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A COMPREHENSIVE PHARMACOGNOSTIC REVIEW: *MANILKARA HEXANDRA* (ROXB.) DUBARD

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ABSTRACT: The aim of this review paper is to provide throughout the information of *Manilkara hexandra* (Roxb.) Dubard, used as a Khirni or Rayon in most of the tropical regions of India. It is native to India, mainly distributed as a wild tree in the southern part and North-central part of India. It is widely spread in Gujarat, Rajasthan, Madhya Pradesh, Andhra Pradesh, Kerala and Maharashtra our efforts are to collect valuable information with respect to morphology, microscopy, phytoconstituents and pharmacological aspect of the plant. The plant contains major phytoconstituents such as protobassic acid, 16-ahydroxyprotobassic acid, taraxerol, a triterpene ketone, alpha and beta-amyrin, cinnamates, alpha-sipnasterol, beta-sitosterol, its beta-D-glucoside, quercitol, quercetin and its dihydroderivatives, ursolic acid. Traditionally, the whole plant is employed as astringent, refrigerant, aphrodisiac, alexipharmic, stomachic, anthelmintic, for reliving fever, flatulence, colic, dyspepsia, helminthiasis, hyperdipsia, burning sensation. All these compounds claimed to possess various pharmacological properties such as antioxidant, antiulcer, anti-inflammatory, antidiuretic and so on.

INTRODUCTION: *Manilkara hexandra* (Roxb.) Dubard, synonym: *Mimusops hexandra* Roxb, widely spread in central India as well as Deccan Peninsula. It is cultivated throughout India covering major regions. It is also equated with Khirni. The fruits of the plant are one of the most underutilized fruits in the Gujarat state. It is popularly known as 'Rayan'¹.

1. Origin and Distribution:

1.1 Geographical Source: It is native to India, mainly distributed as a wild tree in the southern part and North-central part of India.

It is widely spread in Gujarat, Rajasthan, Madhya Pradesh, Andhra Pradesh, Kerala, and Maharashtra³. It is also found in Malaya; mainly grown in gardens.

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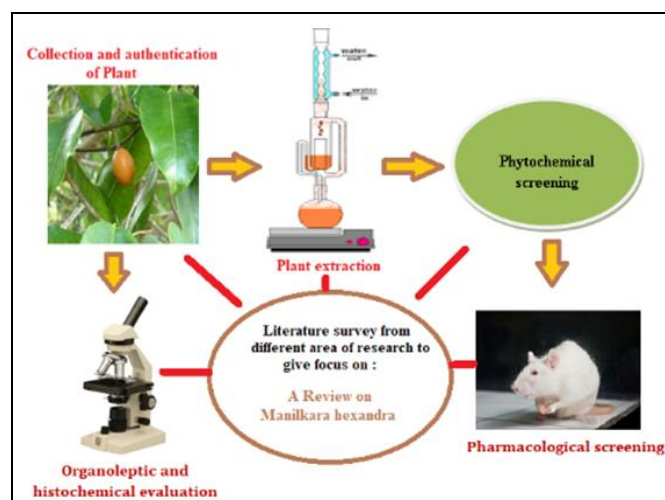


FIG. 1: GRAPHICAL REPRESENTATION PHARMACOGNOSY STUDY OF *M. HEXANDRA*

Vernacular Names: ^{1, 2}

Hin	:	Khirni, Khirani
Eng	:	Obtuse leaved mimusops, Kauki
San	:	Raajaadan, Phalaadhyakhsa, Rajanyaa, Khsirikoo
Tam	:	Ulakkaippa-lai Palai
Tel	:	Patla, Pola, Kirni
Ayurvedic	:	Khirni
Siddha	:	Palai

Local name	:	Reni
Synonyms	:	<i>Mimusops hexandra</i> Roxb. <i>Mimusops indica</i> (A. DC.)
Other Similar Plant	:	<i>Manilkara kauki</i>
Part Used	:	Fruit, Seed, Seed oil, Bark
Botanical Name	:	<i>Manilkara hexandra</i> (Roxb.) Dubard.
Family	:	Sapotaceae

Botanical Classification:

Kingdom	:	Plantae
Phylum	:	Tracheophyta
Sub-phylum	:	Euphyllophytina
Class	:	Magnoliopsida
Sub-class	:	Magnoliidae
Order	:	Ericales
Family	:	Sapotaceae
Genus	:	Manilkara
Species	:	<i>Manilkara hexandra</i>

2.2 Cultivation, Collection and Harvesting:

Propagation of the plant is usually done by seed germination, air layering or by vegetative propagation, including cutting. It is a tropical based crop. It can be grown very well at an altitude of 1000 m. Any type of soil is favorable for the growth of the plant. It can also be planted by rootstock. Sowing can be done during June-December. The space of 8 × 8 m must be recommended in between the crop for conventional planting. It requires proper irrigation soon after planting. Manures and fertilizers may be applied in the month of September-October, about 45 cm away from the trunk upto the leaf apex. The rootstock sprouts, water shoots, and lower branches should be removed after cultivation. The legumes

and vegetable crops must be cultivated as intercrop during pre-bearing stage of cultivation. Farmyard manure can be preferable. The fertilizer must require appropriate amount of nitrogen, phosphorus and potassium. The mature fruits should be harvested by hand picking method in the month of February to June and September to October. Alternatively, fruits can be exposed to ethylene gas at 100 - 200 ppm for 18-20 h to induce ripening ^{4, 5}.

3. Pharmacognostic Study:

3.1 Macroscopy Study: According to the Ayurvedic book, the organoleptic characters are as follow:

Habitat: A medium-sized to a large glabrous evergreen tree, height 15-20 m; stem:bark: blackish-grey, deeply furrowed; leaf: simple, alternate, 5-15 cm by 2.5-5 cm, elliptic-obovate or oblong, coriaceous, rounded or emarginated, at the apex, dark green and polished above, light green beneath, glabrous on both sides main nerves 12-20 pairs, petioles 1.25 cm long, channeled above glabrous; flower: white r pale yellow small odorous, axillary, solitary or in 2-6 flowered fascicles pedicels ⁶⁻¹³ mm long, glabrous or nearly so; Fruit: berries ovoid or ellipsoid, milky one rarely seeded two 1.25 cm long, green, when unripe, reddish-yellow; when ripe, shape like the fruit of *Azadirachta indica*; Seed: ovoid, 1 cm long, brownish-black, shinning with white testa.

Flowering and Fruit Period: March - April and May-June:

Collection: April - May:

3.1.1 Seeds: Type: berry with one-seeded, sometimes two seeds are found; shape: oblique to ovoid, compressed with shining appearance, presence of elongated hilum with testa; the presence of thick and fleshy endosperm, cotyledons are thin, papery with prominent reticulate venation, short radicle, and plumule; odor: slight characteristics; taste: bitter; color: reddish brown ⁶.

3.1.2 Leaves: Type: alternate; shape: elliptic, oblong to obovate, sometimes oblong, rounded; apex: emarginated with glabrous; color: dark green; taste: bitter ⁷.

3.1.3 Stem Bark: Shape: longitudinal, quilled; surface: outer surface shows dark brown to greyish, rough, scaly, presence of mosses and lichens

whereas inner surface is pink color, which in turn into reddish-brown on drying, striations are seen;

fracture: fibrous; odor: none; taste: astringent⁸ as shown in **Fig. 2**.



FIG. 2: ORGANOLEPTIC EVALUATION OF MANILKARA HEXANDRA. (A) LEAVES, (B) FRUITS, (C) SEEDS, (D) STEM BARK, (E) POWDER OF STEM BARK

3.2 Microscopy Study: The macroscopical analysis of the plant has been mentioned in detail in **Table 1** and **Fig. 3**.

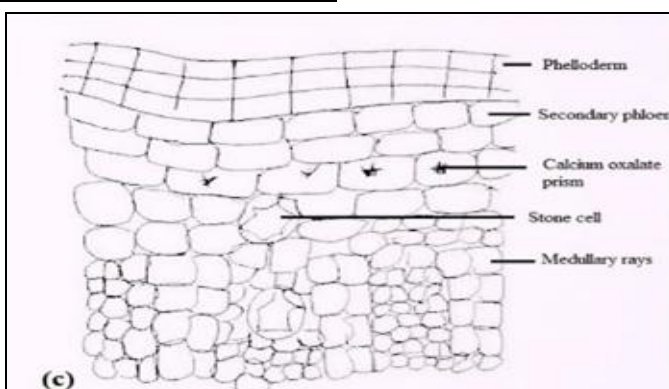
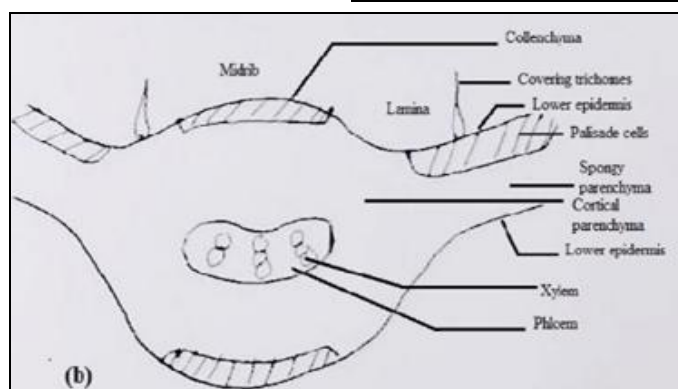
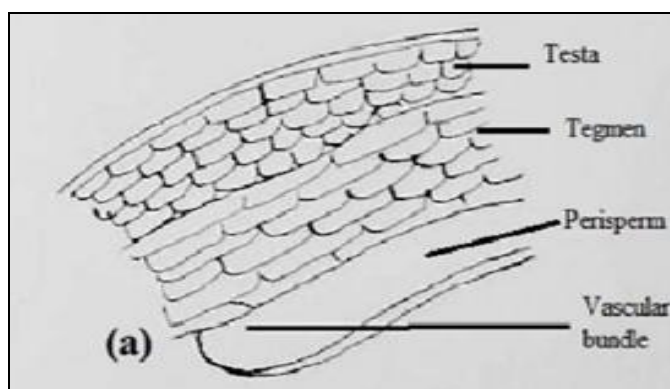


FIG. 3: TRANSVERSE SECTION OF DIFFERENT PARTS OF MANILKARA HEXANDRA. (A) SEED; (B) LEAF; (C) STEM BARK

4. Phytochemistry: A new compound that has been identified by GC-MS was 7, 9-di-tert-butyl-1-oxaspiro (4.5) deca-6, 9-diene-2, 8-dione. The isolated compound showed antibacterial activity as it has high zone of inhibition in the range of 30 to 150 µg/ml. It is assumed that the isolated flavonoid has a great significance, used in the pharmacological applications as main components in the drug delivery system.

Catechin possessed a significant antioxidant activity and has unique biological behaviors, as it acts as a metal chelating agent also. 6 Fruits and seeds of the plant contain phenolic compounds, quercetin, and dihydroquercetin.

For the first time, Benzaldehyde derivatives are reported to present in the plant. Out of which, one compound named as 3, 4-dihydroxy benzaldehyde

was active against *Streptococcus aureus* at a concentration of 500 µg/ml (zone of inhibition of 21.5 ± 0.70 mm) and another compound methyl-p-coumarate was found to be active against *Streptococcus epidermidis* (250 µg/ml level; zone of inhibition of 22 ± 1.41 mm).

As these compounds has a great significance in the treatment of skin infection. Isolation and purification of three bidesmosidic saponins from the seeds of the plant cultivated in Egypt, containing protobassic acid and 16-ahydroxyprotobassic acid as aglycones, showed significant anti-inflammatory, antioxidant and cytotoxic activity. Fruits and seeds of Rayan were

analyzed for total phenolic and flavonoid content. Major phenolic compounds such as asgallic acid, quercetin, and kaempferol were obtained from fruits and quercetin, gallic acid, and vanillic acid from the seeds and were properly analyzed through LC-MS. The seeds also contain 16% of fatty oil and 1% saponin.

All parts gave taraxerol, a triterpene ketone, alpha- and beta-amyrin, cinnamates, alpha-sipnasterol, beta-sitosterol, its beta-D-glucoside, quercitol, quercetin and its dihydroderivatives, ursolic acid^{1, 9-18} (summary of chemical constituents are given in **Table 2** and **Fig. 4**).

TABLE 1: HISTOCHEMICAL CHARACTERISTICS OF DIFFERENT PARTS OF MANILKARA HEXANDRA^{6,7,8}

Part Used	Microscopic Description	Powder Characteristics
Seeds	Transverse section of seed has testa and endosperm. Testa constitutes the outer portion of the seed followed by lignified sclereids. Endosperm consists of thin-walled parenchymatous cells containing oil globules. Starch grains are abundantly found in the region. The cotyledons are compactly arranged with parenchymatous cells.	Colour: light brown; coarse; odour: characteristic; taste: bitter; sclerenchyma cells, parenchyma cell, starch grains, endosperm cells; 26.66 µm in diameter.
Leaves	The leaf has dorsiventral pattern. Transverse section of leaf shows two distinct portion namely, Lamina and midrib region. Lamina is differentiated into upper epidermis, mesophyll and lower epidermis. Upper and lower epidermis has similar features. They consist of single layered, rectangular shaped epidermal cells with glossy thin cuticle layer. It contains covering trichomes and anomocytic stomata. Calcium oxalate crystals are found abundantly present in the lower epidermis. Mesophyll contains palisade layer and spongy parenchyma cells. Midrib showed arc-shaped meristele containing xylem and phloem. Thin strips of collenchyma are seen below upper epidermis and above lower epidermis.	Color: dark green; odor: characteristics; taste: bitter; epidermal cells, anomocytic stomata, covering trichomes, lignified fibers, calcium oxalate crystals, xylem vessels.
Stem bark	Histology of stem bark consists of: Rhytidome contain compact cells of cork. The phelloderm and phloem are the major part of this region A few patches of lignified fibers are found present. Phellem consists of multiple layers of cork cells which are tangentially elongated in nature. Phellogen are formed of periderm layers. Each made up of 2 - 3 layers of thin walled phellogen, which on the outer side forms the phellem and on the inner side the phelloderm. Phellogen consists of thin-walled loosely arranged cells followed by cell inclusions. It contains secondary phloem which is thin walled polygonal cells. Starch grains, stone cells are abundantly present in the region.	Presence of cork cell, stone cells, fibers, starch grains, prism of calcium oxalate crystals .

TABLE 2: DISTRIBUTION OF CHEMICAL CONSTITUENTS IN VARIOUS PARTS OF MANILKARA HEXANDRA⁹⁻¹⁸

Parts of Plant	Phytochemical components
Leaves	Terpenic hydrocarbon, Taraxerol, Hentriacontane, Triterpene ketone, Cinnamic acid, Quercitol, 4-methyl benzaldehyde, p-coumaric acid, 3,4-dihydroxy benzaldehyde
Flowers	Ethyl nicotinate, D-Quercitol
Mesocarp of fruit	Ursolic acid, α-amyrin acetates, β-amyrin acetates, Tetra-hydroxy alcohol, monohydroxy monocarboxylic acid, α-spinasterol, Gallic acid, Quercetin, Kaempferol
Root	Quercitol, α- amyrin cinnamates, β-amyrin cinnamate, Cinnamic acid, Taraxerol, α-spinasterol, β-D-glucoside of β-sitosterol
Bark	Taraxerol, Taraxeryl acetate, α-amyrin cinnamate, α-spinasterol, Triterpenoid acid, Triterpenoid saponin: 1β, 2α, 3β, 19α-tetrahydroxyursolic acid 28-O-β-D-glucopyranoside, β-sitosterol, Flavonoid: 7,9-di-tert-butyl-1-oxaspiro[4.5]deca-6,9-diene-2,8-dione, Flavan- 3- ol,
Seed	Dihydroquercetin, Quercetin, Sterol: ergosterol, β-d-glucoside of β-sitosterol, Quercitol, Xylose, Arabinose, Rhamnose, Glucose, gallic acid, Myrecetin, Vanillic acid

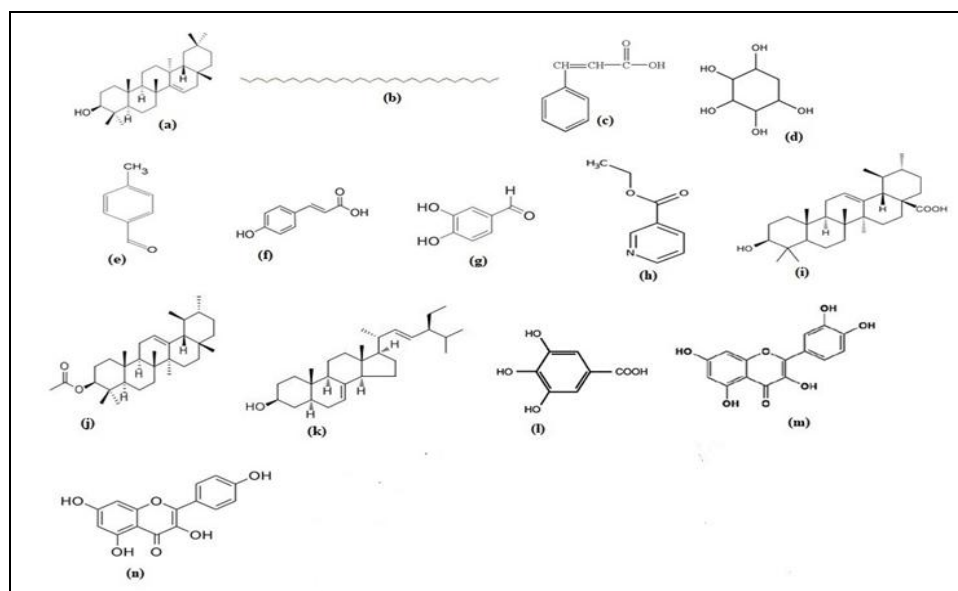


FIG. 4: STRUCTURES OF PHYTOCHEMICAL CONSTITUENTS. (A) TARAXEROL; (B) HENTRIACONTANE; (C) CINNAMIC ACID; (D) QUERCITOL; (E) 4-METHYL BENZALDEHYDE; (F) P-COUMARIC ACID; (G) 3, 4-DIHYDROXY BENZALDEHYDE; (H) ETHYL NICOTINATE; (I) URSOLIC ACID; (J) A-AMYRIN ACETATES; (K) A-SPINASTEROL; (L) GALLIC ACID; (M) QUERCETIN; (N) KAEMPFEROL

5. Pharmacological Activity:

5.1 Antibacterial Activity: Antibacterial potency of herbal gel containing *M. hexandra* leaf extracts, including methanolic and hydroalcoholic with different concentration of carbopol 934 was carried out against *Enterobacter aerogenes*, *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis* and *Proteus vulgaris*, respectively.

Although the other parameters were also evaluated such as homogeneity, color, pH, spreadability of the formulation, the results revealed that formulation containing 1% of gelling agent and 2.5% of the extract showed better stability¹⁹.

Another investigation revealed the fact that the isolated flavonoid, 7, 9- di-tert-buty-1-oxaspiro (4.5) deca-6, 9-diene-2, 8-dione has antibacterial potency at a concentration from 30-150 µg/ml²⁰. Patel K *et al.*, examined the antibacterial activity of the seed extract of the plant prepared from microwave-assisted extraction method. The study showed significant bactericidal action against *Streptococcus mutans* with a minimum bactericidal concentration in the range of 600-900 µg/Ml²¹.

5.2 Antifertility Activity: Seeds of the crude drug have been evaluated for an antifertility property using male albino rats, where it has been observed that there is a markedly decrease in the sperm count of the animals²².

5.3 Antimicrobial Activity: Antimicrobial activity of different leaf extracts of the plant, including petroleum ether, acetone, and methanol, has been tested against gram-positive bacteria, gram-negative bacteria, molds, and yeast. The activity was performed using the agar disc diffusion method at 250 and 500 µg/disc of concentrations. The methanolic extract exhibited maximum antimicrobial potency²³. Aqueous extracts of aerial parts of *Euphorbia thymifolia* and leaves of *M. hexandra* were evaluated for antimicrobial activity using well diffusion method against six different bacterial strains of *Streptococcus mutans*, *Bacillus subtilis*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Salmonella bongori* and *Enterococcus faecalis* and two fungal strains *Candida albicans* and *Aspergillus niger*. The extract of *M. hexandra* was found highly significant when compared to *E. thymifolia* plant extract²⁴. Another study has contributed to the utilization of *M. hexandra* leaf as an antimicrobial compound. *Keshetti et al.*, experimented and showed that the plant extracts, namely petroleum ether, acetone, and methanol, has the potency to exhibit MIC in the range of 250-32,000 µg/ml.

The potency has checked against various microbial strains including, 9 Gram-positive bacteria, 14 Gram-negative bacteria, 7 yeast, and 4 molds, using agar disc diffusion method.

Among all the extracts, methanol extract was found to show maximum antibacterial activity²⁵. The compounds of the plant isolated from the dried leaves and flowers, methyl-p-coumarate and 3, 4-dihydroxy benzaldehyde, are reported to be active against *Streptococcus aureus* and *S. epidermidis*²⁶.

5.4 Antiulcer Activity: Ethyl acetate extract of the plant was examined for the effectiveness of gastric ulcers using ethanol, ethanol-indomethacin, and pylorus ligated gastric ulcer models. It has observed that the extract can significantly reduce the lipid peroxidation in treated animals and also inhibit the increase in vascular permeability. Moreover, it has found that the pre-treatment with ethyl acetate extract increases mucus production and glycoprotein levels when given either orally or intraperitoneal, as there is an increase in the mucin content and TC: PR ratio, respectively²⁷.

5.5 Antidiabetic Activity: The ethanolic bark extract has tested for antidiabetic activity in streptozotocin-induced diabetes models in rats. In

overnight fasted rats, NIDDM was introduced by streptozotocin (60 mg/kg, i.p). During the experiment, the extract dose was given at a single dose for twenty-one days, where it has observed that there is a marked reduction in the biochemical parameters such as serum levels of cholesterol, triglycerides, HDL, and LDL²⁸.

5.6 Antioxidant Activity: The antioxidant property of methanolic extract of fruits and seeds of the plant was measured using six different assays including, FRAP, DPPHRS, ABTSRSA, HRSA, and NORSA, respectively. It has observed that fruits are considered as an excellent source of antioxidants, compared to seeds and showed the presence of phenolic components like gallic acid, quercetin, kaempferol, and vanillic acid, which are the richest source of antioxidant property²⁹. Another study showed the evidence of antioxidant activity of different fractions of leaf extract of *M. hexandra*, using DPPH, Fe³⁺ reducing power assay³⁰ pharmacological activities, as shown in **Fig. 5**.

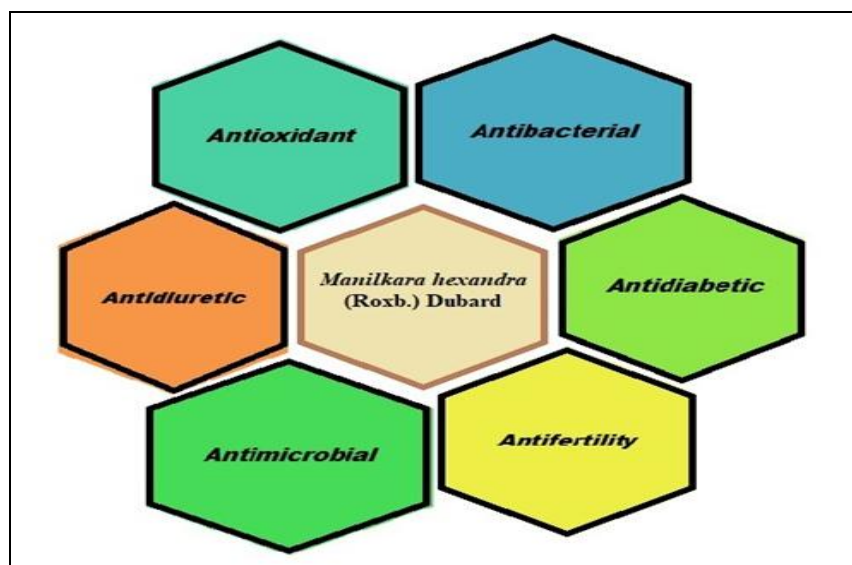


FIG. 5: PHARMACOLOGICAL ASPECTS OF *MANILKARA HEXANDRA*

6. Ethnomedicinal uses:

- ❖ Stem decoction was used to treat diarrhea, fever, and stomach infections by Koli tribe.
- ❖ Bark and roots were known for the astringent property.
- ❖ Powdered seeds were mixed with honey to cure redness in the eyes. It is used as febrifuge, anthelmintic, antileprotic.
- ❖ The bark and root powdered were given to prevent infantile diarrhea.
- ❖ Leaves were used as a poultice for tumors.
- ❖ Epilepsy: Juice of glands of the stem of the described plant 20 mL, Piper longum 500 mg, honey 20 g, is given two times a day for two months.
- ❖ Cloasma: Local application of a paste of leaves of the described plant with fresh milk is usefulness.
- ❖ Dentalgia: Apply latex of the described plant as required.

- ❖ Menorrhagia: Fried leaves powder of the described 10-20 g with water is given two times a day.
- ❖ Scorpion sting: Local application of seed paste of the plant is good for relieves pain.
- ❖ Skin diseases, acne vulgaris, and black spot on face: Local application of a paste of unripe fruit of the plant is very beneficial.
- ❖ Used to treat erectile dysfunction of penis, Usefulness for gaining body weight.
- ❖ Seed oil of the plant 10 drops, sugar candy 10 g with cream of milk 15 g is given two times a day.
- ❖ Oligogalactia, memory weakness: Fruits of the plant 100 g is given twice a day^{31, 32}.

7. Therapeutic uses:

- ❖ The bark is employed as astringent, refrigerant, aphrodisiac, alexipharmic, stomachic, anti-helminthic, for relieving fever, flatulence, colic, dyspepsia, helminthiasis, hyperdipsia, burning sensation.
- ❖ The fruits are refrigerant, aphrodisiac, appetizer, galactagogue, emollient, tonic, anorexia, dyspepsia, nervous weakness, bronchitis, spermatorrhea, consumption, hallucinations and unconsciousness^{31, 32}.

8. Ayurvedic Preparation:

Ras	: Madhur
Gun	: Guru, snigdha
Veerya	: Sheela
Vipaka	: Madhur
Tridosha Effect	: Alleviates
Vaata	: +++; Pitta: ++, aggravates
Kapha	: ++.

9. Dossage:

Fruit	: 25-50 g
Seed	: 5-10 g
Seed Oil	: 5-10 drops
Bark	: 10-20 g

10. Ayurvedic Formulation: Virhat narikel khandā^{31, 32}.

CONCLUSION: The plant belongs to Sapotaceae, is indigenous to India. The literature report revealed its use as an anti-inflammatory, antigout

agent. Sometimes it can be employed in treating various diseases such as colic dyspepsia, hyperdyspepsia. The fruits contain sugar, proteins, fats, carbohydrates, a minor proportion of calcium, iron and phosphorus, Vitamins A, B, and C, respectively. This comprehensive review will support many more properties and activities of the plant, which ultimately play an important role in building steps for further research activities. While gathering information with respect to the plant, it has been analyzed that the genus *Manilkara* holds a great potential of many other pharmacological properties, which has to be flourished in the recent upcoming years through among us.

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CONFLICTS OF INTEREST: The authors declare no conflicts of interest.

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