/ml respectively [10]. Among ethanolic and methanolic pulp and peel extract of sapota, ethanolic peel extract showed the presence of highest flavonoid and phenolic content with maximum multiple radical scavenging activity with least IC_{50} value [11]. Ethanolic bark extract of *M. zapota* was found to be good antioxidant at different concentration [12].

Aqueous methanolic (80%) fruit and seed extract of *M. hexandra* subjected to six different antioxidant assays pointed that *M. hexandra* fruits as better source of antioxidants [13].

Suman and Sanjib carried out four different antioxidant assays on different fractions of leaves of *M. hexandra* and concluded that methanolic extract fraction has strong antioxidant activity with high content of phenolics and flavonoids [14].

Akosung *et al* reported the xanthones and coumarins for the first time in Manilkara. Also isolated new friedelane triterpene lacefriedelic acid and the new prenylated xanthone lacexanthone from extracts of leaves and roots of *M. obovata* showed promising antioxidant activity which is beyond the activity measured for BHA [15].

The stem barks and leaves of *M. kauki* reported the good antioxidant activity with highest amount of phenolic compounds and flavonoids compare to fruits seeds and woods [16].

3.2 Antiurease activity

The isolated compound canophyllol and lupeol from a twig extract of *M. obovata* show better urease inhibition compare to thiourea. It may find promising application in food industry [15].

3.3 Elastase and tyrosinase inhibition

Isolated compound myricetin-3-o-α-L-rhamnoside from methanolic extract of *Zapota* leaves reported moderate elastase and tyrosinase inhibition activities [9].Study

conducted by Sirinada and Chanya showed the significant anti tyrosinase activity of ethyl acetate extract of *M. kauki* stem [16].

3.4 Microbiological activity

Aqueous extract of the leaves of *M. zapota* was noticeably more potent in hindering the growth of against 10 Gram positive, 12 Gram negative bacteria and fungus *Candida tropicalis* [17]. Ethyl acetate extract of both stem bark and leaves of *M. zapota* were found to be good antibacterial/antifungal agent against tested pathogenic Gram positive and negative bacteria and fungi such as *Aspergillus flavus*, *Fusarium* sp and *Vasianfactum* sp [18].Methanolic extract of *M. zapota* leaves was effective against five bacterial strains namely *Bacillus subtilis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Salmonella typhimurium* and *Enterobacter aerogenes* and acetone extract of *Zapota* leaves has highest inhibitory effect on *K. pneumoniae* [6, 7]. Mulvaney *et al* screened ethanolic leaves extract of zapota, its fractions and isolated components for antimicrobial and anthelmintic activity against *Candida albicans*, *Trichophyton rubrum*, *staphylococcus aureus* and *Strongyloides venezuelensis* which indicated *M. zapota* as natural drug for the treatment for microbial and strongyloidiasis drug resistant infections [19].

Among different solvent fractions, acetone, ethyl acetate fractions of *M. zapota seed* showed higher zone of inhibition against *S. aureus*, *E. Coli*, *Haemophilus* sp, *Yersinia* sp, *B. subtilis*, and *Enterobacter faecalis* by agar well diffusion method compare standard drugs whereas aqueous fraction showed inhibition only against *Haemophilus* sp [20].

Acetone extract of seeds of *M. zapota* showed significant antibacterial activity in disc diffusion and broth dilution methods [21].

The antimicrobial study of aqueous root extract of *M. zapota* against *Staphylococcus aureus* and *Escherichia coli* revealed that root can be used to fight infections against both Gram positive and negative bacteria [22]. Methanolic flower extract *M. zapoata* reported maximum zone of inhibition against *B. Subtilis* (29mm) followed by *S. aureus*, *P. aeruginosa* and *S. Typhi* (27.5mm) and aqueous extract showed maximum zone of inhibition for *S. typhi* (28.5 mm) followed by *S. aureus*, *B. subtilis* and *P. aeruginosa* [10]. Rakholiya *et al* reported that fruit peel of *M. zapota* showed good antifungal activity and more active against Gram negative bacteria and. So it has been proved to be a good source of natural antimicrobial compound [23].

Evaluation of antibacterial activity of methanol: water (7:3) extract of stem bark of *M. hexandra* was carried out by disk diffusion method. The sample showed growth inhibitory activity against *Staphylococcus aureus* at ug/ml (7mm) and 150 ug/ml (8mm) and against *Bacillus subtilis* (7 mm) [24].

The optimized topical gel prepared from methanolic and hydroalcoholic leaf extracts of *M. hexandra* showed good antibacterial activity against the strain *Klebsiella pneumoniae* [25]. Study conducted by Mahida *et al.* showed methanol extract of *M. hexandra* effectively inhibited the growth of multidrug resistant *Staphylococcus aureus* and *S. epidermidis* [26]. The different studies revealed that acetone seed extract, methanolic extract of leaves, roots, aqueous extracts of leaves, aerial parts of *M. hexandra*, were found to be having good antimicrobial activity [27-31].

Antifungal activity of some plant extracts was tested against the *Solanum melongena* damping off pathogen, *Pythium aphanidermatum* in PDA cultures. Among that cold water extracts of *M. Kauki* showed (78.8%) inhibitory effect [32].

Fernandes *et al* reported hexanic extract from fruits of *M. subseria* showed good antibacterial activity against *staphylococcus aureus* ATCC25923 and weak cytotoxicity in Vero cells, may be due to high amount of beta and alpha amyrin caproates and caprylates [33].

3.5 Anticancer activity

The methanolic extract *M. zapota* fruit (MESF) showed good cytotoxicity *in vitro* by affecting cell viability in NALM6, human and mouse breast cancer cell lines such as EAC, MCF7 and T47D. This study stated that Zapota fruit induces cytotoxicity in cancer cells by activating intrinsic pathway of apoptosis and *in vivo* Ehrlich ascites carcinoma model showed significant inhibition of tumour growth and a three-fold increase in life span of tumour bearing animals compared to untreated tumour mice. This study revealed that zapota fruit can be used as potential cancer preventing agent [34].

Activity-guided fractionation of a methanol extract from the fruit of *M. zapota* resulted in the isolation of two new antioxidants, in which 4-O-galloyl chlorogenic acid displayed cytotoxicity in the HCT-116 and SW-480 human colon cancer cell lines with IC_{50} values of 154 and 134 µM, respectively [35].

Two new polyhydroxylated pentacyclic triterpenes from *M. pellegriniana* were investigated for cytotoxic effect on SPC212 (human mesothelioma), A549 (human non-small cell lung cancer (NSCLC)), HepG2 (hepatocarcinoma), DLD-1 (colorectal adenocarcinoma) cell lines.

Amongst compound 1β, 2α, 3α, 5, 19α, 24-hexahydroxyurs-11(12), 20(30)-dien-28-oic acid was active against all cell lines and showed promising cytotoxic effect towards SPC212 lung cancer cells with IC50 value of 0.52 µM [36].

Antitumor effect of ethyl acetate extract of *M. zapota* fruits (EEFM) was carried out against Ehrlich ascites carcinoma (EAC) in Swiss albino mice at the doses of 50 and 100 mg/kg body weight. Treatment with EEFM at 100 mg/kg body weight indicated a significant increase in the survival time, decrease in the viable tumour cell count, weight gain in the EAC tumour hosts, improvement in the altered haematological parameters, like haemoglobin content, RBC and WBC count of the tumour bearing mice. It also restored altered biochemical (SALP and SGOT) parameters during tumour progression. In same study, EEFM showed potent cytotoxicity in the brine shrimp lethality bioassay, against brine shrimp nauplii (*Artemia salina*) with LC50 of 3.06 µg/mL, against standard ampicillin trihydrate which showed LC50 of 7.21µg/ml. This study indicated the both antitumour and cytotoxic potential of the zapota fruit [37].

Tan and his co-workers studied the apoptosis-inducing activity of water extract of *M. zapota* leaf in HepG2 cells. This study revealed that leaf water extract causes early apoptosis in hepatocellular carcinoma (HepG2 cells) via modulation of multiple signalling pathways like intrinsic mitochondrial pathways leads suppression of metastasis. All the data recorded indicated that M. zapota leaf water extract has noteworthy apoptotic potentials via the regulation of ERK1/2/Akt1/JNK1 transcriptional activity [38].

The ethyl acetate extract of stem bark of *M. zapota* showed significant antitumour efficacy in Ehrlich ascites carcinoma model. Intraperitoneal administration of this extract reduced viable EAC cells, increased the survival time, and restored

altered haematological parameters [39].
In another study Rashid *et al* used same model to evaluate *in vivo* antitumor activity of ethyl acetate extract of the leaves of *M. zapota* and isolated compound Erythrodiol. Leaf extract increased the life span, weight of the tumour bearing mice, decreased the tumour bearing cell and improved the altered haematological parameters. Erythrodiol reduced the viable tumour cell count by 70.8% in comparison with the untreated control [40].

3.6 Anti-inflammatory, antipyretic, Analgesic activity and antinociceptive activity
The petroleum ether fraction of ethanolic extracts of *M. zapota* leaves showed maximum body temperature lowering effect (36.86 °C) at 4th hr and the ethyl acetate fraction showed anti-inflammatory effect [41]. In another study Ethanol extract and its fractions showed prominent peripheral antinociceptive activity and significant central analgesic activity at 400 mg /kg [42].
Crude methanolic extract of bark and ethyl acetate extract of *M. zapota* leaves has good anti-inflammatory activity [43, 44].
The acetone fraction of *M. hexandra* seed containing the crude saponin mixture possessed a significant inhibitory activity against LPS (Lipo-Poly Saccharide)-induced nitric oxide method indicating a significant anti-inflammatory activity [45].
Study conducted on *M. bidentata* resin extract and isolated fractions for anti-inflammatory activities showed decrease in IL-8 and IL-1β pro-inflammatory cytokines, suggested the use of bidentata resin extract as an anti-inflammatory and anti-aging substance for pharmaceutical and cosmetic industries [3].
The evaluation of analgesic activity of zapota leaves was carried out by using acetic acid-induced writhing test in mice concluded that *M. zapota* leaves possess significant analgesic activity and supported its traditional use as analgesic [46]. The ethanolic extracts of *M. zapota* leaves showed analgesic activity at doses of 200 mg/kg [47]. Another study ethanolic extract of whole plant of *M. zapota* showed dose dependent analgesic activity, suggested the benefits of whole plant of zapota for treating pain and inflammation [48].

3.7 Hepatoprotective activity
In two different studies the crude ethanol extract of bark and cold ethanolic leaf extract of *M. zapota* were tested *in vivo* CCL4 liver damage in rats hepatoprotective model. Results indicated the restoration of altered serum marker enzymes, total bilirubin, total protein and liver weight when compared to standard. These studies suggested that hepatoprotective activity bark and leaves may be due to their antioxidant potential and presence of flavonoids, carotenoids and ascorbic acid [8, 12].
Administration of lyophilized zapota fruit extract in CCL4 intoxicated rats resulted in prominent dose-dependent reversal of elevated serum biomarkers, bilirubin and abnormal lipid profile at (250 and 500 mg/kg proved its hepatoprotective and lipid-lowering effects [49]. Investigation of hepatoprotective activity of methanolic and petroleum ether extracts of *M. obovata* seed against CCL4 induced hepatic damage in rats reported their significant antioxidant and hepatoprotective activities [50].

3.8 Hypocholesterolaemic effect
Aqueous extract of *M. zapota* leaves showed a significant decrease in cholesterol level
close to that of atorvastatin [51].

3.9 Hypoglycemic activity
Alcoholic and aqueous extracts of the *M. zapota* leaves showed the significant decrease in the blood glucose level in hyperglycaemia induced rats but not in normal rats compared to Metformin [51].
The hypoglycaemic activity of petroleum ether extracts of leaves and methanol extracts of seeds of *M. zapota* was tested in alloxan induced diabetes model. The oral glucose tolerance test after 15, 30, 60, 90 and 120 min of administering 2mg/body weight of glucose noted the decrease in blood glucose level in a promising way, indicated hypoglycaemic potency of the leaves and seeds of *M. zapota* [52].
Anti hyperglycaemic activity of 50% hydroalcoholic bark extract of *M. hexandra* out by administering 250 mg/kg or 500 mg/kg body weight of extract orally to the streptozotocin induced diabetic rats once daily for 21 days. Result showed that extract has significant antidiabetic activity and good hypolipidemic activity in diabetic conditions [53].
Another study Nimbekar *et al* investigated the hypoglycaemic activity of the methanolic extracts of *M. hexandara* on normoglycemic and alloxan induced diabetic rats. Methanolic extract of *M. hexandra* at (400mg/kg body weight) showed effective hypoglycaemic activity supports the folklore use in the management of type II diabetes [54].

3.10 Antidiarrhoeal activity
Ganguly *et al* tested antidiarrhoeal activity of crude ethanolic extracts of *M. zapota* leaves and it's different fractions such as petroleum ether, carbon tetra chloride and ethyl acetate by castor oil-induced diarrhoeal model indicated the significant antidiarrhoeal activity of ethanol extract (200 and 400 mg/kg) by inhibition of defecation by 53.57 and 60.71%, respectively compared with that of loperamide 71.42% [42].

3.11 Anti-arthritic Activity
Investigation of *M zapota* ethanolic leaf extract for anti-arthritic activity using *in vitro* protein denaturation inhibition model showed good anti arthritic activity as compared to standard drug acetyl salicylic acid at concentration of 100 mcg/ml and 250 mcg/ml [55].
In another *in vitro* antiarthritic evaluation of methanolic and hydroalcoholic leaf extracts of *M. hexandra* by protein denaturation method and proteinase inhibition method, both the extract inhibited the denaturation of bovine albumin and proteinase enzyme in dose dependent manner against standard drug diclofenac sodium suggested that activity is due to their ability to control production of auto-antigen [56].

3.12 Corneal wound healing
Ethanolic extract of the leaves of *M. zapota* showed cornel wound healing activity on Bovine eyes culture / organ culture suggested that may be due to the occurrence of bioflavonoids and its antioxidant properties [57].

3.13 Immunostimulatory activity
The polysaccharides obtained from *M. hexandra* bark was

tested for Immunostimulatory effect showed dose dependent effect may be due to stimulating macrophage function [58].

3.14 Antifertility Activity
The aqueous powdered drug (2gm/body weight) of seeds of *M. hexandra* showed marked decrease in sperm count in albino male rats in an experiment and proved to be good anti fertility agent [59].

3.15 Antiulcer Activity
Effects of the flavonoid rich fraction of ethyl acetate extract (extract A3) of stem bark of *M. hexandra*, was investigated in experimental animals for ethanol induced, ethanol-indomethacin induced and pylorus ligated gastric ulcers. On administration, extract A3 inhibited the formation of gastric lesions induced by ethanol and pylorus ligation, decreased the ethanol induced vascular permeability, reduced the lipid peroxidation in experimental animals. There was increased mucus production and glycoprotein content in animals pre-treated with extract indicated the protective action of the extract A3 [60].
Another study ether, ethyl acetate and aqueous fractions of acetone extract showed significant inhibition of HCl-ethanol induced gastric ulcer. Amongst ethyl acetate fraction found to be very effective. It sped up the healing of chronic gastric ulcer induced by acetic acid (100mg/kg) and showed protective action in cysteamine -induced duodenal ulcer by reduction in total lesion area and score for intensity [61].

3.16 Inhibition of SARS-CoV-2 main protease activity
Metabolic profiling of secondary metabolites of methanolic leaf extract and ethyl acetate bark extract of *M. hexandra* using LC-HRESIMS (Liquid chromatography-high resolution electrospray ionization mass ionization spectrometry) leads to elucidation of eighteen compounds. Amongst major components were polyphenolics, flavonoids and triterpenes. Flavonoids like rutin, myricitrin, mearnsitrin, and quercetin 3-o-β-D-glucoside showed considerable SARS-CoV-2 main protease inhibitor activity. Amongst rutin showed highest inhibition. It can be promising lead against SARS-CoV-2 pandemic [62].

3.17 Pesticidal Activity
Fernandes *et al* reported that hexane soluble fraction from ethanolic fruit extract of *M. subseria* and its triterpenoids were active against cotton pest *Dysdercus peruvians* [63]. Insecticidal nano emulsion prepared from polar fraction of fruits of *M. subsericea* (5%) showed mortality in *D. peruvians* [64].

3.18 Formulation of fruit extract for cosmeceutical application
Nano emulsion prepared using ethyl acetate peel extract as active constituent was subjected to accelerated stability and cytotoxicity study and it indicated the extract as non-toxic and safe to be used as active ingredient in cosmeceutical application against skin aging [65].

Methanolic extract and its six isolated phenylethanoids from *M. zapota* seeds were screened for antioxidant activity using DPPH assay. Methanolic crude extract exhibited significantly high antioxidant values (IC_{50} 8.50 µg/mL) and phenylethanoid compounds showed moderate antioxidant activities with (IC_{50} 62.52-70.20) mM compared to standard BHA (butylated hydroxy anisole) with (IC_{50} 44.20 mM) [66].

4. Phytochemistry of manilkara
Chemical investigation of different plants of Manilkra species have led to the isolation and characterisation of many primary and secondary metabolites. These chemical constituents can be categorised as triterpenoids, saponins, phenolic compounds, volatile compounds, phytosterols, saturated and unsaturated fatty acids and others.

4.1 Triterpenoids
Many triterpene esters and pentacyclic triterpenoids have been identified in Manilkara species. In study conducted by Fernandes *et al*, the mixture containing the triterpenes β-amyrin acetate (76.3%) and α-amyrin acetate (23.7%) showed inhibition of acetylcholinesterase activity and suggested that these two compounds as chemical markers of *M. subseria* [67].

4.2 Phenolic Compounds
Phenolic compounds such as simple phenols, phenolic acids, flavonoids, coumarins and xanthones are present in genus Manilkara. The most common flavonoids present in this genus are quercetin, quercitol, kaempferol, ferulic acid, chlorogenic acid and catechin. (Table 2 and 3, 33-96 and 173-185).

4.3 Saponins
Few saponins including pentacyclic triterpenoid saponin Manilkoraside was isolated from stem bark of *M. zapota*. It showed potent inhibitive effects on HL-60 and HT-29 and moderate activity on A 549, A 431 and MCF-7 cell lines [68]. There was isolation of novel saponin along with other 2 saponins from *M. hexandra* seeds [45].

4.4 Phytosterols
β-sitosterol, stigmasterol, α-spinosterol and other few phytosterols have been reported from Manilkra species. (Table 3, 113-123).

4.5 Volatile compounds
34 volatile compounds were identified from leaves of *M. subseria*. (Table-3,127-165).

4.6 Fatty Acids
Many saturated and unsaturated fatty acids have been isolated from Manilkara species. (Table-3, 97-112).
Other phytoconstituents and isolated compound from different species of genus Manilkra are given in Table 3.

Table 2: Some important chemical compounds present in Genus Manilkara

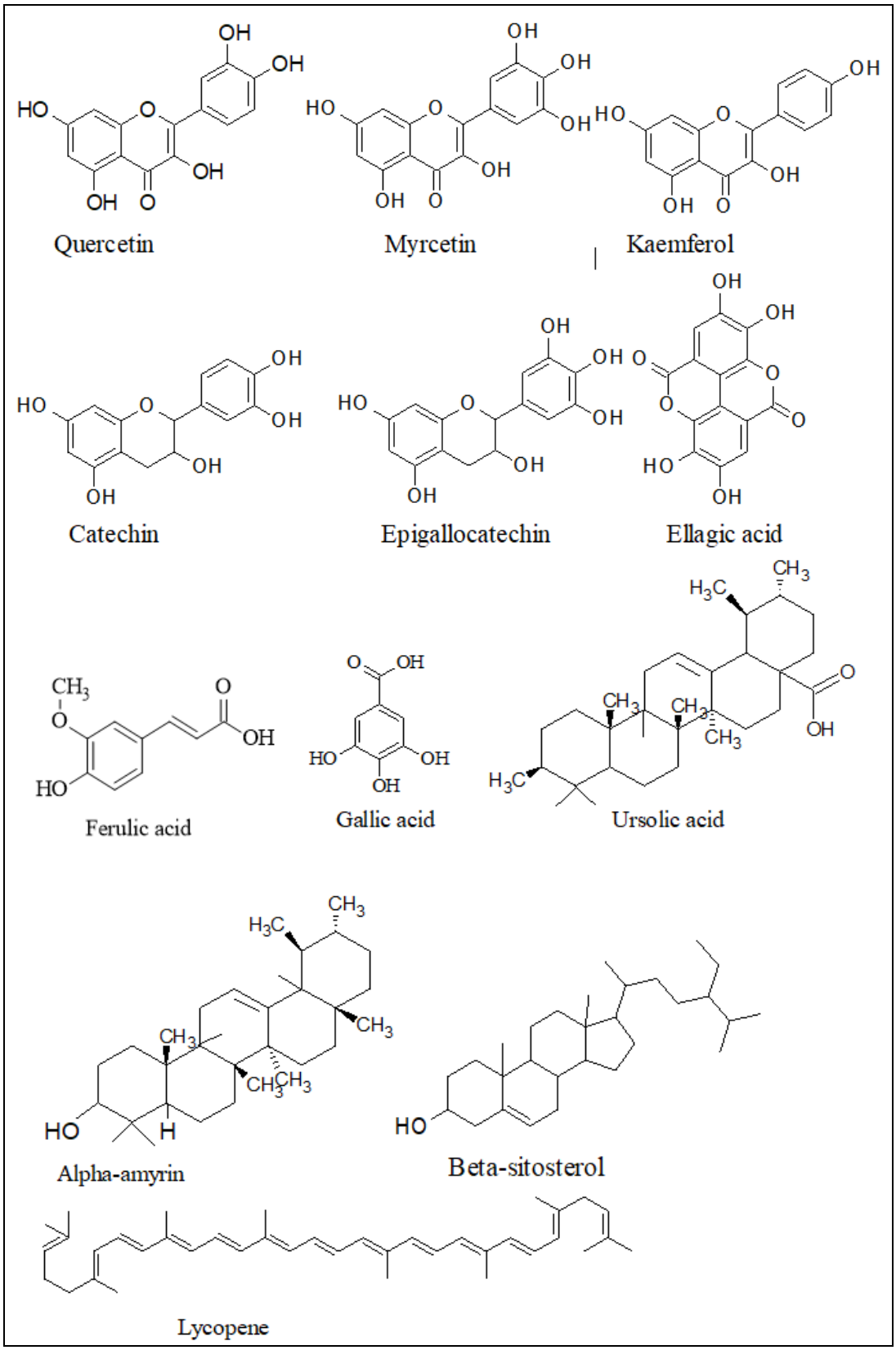

Table 3: Bioactive Constituents from Manilkara

SI NO	COMPOUND	SPECIES	PART USED	REFERENCE
	Triterpenoids			
1	Erythrodiol	*M. zapota*	Leaf	[35]
2	α-amyrin	*M. hexandra*	Roots	[71]
3	β- amyrin	*M. hexandra* *M. zapoata*	Roots seeds	[61, 71]
4	α-amyrin acetate	*M. subseria* *M. hexandra*	Fruits Fruits	[20, 62, 72, 73]

5	β- amyrin acetate	*M. subseria* *M. pellegriniana*	Fruits Stem bark	[20, 31, 62, 72]
6	Alpha amyrin caprolates & caprylates	*M. subseria*	Fruits	[20]
7	Beta amyrin caprolates &caprylates	*M. subseria*	Fruits	[20]
8	Pomoleic acid	*M. subseria*, *M. zapota*	Fruits Leaves	[72]
9	Oleanolic Acid	*M. subseria* *M. obovate* *M. zapota*	Leaves Root, stem bark, Seeds	[11, 46, 61]
10	Obovatol	*M. subseria* *M. obovata*	Zapota Root, stem bark, leaves	[72, 74]
11	Ursolic acid	*M. subseria* *M. obovata* *M. hexandra* *M. pellegriniana*	Fruits Twig Fruits Stem bark	[11, 31, 62, 71]
12	1β-hydroxyeucaphic acid	*M. pellegriniana*	Stem bark	[31]
13	Lacefriedelic acid	*M. obovata*	Leaves	[11]
14	Friedelin	*M. obovata*	Twig	[11]
15	Friedelanol	*M. obovata*	Stem bark	[11]
16	Canophyllol	*M. obovata*	Twig	[11]
17	Canophyllic acid	*M. obovata*	Leaves	[11]
18	Ethylcanophyllate	*M. obovata*	Root, stembark, leaves	[74]
19	Lupeol	*M. obovata* *M. zapota*	Twig Seeds	[11, 61]
20	Betulinic acid	*M. subseria* *M. zapota* *M. obovata*	Root Seeds Root	[11, 61, 62]
21	Maslinic acid	*M. obovata*	Twig	[11]
22	Taraxerol	*M. hexandra* *M. pellegriniana*	Leaves, Roots Stem bark	[73, 75, 31]
23	Taraxeryl acetate,	*M. hexandra* *M. pellegriniana*	Bark Stem bark	[75, 31]
24	α-amyrin cinnamate	*M. hexandra*	Bark	[75]
25	3β-O-acetyl-α-amyrin	*M. hexandra* *M. bidentata*	Seeds Resin	[41, 75]
26	3β-O-trans cinnamyl-α-amyrin	*M. bidentata*	Resin	[41]
27	3β-O-trans cinnamyl lupeol	*M. bidentata*	Resin	[41]
28	3β,6α,19α,23-tetrahydroxyurs-12-en-28-oic acid 1	*M. argentea*	Stem bark	[31]
29	1β-hydroxyeucaphic acid	*M. pellegriniana*	Stem bark	[31]
30	2α-hydroxy-ursolic acid	*M. argentea*	Stem bark	[31]
31	2α, 3α, 19α,20β, 23-pentahydroxyurs-12-en-28-oic acid,	*M. pellegriniana*	Stem bark	[31]
32	1β, 2α, 3α, 5, 19α, 24-hexahydroxyurs-11(12), 20(30)-dien-28-oic acid	*M. pellegriniana*	Stem bark	[31]
Phenolic Compounds				
33	D-quercitol,	*M. subseria*, *M. zapota* *M. hexandra*	Seeds Leaves, seeds Leaves, seeds	[6, 60, 73]
34	Methyl chlorogenate	*M. zapota*,	Fruits	[30]
35	Myricetin	*M. subseria*, *M. zapota*	Leaves Leaves	[72, 76]
36	Myricitrin	*M. zapota*, *M. subseria*	Fruits Leaves	[30, 72]
37	Dihydromyricetin	*M. zapota*	Fruits, leaves	[30,76]
38	Myricetin-3-O-α-L-rhamnoside	*M. zapota*	Seeds, leaves,	[6, 46]
39	Myricetin-3-O-β-D-glucopyranoside	*M. zapota*	Leaves	[17]
40	Quercetin	*M. hexandra*, *M. subseria* *M. zapota*	Seeds, fruits Leaves Seeds, fruits	[9, 30, 72, 75]
41	Quercitrin	*M. zapota* *M. subseria*	Fruits Leaves	[30, 72]
42	Dihydroquercetin	*M. hexandra*	Seeds	[75]
43	Chlogeneic acid	*M. zapota*	Leaves	[17, 76]
44	Methyl 4-galloylchlorogenate	*M. zapota*	Fruits	[30]
45	4-O-galloylchlorogenic acid	*M. zapota*	Fruits	[30]
46	Catechin	*M. zapota*, *M. hexandra*	Leaf, fruits, seeds Fruits	[30, 72, 77]
47	Epicatechin,	*M. zapota*	Fruits	[30]
48	Gallocatechin,	*M. zapota*	Fruits	[30]
49	Gallic acid,	*M. zapota*	Fruit, seed	[60, 77]
50	Apigenin-7-O-α-L-rhamnoside,	*M. zapota*	Leaves	[46]

51	Leucodelphinidin,	*M. zapota*	Fruits	[78]
52	Leucocyanidin	*M. zapota*	Fruits	[78]
53	Leucopelargonidin	*M. zapota*	Fruits	
54	Saccharose	*M. zapota*	Leaves, seeds	[6]
55	Caffeic acid	*M. zapota*	Leaves	[46]
56	Trans-cinnamic	*M. zapota*	Fruit	[79]
57	Ellagic acid	*M. zapota*	Fruit	[79]
58	Catechol	*M. hexandra*	Fruits, seed	[9]
59	P-hydroxybenzoic acid	*M. hexandra*, *M. zapota*	Fruits Fruits	[9,79]
60	Kaempferol	*M. subseria*, *M. zapota* *M. hexandra*	Leaves Fruits Fruits	[9,72,77]
61	5-caffeoyl quinic acid conjugates	*M. zapota*	Fruit	[80]
62	Catechin	*M. subseria*, *M. zapota* *M. hexandra*	Leaves Fruits, seeds Fruits, seeds	[9,30,60,79]
63	Salicylic acid,	*M. zapota*, *M. hexandra*	Leaves Fruit, seeds	[9,76]
64	3,4-Dihydroxybenzoic acid	*M. zapota*	Fruit pulp, seeds	[60]
65	Vanillic acid	*M. zapota*, *M. hexandra*	Leaves seeds	[9,76]
66	Gallic acid	*M. zapota* *M. hexandra* *M. zapota*	Immature fruits, leaves Seeds, fruits fruit	[9, 30, 76, 79]
67	Caffeic acid	*M. zapota*	Leaves	[46, 76]
68	Coumaric acid	*M. hexandra*	Leaves and fruits	[9]
69	Ferulic acid	*M. zapota*, *M. hexandra* *M. zapota*	Leaves Fruits, seeds fruits	[9, 76, 79]
70	Chlorogenic acid	*M. sapota*	Leaves, Immature fruits	[30, 76, 79]
71	Syringic acid	*M. subseria* *M. zapota*	Leaves Leaves	[76]
72	Afzelechin	*M. zapota*	Leaves	[76]
73	Epicatechin	*M. zapoata* *M. hexandra*	Leaves Seeds, fruits	[9, 76]
74	Epigallocatechin	*M. zapota*, *M. hexandra*	Leaves Fruit, seeds	[9, 76]
75	flavanol	*M. hexandra*	Fruit, seeds	[9]
76	Flavan-3-ol	*M. hexandra*	Fruit, seeds	[9]
77	Laricitrin	*M. zapota*	Leaves	[76]
78	Myricetin-3-O-rhamnoside	*M. zapota*	Leaves	[76]
79	Laricitrin-3-O-rhamnoside	*M. zapota*	Leaves	[76]
80	Prodelphinidin B	*M. zapota*	Leaves	[76]
81	2-Hydroxybenzaldehyde	*M. zapota*	Leaves	[76]
82	Guaiacol	*M. zapota*	Leaves	[76]
83	Pyroglutamic acid	*M. zapota*	Leaves	[76]
84	Threonic acid	*M. zapota*	Leaves	[76]
85	Vanillin	*M. zapota*	Leaves	[76]
86	7,9- di-tert-butyl-1-oxaspiro [4.5] deca-6,9- diene-2,8-dione.	*M. hexandra*	Stem bark	[21]
87	3-Hydroxycoumarin	*M. zapota*	Leaves	[17]
88	Mearnsitrin	*M. zapota*	Leaves	[17]
89	Germanicol	*M. zapota*	Leaves	[17]
90	Germanicol acetate	*M. zapota*	Leaves	[17]
Saponins				
91	Manilkoraside	*M. zapota*	Stem bark	[63]
92	Aridanin	*M. hexandra* *M. obovata*	Stem bark Stem bark	[11, 81]
93	1 β, 2α, 3β, 19α-tetrahydroxyursolic acid 28-O-beta -D-glucopyranoside	*M. hexandra*	Stem bark	[81]
94	Saponin 1 (16-a-hydroxyprotobassic acid)	*M. hexandra*	Seeds	[40]
95	Saponin 2 (16-a-hydroxyprotobassic acid)	*M. hexandra*	Seeds	[40]
96	Saponin 3(protobassic acid)	*M. hexandra*	Seeds	[40]
Fatty acids (saturated and unsaturated)				
97	Oleic acid	*M. zapota*	Leaves	[46]
98	Ethyl oleate	*M. bidentata*	Seeds	[82]
99	α-linolenic acid	*M. zapota*	Leaves	[46]
100	Linoleic acid,	*M. zapota*	Leaves	[46]
101	Lupeol acetate	*M. zapota*	Leaves	[46]
102	Oleanolic acid	*M. zapota* *M. obovata*	Seeds, Leaves Stem bark	[46, 61]

103	Lupeol-3-acetate	*M. zapota*	Leaves	[46, 6]
104	Palmitic acid	*M. zapota*	Leaves, fruit, seeds	[46, 60]
105	Capric acid	*M. zapota*	Leaves	[46]
106	Stearic acid	*M. zapota*	Leaves	[46, 83]
107	Linoleidic acid	*M. zapota*	Leaves	[46]
108	Oleic acid	*M. zapota*	Fruits, seeds	[83]
109	Myristic acid	*M. zapota*	Fruit, seed	[83]
110	Garbanzol	*M. argentea*	Stem bark	[31]
111	3,5,7,4′,5′-pentahydroxyflavan	*M. argentea*	Stem bark	[31]
112	(+)-proto-quercitol	*M. argentea*	Stem bark	[31]
	Phyto sterols			
113	β-sitosterol	*M. zapota*	Leaves, stem bark	[46, 75, 81]
114	Stigmasterol	*M. zapota*	Leaves	[46]
115	A mixture of stigmasterol and b-sitosterol	*M. obovata* *M. zapota*	Twig Seeds	[11,61]
116	Stigmasterol-3-O-β-D-glucoside	*M. obovata*	Twig	[11]
117	b-sitosterol-3-O-β–D-glucoside	*M. obovata*	Leaves	[11]
118	Stigmasterol-3-O-β-D-glucopyranoside	*M. zapota*	Seeds	[61]
119	β-D-glucoside of β-sitosterol	*M. hexandra*	Seeds	[73]
120	α-spinosterol	*M. hexandra*	Bark, seed	[75]
121	3α- spinasterol	*M. pellegriniana*	Stem bark	[31]
122	Spinasterone	*M. pellegriniana*	Stem bark	[31]
123	α-spinasterol glucoside	*M. argentea*	Stem bark	[31]
	Carotenoid			
124	β-carotene	*M. zapota*	Fruits	[84]
125	Lycopene	*M. zapota*	Fruits	[85]
126	α-tocopherol (Vitamin E)	*M. zapota*	Fruits	[84]
	Volatile compounds essential oils			
127	Hexanol	*M. subseria*	Leaves	[72]
128	Trans-2-decenal	*M. subseria*	Leaves	[72]
129	3-hexen-1-ol	*M. subseria*	Leaves	[72]
130	Octanal	*M. subseria*	Leaves	[72]
131	Heptanol	*M. subseria*	Leaves	[72]
132	Heptanal	*M. subseria*	Leaves	[72]
133	2-heptanone	*M. subseria*	Leaves	[72]
134	(3E) -3-hexenyl acetate	*M. subseria*	Leaves	[72]
135	Beta-ocimene	*M. subseria*	Leaves	[72]
136	Octanol	*M. subseria*	Leaves	[72]
137	Linalool oxide	*M. subseria*	Leaves	[72]
138	2-nonanone	*M. subseria*	Leaves	[72]
139	Linalool	*M. subseria*	Leaves	[72]
140	Terpineol	*M. subseria*	Leaves	[72]
141	Pentacosane	*M. subseria*	Leaves	[72]
142	Methyl salicylate	*M. subseria*	Leaves	[72]
143	Heptacosane	*M. subseria*	Leaves	[72]
144	Safranal	*M. subseria*	Leaves	[72]
145	Squalene	*M. subseria*	Leaves	[72]
146	Beta-cyclocitral	*M. subseria*	Leaves	[72]
147	Nonacosane	*M. subseria*	Leaves	[72]
148	Geraniol	*M. subseria*	Leaves	[72]
149	Beta-damascenone	*M. subseria*	Leaves	[72]
150	Beta-damascone	*M. subseria*	Leaves	[72]
151	Beta-caryophyllene	*M. subseria*	Leaves	[72]
152	Farnesene	*M. subseria*	Leaves	[72]
153	Caryophyllene oxide	*M. subseria*	Leaves	[72]
154	1,2,3-Propanetriol	*M. zapota*	Fruits, Seeds	[83]
155	5-Methyl-2(3H) furanone	*M. zapota*	Fruits, Seeds	[83]
156	Octadecanoic acid	*M. hexandra*	Stem bark	[21]
157	Hexadecanoic acid	*M. bidentata* *M. subseria* *M. hexandra*	Seed Leaves and fruits Stem bark	[82, 69, 21]
158	Hexadecanoic acid ethyl esters	*M. subseria M. bidentata*	Fruits Seed	[69, 82]
159	Octadecanoic acid ethyl esters	*M. subseria*	Fruits	[69]
160	Eicosene	*M. subseria*	Leaves	[72]
161	Heneicosane	*M. subseria*	Leaves	[72]
162	Phytol	*M. subseria*	Leaves	[72]
163	Docosene	*M. subseria*	Leaves	[72]
164	Tricosane	*M. subseria*	Leaves	[72]
165	Untriacontane	*M. subseria*	Leaves	[72]

Carboxylic And Dicarboxylic Acid				
166	Succinic acid	*M. zapota*	Leaves	[76]
167	Malic Acid	*M. zapota*	Leaves	[76]
168	Adipic acid	*M. zapota*	Leaves	[76]
169	3-Oxoadipic acid	*M. zapota*	Leaves	[76]
170	Cinnamic acid	*M. hexandra*	Leaves	[71]
171	Trans-cinnamic acid	*M. zapota*	Fruit	[79]
172	Formic acid	*M. zapota*	Fruit, seed	[83]
Coumarins				
173	Isocallophyllic acid	*M. obovata*	Leaves	[11]
174	Calophyllolide	*M. obovata*	Leaves	[11]
175	3-methoxyphenol	*M. obovata*	Twig	[11]
176	Calaustralin	*M. obovata*	Twig	[11]
177	Callophyllic acid	*M. obovata*	Stem bark	[74]
178	Obovacoumaric acid	*M. obovata*	Stem bark	[74]
Xanthones				
179	Lacexanthone	*M. obovata*	Root	[11]
180	Gerontoxanthone A	*M. obovata*	Roots	[11]
181	6-deoxyjacareubin	*M. obovata*	Twig	[11]
182	1,3-dihydroxy-2-methoxyxanthone	*M. obovata*	Stem Bark	[11]
183	1,2-dihydroxy-3-methoxyxanthone	*M. obovata*	Stem bark	[11]
184	2-hydroxyxanthone	*M. obovata*	Roots	[11]
185	Norathyriol	*M. zapota*	Leaves	[76]
Phenylethanoid				
186	2-(4-Hydroxyphenethyl) tetratriacontanoate	*M. zapota*	Seeds	[61]
187	2-(4-Hydroxyphenethyl) tetracosanoate	*M. zapota*	Seeds	[61]
188	2-(4-Hydroxyphenethyl) docosanoate	*M. zapota*	Seeds	[61]
189	2-(4-Hydroxyphenethyl) eicosanoate	*M. zapota*	Seeds	[61]
190	2-(4-Hydroxyphenethyl) octadecenoate	*M. zapota*	Seeds	[61]
191	2-(4-Hydroxyphenethyl) hexadecanoate	*M. zapota*	Seeds	[61]
Carbohydrates				
192	Rhamnose	*M. hexandra* *M. zapota*	Seed Leaves	[73, 76]
193	Glucose	*M. hexandra* *M. zapota*	Seeds Leaves	[73, 76]
194	Xylose,	*M. hexandra*	Seeds	[73]
195	Arabinose	*M. hexandra*	Seeds	[73]
196	Sucrose	*M. zapota*	Leaves	[76]
Minerals				
197	Iron, copper, zinc, calcium. potassium	*M. zapota*	Fruits	[77]
Amino Acids				
198	Aspartic acid and glutamic acid, lysine, proline, hydroxyproline	*M. zapota* *M. hexandra*	Fruit Fruit	[86, 78, 73]
Hydrocarbons				
199	n-hexadecane	*M. zapota*	Leaves	[46]
200	n-tricontane	*M. zapota*	Leaves	[46]
201	n-octacosane	*M. zapota*	Leaves	[46]
202	n-docosane	*M. zapota*	Leaves	[46]
203	n-tetracosane	*M. zapota*	Leaves	[46]
204	Hentriacontane	*M. zapota*	Leaves	[71]
Others				
205	Shikimic acid	*M. zapota*	Leaves	[76]
206	3-O-Galloylquinic acid	*M. zapota*	Leaves	[76]
207	Esculetin	*M. zapota*	Leaves	[76]
208	Quinic acid	*M. zapota*	Leaves	[76]
209	Hydroquinone glucuronide	*M. zapota*	Leaves	[76]
210	Glyceraldehyde	*M. zapota*	Fruit, seed	[83]
211	3-Glucogallic acid	*M. zapota*	Leaves	[76]
212	3-p-Coumaroylquinic acid	*M. zapota*	Leaves	[76]
213	2-Propyl tetrahydropyran-3-ol	*M. bidentata*	Seeds	[87]
214	2-Furancarboxyaldehyde, (hydroxymethyl)-	*M. bidentata*	Seeds	[87]
215	5-methyl-2-furancarboxaldehyde	*M. bidentata*	Seeds	[87]
Glycosides				
216	Cyanogenetic glycosides	*M. zapota*	Latex	**[88]**

5. Conclusion

This review highlighted the phytopharmacological findings of different plant extracts from genus Manilkra. Quite majority of the species remain unknown or scientifically unexplored. Thus, it justifies the need for the advanced research studies on Manilkara species on their therapeutic potential. It will pave the way for future drug design.

6. Acknowledgement
The author is thankful to Management of Faculty of Pharmaceutical Sciences, PES University, Bangalore and Nargund College of Pharmacy, RGUHS, Bangalore, for providing necessary facilities for research work.

7. Conflict of interest
We declare that the authors have no conflict of interest

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