CHAPTER - II

REVIEW OF LITERATURE
<table>
<thead>
<tr>
<th>Chapter 2</th>
<th>LITERATURE REVIEW</th>
<th>23-61</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Literature review</td>
<td>23</td>
</tr>
<tr>
<td>2.1</td>
<td><em>Gmelina arborea</em> Roxb.</td>
<td>23</td>
</tr>
<tr>
<td>2.1.1</td>
<td>Description</td>
<td>23</td>
</tr>
<tr>
<td>2.1.2</td>
<td>Morphology</td>
<td>24</td>
</tr>
<tr>
<td>2.1.3</td>
<td>Ethnobotanical uses</td>
<td>25</td>
</tr>
<tr>
<td>2.1.4</td>
<td>Phytochemical Review</td>
<td>27</td>
</tr>
<tr>
<td>2.1.5</td>
<td>Biological Review</td>
<td>29</td>
</tr>
<tr>
<td>2.2</td>
<td><em>Careya arborea</em> Roxb.</td>
<td>35</td>
</tr>
<tr>
<td>2.2.1</td>
<td>Description</td>
<td>35</td>
</tr>
<tr>
<td>2.2.2</td>
<td>Morphology</td>
<td>36</td>
</tr>
<tr>
<td>2.2.3</td>
<td>Ethnobotanical uses</td>
<td>37</td>
</tr>
<tr>
<td>2.2.4</td>
<td>Phytochemical Review</td>
<td>38</td>
</tr>
<tr>
<td>2.2.5</td>
<td>Biological Review</td>
<td>40</td>
</tr>
<tr>
<td>2.3</td>
<td>References</td>
<td>45-61</td>
</tr>
</tbody>
</table>
2. LITERATURE REVIEW

2.1 Gmelina arborea Roxb.

2.1.1 Description

_Gmelina arborea_ Roxb. is an unarmed, moderately sized to large deciduous tree, about 30m or more in height and a diameter of up to 4.5m. The genus was named after 18\textsuperscript{th} century German botanist J.C. Gmelin. The name _arborea_ means tree-like, derived from the Latin word ‘arbor’ means tree. The great sage _Charaka_ has categorized gambhari as _sothahara_-relieves oedema, _virecanopaga_-adjunct to purgation and its fruit as _dahaprasamana_-relieves burning sensation of the skin. In Ayurvedic texts, gambhari has numerous synonyms like _kasmari_- a beautiful tree, _sriparni_- has beautiful leaves, _madhuparnika_- has leaves with sweetish taste, _pita rohini_- has yellow flowers.

A. Taxonomical profile

<table>
<thead>
<tr>
<th>Kingdom</th>
<th>: Plantae</th>
</tr>
</thead>
<tbody>
<tr>
<td>Division</td>
<td>: Magnoliophyta</td>
</tr>
<tr>
<td>Class</td>
<td>: Magnoliopsida</td>
</tr>
<tr>
<td>Order</td>
<td>: Lamiales</td>
</tr>
<tr>
<td>Family</td>
<td>: Verbenaceae</td>
</tr>
<tr>
<td>Genus</td>
<td>: <em>Gmelina</em></td>
</tr>
<tr>
<td>Species</td>
<td>: <em>Gmelina arborea</em> Roxb</td>
</tr>
</tbody>
</table>


B. Common names (Vernacular names)

<table>
<thead>
<tr>
<th>Language</th>
<th>: yemane, yemani, yemari</th>
</tr>
</thead>
<tbody>
<tr>
<td>English</td>
<td>: beechwood, gmelina, goomar teak, Kashmir tree, white teak.</td>
</tr>
<tr>
<td>French</td>
<td>: gmelina, melina, peuplier d Afrique</td>
</tr>
<tr>
<td>German</td>
<td>: Gumar-Teak</td>
</tr>
<tr>
<td>Nepali</td>
<td>: gamari, gambari, gumhari, khamari</td>
</tr>
<tr>
<td>Bengali</td>
<td>: gamari, gambar, gumbar</td>
</tr>
<tr>
<td>Gujarati</td>
<td>: Shewan, Sivan</td>
</tr>
</tbody>
</table>
2.1.2 Morphology

Figure 2.1 Gmelina arborea Roxb

A. Leaves: They are opposite, decussate, petioles cylindrical, 5-15cm long, leaf blades broadly ovate, 10-25cm x 7-20cm wide, apically long acuminate or caudate, entire on mature plants but strongly toothed or lobed on young plants, usually cordate or trunkate basally, with a short cuneate attenuation into the petiole, densely tomentose above when young, becoming glabrous above when mature, permanently densely fulvous, tomentellous with stellate hairs beneath, glanduliferous just above the petiole on the basal attenuation.
B. **Flowers:** Flowers are abundant, scented, reddish, brown or yellow, in terminal and axillary 1-3 flowered cymes on the panicle branches, which are about 8-40cm long. Flower is 2.5-5cm in diameter; bracts 8mm long, linear lanceolate. Calyx is broadly campanulate, about 5mm long, densely fulvous-tomentose externally, the rim with 5 small, triangular, acute teeth. Corolla are large, showy, varying from yellow to orange or brilliant orange to reddish or brownish yellow, dull yellow brown, tubular below, obliquely funnel shaped at the throat, the tube densely pubescent externally, the limb 2-lipped, the upper lip often orange-pink, deeply divided into 2 oblong, obtuse, backwardly curled lobules, the lower lip often lemon yellow, up to twice as long as the upper and 3-lobed.

C. **Fruit:** It is a drupe, 1.8-2.5cm long, obovoid, seated on the enlarged calyx; glossy and yellow when ripe, exocarp is succulent and aromatic. Endocarp is bony and usually 2-celled. Seeds are 1-3, lenticular and exalbuminous.

D. **Bark:** It is smooth, pale ashy-grey or grey to yellow with black patches and corky circular lenticels. Internal surface of bark is brown coloured, exfoliates into thick woody plates or flakes.

E. **Geographical distribution:** *Gmelina arborea* extensively found in the sub-Himalayans tracts eastwards from the Ravi river, common throughout Assam and adjoining areas of Northern West Bengal, also in South Bihar and Orissa, sporadically found in western and southern India and planted on a large scale.

### 2.1.3 Ethnobotanical uses

*Charaka* prescribed a paste of the leaves as ingredients of a medicated clarified butter for stiffness of the back, facial paralysis; prescribed the soup of fruits in diarrhoea. *Sushruta* prescribed the drug internally in bilious fever, haemoptysis, breathing trouble, asthma and for promoting adhesion of fracture bones. *Chakradatta* gave ripe fruits with honey for checking hemorrhage. Ripe fruits dried and cooked with cow’s milk, for urticaria. Pulverized root is applied on gout. It is important ingredient of *Dashamularista* as tonic and *Shriparnayaadi kwaath* used in fever. Leaf paste is used in cephalgia. Fruits are used for reducing fever.⁴
In Ayurveda, it has been observed that gamhar fruit is acrid, sour, bitter, sweet, cooling, diuretic, tonic, aphrodisiac, alternative astringent to the bowels, promote growth of hairs, useful in 'vata', thirst, anaemia, ulcers, alopecia, consumption, leprosy, strangury, thirst and vaginal discharges. The flower used for blood disorders and leprosy. The root is anthelmintic, laxative, burning sensations, fever, hallucinations, piles and urinary discharges. The leaves are used for treatment of diarrhoea, high blood pressure, malaria, scorpion and insect stings.  

Leaves used in herpes zoster. The juice of leaves is used as demulcents in cough, gonorrhoea, to remove foetid discharge and worms from ulcer. Leaf is used as carminative, in headache, anasarca, asthma, bronchitis, cholera, colic pain, diarrhoea, dropsy, dyspepsia, epilepsy, fever, phthisis, rheumatism, small pox, sore, spleen complaints, syphilis, throat swelling, urticaria, as antidote to snake bite and some other poisons, cough and gonorrhoea. Leaves used in high blood pressure, malaria, diarrhoea, scorpion and insect sting. The tender leaves are demulcents, carminative, purgative, diuretic and anti-inflammatory, also used in gonorrhoea, cough and ulcer. Leaf-paste is applied on wounds. The juice of leaves is used as demulcent in cough, gonorrhoea. The leaves are used in headache, gonorrhoea, cough, bronchitis, dyspepsia and wound treatment.

Stem used in diabetes, cough, hoarseness, sore throat, asthma and dysuria. 

Fruits are used in shortness of breath. Flowers used in blood disease. Fruits are astringent, insecticide, wound dressing, fever, skin disease, urticaria, biliousness. Ripe fruit juice is given with sugar in dysentery. The flowers are sweet, cooling, bitter, acrid; astringent; useful in leprosy and blood diseases.

The roots are used as anthelmintic, stomachic, tonic, hyperdipsia, stomachalgia, leucorrhoea, colitis, trichogeneous, leprosy, anemia, and strangury and skin disease. Root is used as blood purifier, in catarrh of bladder. Decoction of root is used as tonic. The root is stomachic, laxative, anthelmintic; improves the appetite; useful in hallucinations, thirst, piles, abdominal pains, burning sensations, fevers, tridosha. Root is bitter tonic, stomachic, laxative and galactogogue. Infusion used in indigestion, fever and anasarca. Pulverized root is applied on gout. The bark is bitter tonic and stomachic. The
flowers are given in blood disorder. Root is an ingredient of the Dasamulas, used with liquorice, sugar and honey used as galactogogue. Root used in fever, indigestion, anasarca and blood purifier.

Bark used in bone fracture, stomach disorder and as antidote to poison. Bark used in stomach ailments scabies, antidote, used in whitlow. It uses as galactogogue, appetite stimulant, used in liver disorder, wound healer, gout. The roots are used in catarrh of bladder and constipation. The plant used in epilepsy, dropsy and rheumatism. Fruits are used as cooling agent.

Root bark is appetizing, digestive, brain tonic, laxative and vertigo, emaciation, abdominal colic, insanity, piles, burning, oedema and dyspepsia. The fruits are diuretic, nutritive, used in tuberculosis; promote hair growth, menorrhagia and burning sensation. Flower used in burning pain, bleeding from internal organ, disease of impure blood.

Bark-paste is applied on bone fracture.

The plant is recommended in combination with other drugs for the treatment of snakebite and scorpion sting. In snakebite a decoction of the root and bark (1 in 16) is given internally. The root decoction is used in folk remedies for abdominal tumors in India. It is also a folk remedy for anasarca, anthrax, asthma, bilious disorder, bites, blood disorder, cholera, convulsions, delirium, gravel, phthisis, bronchitis, diarrhea, dropsy, dyspepsia, epilepsy, fever, gout, headache, hemorrhage, intoxication, madness, rat bite, rheumatism, rinder pest and septicemia.

2.1.4. Phytochemical Review

The leaves of *G. arborea* reported to contain iridoids 6-O-alpha-L-rhamnopyranosyl-catalpol, 6-O-(3”-O-trans-feruloyl)-alpha-L-rhamnopyranosyl-catalpol-6-O-(2”-O-acetyl-3”,4”-O-di-trans-cinnamoyl)-alpha-L-rhamnopyranosylcatalpol, phenylpropanoid glycosides verbascoside (acteoside) and martynoside, acylated iridoid glycosides named gmelinosides A-L. Three iridoid glycosides 6-O-(3”-O-benzoxy)-alpha-L-rhamnopyranosyl catalpol, 6-O-(3”-O-trans-cinnamoyl)-alpha-L-rhamnopyranosylcatalpol and 6-O-(3”-O-cis-cinnamoyl)-alpha-L-rha-mnopyranosylcatalpol,6-O-(3””,4”-O-dibenzoxy)-alpha-L-rhamno-pyrano-sylcatalpol have been isolated from aerial parts of *Gmelina arborea*. 
Figure 2.2 Chemical constituents of *Gmelina arborea* Roxb

Bark reported to contain lignan such as tyrosol [2- (4- hydroxyphenyl) ethanol], (+) - balanophonin, 8- 5’ neolignan, (-) - balanophonin and gmelinol. Phenylethanoid glycoside e.g. (-)- p- hydroxyphenylethyl[5”- O- (3,4dimethoxycinnamoyl)-ß- d- apiofuranosyl (1' →6')]-ß- d- glucopyranoside and also reported to contain 2,6-dimethoxy-p- benzoquinone and 3,4,5- trimethoxyphenol.\\(^{33}\)

Arborone and 7-oxo dihydrogmelinol,\\(^{34}\) 6“- bromo - isoarborone, 4 - hydroxysesamin, 4,8-dihydroxysesamin, 1,4-dihydroxysesamin(gummiadiol), 2-piperonyl-3-hydroxyl- methyl - 4 - (α - hydroxy - 3,4- methylenedioxybenzyl) - 4 - hydroxytetrahydrofuran, and
the 4-O-glucoside of 4-epigummadiol. Gummmadiol (1,4-dihydroxy-2, 6-dipiperonyl-3, 7-dioxabicyclo-[3, 3, 0]-octane) is a dihydroxylignans. Quercetagetin, glycosides of kaempferol, apigenin and luteolin. Root contains umbelliferone 7-apiosylglucoside, arboele, gmelanone has been reported from Gmelina arborea.

The root of G. arborea is also reported to contain ceryl alcohol, gmelofuran, gmelinol, hentriacontanol-I, n-octacosanol, β-sitosterol, sesquiterpene. Stem; bromoisoboreol, cluytferulate, gmelanone, gmelinol, gummidiol, lignans, lignan hemiacetal, n-hentriacontanol-I, n-octacosanol, β-sitosterol; Leaf: apigenin, hentriacontanol, luteolin, quercetin, quercetogenin, β-sitosterol.

The heartwood contains lignans, arborone, oxodihyrgmenol, paulownin acetate and epieudesmin; trans- p-methoxycinnamate and trans p-hydroxycinnamic acid.

The roots contain sesquiterpenoid, apiosylskimmin, and gmelofuran. The heart wood gives ceryl alcohol, cluytferulate, lignans, arboele, gmelonone, 6-bromo isoarboreol, lignin, hemiacetal and gummidiol.

Leaves yield luteolin, apigenin, quercetin, hentriacontanol, β-sitosterol, quercetogenin and other flavons. Fruits contain butyric acid, tartratic acid, and saccharine substances. It also reported to contain alkaloid Premnazole.

### 2.1.5 Biological Review

#### A. Antiulcer activity:
Giri et al. reported antiulcer activity on hydro-alcohol extracts of leaves of G. arborea when evaluated using experimentally induced ulcer in Wistar rats using different experimental models such as aspirin induced ulcer, pylorus ligation induced ulcers, and ethanol induced ulcers and cold restrain stress induced ulcers.

The Methanol extract of G. arborea showed anti-ulcer activity in pylorus ligation and ethanol induced ulcer models in Wistar albino rats. Extracts inhibits of the gastric lesions induced by pylorus ligation induced ulcer and ethanol induced gastric ulcer. The extract showed significant reduction in gastric volume, free acidity and ulcer index as compare to control.
B. Anthelmintic activity\textsuperscript{49}: Ambujakshi et al. showed that the crude alcohol and water extracts of leaves of \textit{G. arborea} has reported anthelmintic activity against \textit{Pheretima}, \textit{Posthuma} and \textit{Ascardiagalli}, as compared with standard reference Piperazine citrate.

C. Cardioprotectives activity\textsuperscript{50}: Vijay et al, showed cardioprotective activity of ethanol extract of \textit{Gmelina arborea} against DOX-induced cardiotoxicity in rats. It protect against DOX-induced increased the levels of marker enzymes. It significantly inhibits DOX-provoked glutathione (GSH) depletion in cardiac tissues. The reductions of cardiac activities of catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GSH-Px) and glutathione reductase (GR) were significantly mitigated.

D. Vasodilating activities\textsuperscript{51}: Wansi et al. reported the hexane extract of leaves of \textit{G. arborea} possesses antioxidant and vasorelaxant properties. The oxidative stress and its vasorelaxant effects were carried out on isolated rat aorta. The \textit{in vitro} vasodilating effects of the extract were evaluated using intact and denuded rat thoracic aortic rings or aorta pre-incubated in L-NAME, indomethacin or glibenclamide and contracted with phenylephrine. The \textit{in vivo} effects of \textit{G. arborea} hexane extract prevented both left ventricular and vascular hypertrophy, it also affect lipid metabolism, prevent lipid peroxidation, increased superoxide dismutase and catalase activity.

E. Anti-hyperglycemic activity\textsuperscript{52}: Punitha et al. evaluated anti-hyperglycemic activity of the ethanol extract of \textit{G. arborea} leaf in streptozotocin induced male Wistar albino rats using glibenclamide as standard. The lipid profile such as TC, TG and LDL levels were significantly increased in diabetic control animals whereas HDL levels were decreased when compared to the control rats.

F. Antidiabetic activity\textsuperscript{53}: Opara et al. Showed antidiabetic properties and ability to enhance renal function of aqueous extracts of \textit{G. arborea} by haematological and biochemical responses using rabbits. Red blood cells of the animals were significantly increased, neutrophils progressively decreased while glucose analysis of the rabbits recorded a progressive decrease dose dependent.
G. Wound healing activity\textsuperscript{54}: Shirwaikar et al. evaluated wound healing activity of alcohol extract of leaves powder of \textit{G. arborea} using incision, excision and dead space wound models in rats. The extract significantly increase in wound contraction rate, skin breaking strength, granuloma breaking strength, hydroxyproline content and dry granuloma weight and decrease in epithelization period was observed.

H. Hepatoprotective activity\textsuperscript{55}: Sinha et al. reported hepatoprotective activity of the aqueous extracts of bark and fruit of \textit{G. arborea} against paraquat- and hydrogen peroxide induced oxidative stress using liver slice culture.

I. Antidiarrheal activity\textsuperscript{56}: Agunu et al. showed \textit{G. arborea} possesses antidiarrheal activity when tested by perused isolated rabbit jejunum and castor oil-induced diarrhoea in mice.

J. Antioxidant Activity\textsuperscript{57,58}: Patel et al. reported antimicrobial and antioxidant activity of the Methanol and Chloroform extracts of \textit{G. arborea}. Antioxidant activity was tested using 2, 2 diphenylpicryl - 1- hydrazyl (DPPH) and β-carotene bleaching methods.

The methanol extracts of stem bark of \textit{G. arborea} (MEGA) has reported for antioxidant activity by using the free radical scavenging activity assay (DPPH method), reducing power assay, nitric oxide scavenging activity, hydroxyl radical scavenging activity and \( \text{H}_2\text{O}_2 \) scavenging activity.\textsuperscript{59}

Aqueous extract (AE) and methanol extract (ME) of \textit{G. arborea} bark has reported antioxidant activity when studied by various \textit{in vitro} techniques using stable 1, 1-diphenyl-2-picryl hydrazyl radical (DPPH) assay, free radical scavenging assay, reducing power assay and nitric oxide screening activity.\textsuperscript{60}

K. Antifungal activity\textsuperscript{61}: Kawamura et al. reported antifungal activity of the heartwood of \textit{G. arborea} against \textit{Trametes versicolor} and \textit{Fomitopsis palustris} using a sensitive bioassay system for antifungal activity against basidiomycetes has been developed which uses a medium in which homogenized hyphae has dispersed. Ethyl acetate solubles from the heartwood showed the highest activity five constituents has been isolated and identified as (+)-7'-O-ethyl arboreol, (+)-
paulownin, (+)-gmelinol, (+)-epieudesmin and (−)-β-sitosterol. The four lignans showed antifungal activity, gmelinol has reported antifungal constituent.\textsuperscript{62}

L. \textbf{Antimicrobial activity}\textsuperscript{63}: El-Mahmood et al. reported antibacterial activity on leaf and stem of bark extracts of \textit{G. arborea} against \textit{Escherichia coli}, \textit{Klebsiella pneumoniae}, \textit{Proteus mirabilis}, \textit{Shigella dysenteriae} and \textit{Salmonella typhi}.

M. \textbf{Analgesic activity}: Gangwar et al. reported the methanol extract of leaves of \textit{G. arborea} possesses analgesic activity studied using acetic acid-induced writhing in mice and by Randall-Selitto assay. The central analgesic of alcohol extract of \textit{G. arborea} was evaluated using hot plate method and tail clip method. \textsuperscript{64}

Parhi et al. showed the analgesic and antipyretic activity on various extracts of the heart wood bark of \textit{G. arborea}. The peripheral analgesic and central analgesic activity of different extracts of \textit{Gmelina arborea} was evaluated by the acetic acid induced writhing test and tail-Immersion test in mice respectively. The antipyretic activity was evaluated using Yeast induced Pyrexia in Wister strain albino rats. Paracetamol was used standard as drug. \textsuperscript{65}

N. \textbf{Anti-inflammatory activity}\textsuperscript{66}: Barik et al. isolated premnazole, an isoxazole alkaloid isolated from \textit{G. arborea}. It exhibited significant anti-inflammatory activity in reducing cotton pellet-induced granuloma formation in rats.

O. \textbf{Anti-inflammatory and anti-nociceptive activities}\textsuperscript{67}: Kulkarni et al. showed that the aqueous and methanol extracts of stem bark of \textit{G. arborea} possess significant anti-inflammatory and anti-nociceptive activities evaluated using Wistar albino rats in a model of acute plantar inflammation induced by carrageenan and anti-nociceptive activity by using hot plate test and writhing test in Swiss albino mice.

P. \textbf{Toxicity study and analgesic activity}\textsuperscript{68}: Kulkarni et al. showed that the alcohol extract (AlcE) and its various fractions of stem bark of \textit{G. arborea} exhibited analgesic activity. The acute toxicity of AlcE and its fractions was investigated in female Swiss albino mice using the OECD guidelines. The analgesic activity was evaluated in Swiss albino mice by using acetic acid-induced writhing method. These results indicate that AlcE and its fractions are safe after oral administration.
Q. **Antibacterial, antioxidant and antidiabetic activities**\(^{69}\): Nayak et al, suggested the fruits of *G. arborea* possess antibacterial, antioxidant and antidiabetic activities evaluated on human pathogens like *B. subtilis*, *S. aureus* and *Pseudomonas aeruginosa*. *In-vitro* antioxidant activity of *G. arborea* fruits was studied by DPPH free radical scavenging and reducing power assay. The antidiabetic activity of extracts was carried out using alloxan induced diabetic model of Wistar rats.

R. **Diuretic activity**: Sravani et al. studied the diuretic effect of methanol extracts of the *G. arborea* (MEGA) activity in albino rats. Acute oral toxicity study was evaluated as per OECD guidelines. The diuretic effect of the extract was evaluated by measuring urine volume, sodium and potassium content. Urine volume is significantly increased in MEGA in treated rats. The diuretic effect of the extract was similar to furosemide.\(^{70}\)

Nayak et al. evaluated diuretic activity of different extracts of *G. arborea* fruit by determining urine volume, urine pH and electrolyte (Na+) concentration in male Wistar rats using urea as standard drug and saline water was used as control. There was no significant change in the pH of urine after administration of the *G. arborea* extracts. The excretion of sodium was also increased by all the extracts.\(^{71}\)

S. **Immunomodulatory effects**\(^{72}\): Shukla et al. evaluated immune stimulant activity on methanol extract of root of *G. arborea* (MEGA) and its ethyl acetate fraction (EAFME) on humoral and cell-mediated immune response using animal models like cyclophosphamide-induced myelo-suppression, delayed-type hypersensitivity (DTH) response, and humoral antibody (HA) titre. Extracts produced significant increase in HA titre, DTH response, and levels of total white blood cell count.

T. **In vitro cytotoxic activity**\(^{73}\): David et al. showed that the ethanol extracts of *G. arborea* leaf has exhibited *in vitro* cytotoxic activity. *In vitro* cytotoxic tested against Colon cancer (COLO 201), Gastric cancer (HT-29) and Human oesophageal cancer (TE-2) cell lines using the thiazolyl blue test (MTT) assay.

Shoeb et al. evaluated antioxidant and cytotoxic activities of methanol extracts and the derived sub-fractions of 90% methanol extract of *G. arborea* leaves using DPPH antioxidant activity and reducing power assay. The cytotoxic activity was
carried out via brine shrimp test and toward human cancer cell line; HepG\textsubscript{2} using Sulphorhodamine-B assay.\textsuperscript{74}

### Table 2.1 List of marketed formulation containing \textit{G. arborea}

<table>
<thead>
<tr>
<th>Manufacturing Company</th>
<th>Formulation</th>
<th>Medicinal uses</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVN Ayurveda Formulations Pvt. Ltd, Madurai</td>
<td>Sukumarakashaya</td>
<td>Pain during Menstruation, Backache, Constipation.</td>
</tr>
<tr>
<td>Ayurveda For You, Pune</td>
<td>Dahamoolachurna/ powder</td>
<td>\textit{Vata} diasorders, Imbalance, Oedema, Fever</td>
</tr>
<tr>
<td>Ayurvedic Formulary of India</td>
<td>Elanirkujambu (eye drop)</td>
<td>Cataract, Wounds in eye</td>
</tr>
<tr>
<td>Chandra Ayurved Bhavan Pvt. Ltd.(Mumbai)</td>
<td>DashmulaKwath</td>
<td>Fatigue, Nervous, Worries, Insomnia, Relieve mental and physical tensions</td>
</tr>
<tr>
<td>Classical Ayurvedic preparation</td>
<td>Sriparnyadikvatha, Sriparnitaila, Brhatpancamulakvath</td>
<td>Obesity, Dyspnoea</td>
</tr>
<tr>
<td>Dabur India Ltd</td>
<td>Chyawanprashawaleha</td>
<td>Tonic, Immunomodulator</td>
</tr>
<tr>
<td></td>
<td>Brahmf rasayan</td>
<td>Cerebral tonic, Headache, Immunomodulator</td>
</tr>
<tr>
<td></td>
<td>Dasamhulataila</td>
<td>Headache and Respiratory disorder</td>
</tr>
<tr>
<td></td>
<td>Dasmularista</td>
<td>Jaundice, Leprosy, Piles, Aversion and develops sprit and semen.</td>
</tr>
<tr>
<td>Himalaya Drug company, Bangalore</td>
<td>Chyawanprash</td>
<td>Tonic, Immunomodulator</td>
</tr>
<tr>
<td></td>
<td>Diabecon - Tablets 60</td>
<td>Anti-diabetic</td>
</tr>
<tr>
<td></td>
<td>GlucoCare capsule</td>
<td>Antidiabetic</td>
</tr>
<tr>
<td>KM Siddha and Ayurvedha Company (India) Limited</td>
<td>Dasamoolaharitakilehya</td>
<td>Discoloration, Dysuria, Vitiation of semen, Asthma, Fever and Bleeding disorder</td>
</tr>
<tr>
<td>Little India</td>
<td>Hassnar’s Brestone firming cream</td>
<td>Firming breast</td>
</tr>
<tr>
<td>Sandu Pharmaceuticals Limited, Mumbai,</td>
<td>Kutajarista</td>
<td>Sprue, Dysentery.</td>
</tr>
<tr>
<td>Sharangdhar Pharmaceuticals Pvt. Ltd, Pune</td>
<td>Chyawanprash</td>
<td>Tonic, Anti-oxidant and Immunomodulator</td>
</tr>
</tbody>
</table>
2.2 Careya arborea Roxb

2.2.1 Description\textsuperscript{75,76,77,78}

Careya arborea Roxb (Lecythidaceae) is a large deciduous tree grows up to 20meters height. It is named Kumbhi in Sanskrit on account of the hollow on the top of the fruit giving its appearance somewhat of a water-pot. Tamil name Puta-tanni-maram signifies "water-bark-tree" in allusion to the exudation trickling down the bark in dry weather. The bark of the tree, the calices of the flowers and astringent gum exudes from the fruit and stem are valued on account of their astringent and mucilaginous properties, being administered internally in coughs and colds and applied externally in embrocation. It states that wild pigs are very fond of the bark hence, hunters use to attract them.

A. Taxonomical profile

- **Kingdom**: Plantae
- **Division**: Magnoliophyta
- **Class**: Magnoliopsida
- **Order**: Lecythidales
- **Family**: Lecythidaceae
- **Genus**: Careya
- **Species**: Careya arborea Roxb.

B. Vernacular names

- **Hindi**: Kumbhi, Kaloikatbhi
- **English**: Patana Oak, Slow Match Tree, wild guava
- **Kannada**: Dolli, Kaulu
- **Sanskrit**: Katabhi, Svadupushpa, Madhurenu, Katambhara, Kumbhi
- **Tamil**: Kumbi
- **Malayalam**: Pezuntol
- **Marathi**: Kumbhaa
- **Hindi**: SthalaKumbhi
- **Kannada**: Daddala, Gudda, Daddippe
2.2.2 Morphology

A. **Leaves:** Leaves are simple, alternate, glabrous, ovate, apex obtuse with short tip, base attenuate and margin finely toothed. Midrib is flat, secondary veins obtuse, widely parallel, tertiary veins oblique (ladder-like or percurrent). Stipules are absent.

B. **Flowers:** Flowers are yellowish green with red purple stamens, arranged in 1-10 flowered inflorescences, bisexual, sessile and flowering in summer. Stamens are numerous, twice as long as the petals, in 3 layers, cream tinged purple-red at base.

C. **Fruits:** Fruits are simple, berry, fleshy, up to 6cm, skin leathery, pulp fleshy, not splitting and fruiting in monsoon.

D. **Seed:** Seeds are exalbuminous, dark brown, oval ellipsoid, 1.5-2cm long, up to 1cm width; indehiscent; testa hard and wrinkled; pleasant odour and astringent taste.\(^7^9\)

E. **Bark:** Bark is thick, rough, dark grey in colour, showed shallow cracks, exfoliating in narrow flakes and odorless with astringent taste.

F. **Distribution:** It is found in Afghanistan, Pakistan, India, Nepal, Burma (Myanmar), Malay Peninsula, Thailand, Indochina, Laos (Khammouan).
2.2.3 Ethnobotanical uses

Stem barks of *Careya arborea* was traditionally used in the treatment of tumors, anthelmintic, bronchitis, epileptic fits, astringents, dyspepsia, urinary discharge, piles, lecoderma antidote to snake-venom, scorpio bite and skin disease. In snake bite the fresh bark is applied to the bitten part and infusion of same is taken internally. In Cambodia the bark is used in small pox.\(^{80}\)

It was also used as leech repellent, fish poison and antivenin activities as per reported literature. The aqueous extract of fresh root bark used as fish poison. The tribal peoples of Kolli hills of Tamil Nadu used the stem bark for the treatment of various tumor, liver disorders, in fever, best wound healer-medicated oil in sinus and fresh wounds.\(^{81,82}\)

It is applied to the wound in snake bite. Internally used in the form of infusion. Leaves made into poultice applied 3to 4 times a day rapidly heal obstinate ulcers. Flower is given in sharbat or in infusion after child birth to heal rupture caused by child birth. Juice of the fresh bark as well flower is administered with honey as demulcent in cough and colds. Boils, abscesses and ulcers cleaned and washed with the decoction of the barks will heal rapidly. It also used in indigestion and dysentery.\(^{83,84}\)

Fresh root paste is taken in the morning in empty stomach for five days against joint pain. Bark juice is mixed with cow’s milk and taken orally 3 times a day, for dysentery with vomiting. Bark is used as an astringent, bitter, thermogenic, alexeteric, anti-pyretic, antipruritic. Also used in tumors, cough, bronchitis, catarrh, dyspepsia, colic, intestinal worms, epilepsy, leucoderma, ulcer and aphrodisiac.\(^{85}\)

Bark is used as anthelmintic, antipyretic, demulcent and diarrhea. Flower is used as aphrodisiac. Fruit is used as an astringent, demulcent,\(^{86}\) safe abortion,\(^{87}\) dysentery with bloody stools and ear pain.\(^{88,89,90,91}\)

The stem bark is used as demulcent in fistula, pruritis, smallpox, sore, cough and cold, as antipyretic, anthelmintic. The decoction of the bark is used in diarrhea and used for washing eyes. The flowers are used as an aphrodisiac and infusion is given after child birth. The stem bark is used as demulcent in cough and cold. The dried calyces are tonic and demulcent.\(^{92,93,94}\) Bark juice with cow milk is administered to cure dysentery,\(^{95}\) also
used in inflammation cough, cold and joint pain. Stem bark is boiled with water and taken in empty stomach once a day for 7 days in pile treatment. A Paste of bark with coconut oil is applied on infected areas of skin. The bark is grinded and mixed with salt, applied externally against the foot and mouth disease of cattle. Various parts of the tree are known as padmaka in Ayurvedic system of medicine. Bark, leaf and fruits are used as thermogenic and antipyretic, also in tumours, colic, intestinal worms, epileptic fits and healing of vaginal ruptures.

Fruits are edible, aromatic, also used in snake bite and fever. The fruits are eaten at the time of fast in some festivals like Mahashivratri. Fruits powder is used for reduce cough and overweight. Fruit pulp is applied to scalp for hair growth.

Leaf extract is administered for stomach pain. A Cup of juice of leave is given once day at morning with empty stomach to treat cough and cold. Extract of stem in water with equal amount of cow ghee is given after every two hour for hemorrhage.

Leaves are used in treatment of dislocated bones, body pain, abdominal pain, myalgia, and rheumatic pain. Leaf paste is applied on the face to reduce the swellings, skin diseases and tongue ulcer.

2.2.4 Phytochemical Review

The physical evaluation parameters C. arborea bark revealed total ash (12%), sulphated ash (9.49%), water soluble ash (2%), acid insoluble ash (0.9%), water soluble extractive value (16%), alcohol soluble extractive value (7.2%) and loss on drying (14%). Leaves reported ash content 6.94%, fibers 22.12%, tannins 19.00%, and fats 5.85%. It is reported to contain triterpenoids, flavonoids, coumarin, saponins, and tannins. Mandal et al. isolated triterpenoid saponin, arboerenin and desacylescin III from the methanol extract of the leaves of C. arborea by bioguided-fractionation. It also contains alkaloid piperine, sapogenin, taraxerol, arboerenin, desacylescin III, sapogenols, careyagenolide, maslinic acid and 2α-hydroxyursolic acid. It is 2α, 3β-dihydroxytaraxastan-28, 20β-olide, α-spinasterol; α-spinasterone, baringtogenol-C and careyagenol-E. Bark contains lupeol and botulin. Leaf contains ellagic acid,
hexacosanol, quercetin, β-sitosterol, β-spinasterol, taraxerol and taraxeryl acetate, valoneic acid, careaborin, β-amyrin; Seed contains α-spinasterol.\textsuperscript{126}

Fruit is reported to contain dihydroxybenzoic acid (gallic acid, kaempferol 3-\textit{O}-glucopyranoside, quercetin 3-\textit{O}-glucopyranoside, quercetin 3-\textit{O}-(6-\textit{O}-glucopyranosyl)-gluco pyranoside,\textsuperscript{127} and careaborin.\textsuperscript{128}

\textbf{Figure 2.4} Chemical constituents of \textit{Careya arborea}
2.2.5 Biological Review

A. Central nervous system depressant activity: Kumar et al. reported CNS depressant activity on methanol extract of barks of *C. arborea* in Swiss albino mice and Wistar albino rats by general behavior, exploratory behavior, muscle relaxant activity and phenobarbitone sodium induced sleeping time were revealed a significant reduction in the spontaneous activity.

B. Anticonvulsant activity: Shinde et al. reported anticonvulsant activity of methanol and aqueous extract of Bark of *C. arborea* by inducing convulsion using maximal electroshock seizures (MES), pentylenetetrazol (PTZ) and PTZ induced kindling model had shown anticonvulsant effect by decreasing extensor phase, clonus and also the duration of stupor phase, as compared with control in MES and PTZ and the extracts also inhibited seizure score in PTZ induced kindling model.

C. Antidiarrhoeal activity: Rahman et al. reported antidiarrhoeal activity. The methanol extract of the *C. arborea* bark significantly reduced castor oil-induced diarrhea in mice supporting traditional use of the plant against diarrhoea.

D. Gastroprotective activity: Gupta et al. reported significant gastro-protective activity of the 70% ethanol extract of *C. arborea* leaves, evaluated using aspirin, EtOH, pylorus ligation, and cold restraint stress induced ulcer in rats. The H⁺K⁺ATPase, volume of gastric juice, and acid output was decreased significantly while gastric wall mucus secretion was increased significantly.

E. Wound healing activity: Ramesh et al. reported wound healing activity of the leaf extract of *C. arborea* in rats using excision wound model, incision wound model, burn wound model and dead space wound model.

F. Antibacterial activity: Prabhakaran et al. exhibited antibacterial activity with the ethyl acetate, ethanol and hexane extracts of *C. arborea* fruits evaluated by agar diffusion assay. The bacterial strains found sensitive were, *E. coli*, *S. typhimurium*, *Listeria monocytogenes*, *S. aureus* and *S. epidermidis*.

Rathod et al. reported an *in vitro* antitumor and antibacterial activities on ethanol extract of *C. arborea* leaves on inhibition of Vero cell line screened by MTT assay.
against HEp-2 cell lines and antibacterial activity were tested by disc diffusion and tube dilution method against gram positive and gram negative bacteria.\textsuperscript{135}

Kumar et al reported antimicrobial and antioxidant activities on methanol extract of \textit{C. arborea} (MECA) stem barks in various \textit{in-vitro} systems using disc diffusion methods with gram positive and gram negative bacteria and some fungal species. MECA showed broad spectrum antimicrobial activity against all tested microorganisms. Antioxidant and free radical scavenging activities of MECA was assessed by using DPPH, superoxide anion radical, nitric oxide radical and hydroxyl radical scavenging assays and was found to be antioxidant.\textsuperscript{136}

G. \textbf{Antileishmanial activity}\textsuperscript{137}: Mandal et al. Isolated triterpenoid saponin, arborenin and desacylescin III from the methanol extract of the leaves of \textit{C. arborea} by bioguided fractionation. The saponin showed \textit{in vitro} antileishmanial activity against \textit{Leishmania donovani}.

H. \textbf{Anticoagulant activity}\textsuperscript{138}: Varadharajan et al. anticoagulant activity of extracts of \textit{C. arborea} barks when compared with the standard warfarin. Methanol extract of \textit{C. arborea} bark prolonged the blood clotting time with the assay of activated partial thromboplastin time (PTT), prothrombintime (PT) and thrombin time (TT).

I. \textbf{Antiulcer activity}\textsuperscript{139}: Kumar et al. studied antiulcer activity of the ethanol extract of \textit{C. arborea} stem bark on the Wister strain albino rats against ethanol induced, cold restraint stress induced and pylorus ligation induced models. Ulcer protection was calculated by ulcer index and gastric juice volume, pH and acidity of gastric juice. The extract had shown significant antiulcer activity.

J. \textbf{Antioxidant activity}\textsuperscript{140}: Ariyaratna et al. reported the n-hexane, dichloromethane, ethyl acetate and methanol extract of fresh fruits of \textit{C. arborea} has antioxidant potential when evaluated by the DPPH radical scavenging method

K. \textbf{Antioxidant and hepatoprotective activity}: Senthilkumar et al. showed that the methanol extract of \textit{C. arborea} bark (MECA) has exhibited antioxidant and hepatoprotective activity in Ehrlich ascites carcinoma (EAC) tumor bearing mice. Tumor control animals inoculated with EAC showed alteration in the levels of antioxidant and hepatoprotective parameters. The extract treatment given orally
produced significant reversal of biochemical changes towards the normal in serum, liver and kidney when compared to tumor control animals indicating the potent antioxidant and hepatoprotective nature of the standardized extract.\textsuperscript{141}

MECA has reported hepatoprotective and antioxidant activities in Wistar albino rats. The MECA and silymarin produced significant (p<0.05) hepatoprotective effect by decreasing the activity of serum enzymes, bilirubin, uric acid, and lipid peroxidation in CCl\textsubscript{4} treated rats.\textsuperscript{142}

\textbf{L. Anti-inflammatory and analgesic activity:} Nethaji et al. reported anti-inflammatory and analgesic activities on MECA. The effects of MECA on the acute and chronic phases of inflammation were studied in carrageenan, dextran and mediators (histamine and serotonin) induced paw oedema and cotton pellet induced granuloma respectively. Analgesic effect of MECA was evaluated in acetic acid induced writhing and hotplate tests.\textsuperscript{143}

Bioactivity guided isolation of piperine from the bark of \textit{C. arborea} was found to possess significant central and peripheral analgesic activity. Analgesic activity was tested using acetic acid induced writhing in mice and prolongation of tail flicking time of mice 30min after the treatments determined by the radiant heat method.\textsuperscript{144}

\textbf{M. Anti-fertility activity:} Kalita et al indicated the methanol extract of \textit{C. arborea} root possesses antifertility effects in Albino mice. A short term treatment of the methanol root extract for a period of 14 days revealed strong antifertility effects in mice and was found severely affected estrous cyclicity in normal adult cyclic mice by the root extracts.\textsuperscript{145}

Haloi et al. found reversible anti-fertility activity in adult female Albino mice with methanol root extract of \textit{C. arborea} by reduction in number of mature graffian follicles& corpora lutea and degeneration of corpus luteum with frequent haemorrhage.\textsuperscript{146}

\textbf{N. Cytotoxic activities:} Subhadradevi et al. reported anticancer activity in MECA. Cytotoxicity was evaluated by Trypan blue dye exclusion method, MTT assay and apoptosis was determined by DNA fragmentation assay. Extracts were found to be
cytotoxic to DLA and EAC cell lines in a dose dependent manner in Trypan blue dye exclusion method. The cytotoxic effect of extract was associated with apoptosis on DLA cell lines by determination of morphological changes and DNA fragments.\textsuperscript{147}

Senthilkumar et al. reported anticancer activity on the successive chloroform and ethyl acetate extracts and crude 50\%MECA against cancerous RD, HEp-2 and HeLa cell lines. They were found to be safe against the normal Vero cell line. The methanol and aqueous extracts possessed strong antioxidant activity against many oxidants in the \textit{in vitro} antioxidant screening.\textsuperscript{148}

Natesan et al. reported anticancer potentials of MECA against Dalton's lymphoma ascites (DLA) induced ascitic and solid tumors. The methanol extract given orally to mice caused significant reduction in percent increase in body weight, packed cell volume, and viable tumor cell count when compared to the mice of the DLA control group. Restoration of hematological and biochemical parameters towards normal was also observed. Histological observations of liver and kidney also indicated repair of tissue damage caused by tumor inoculation indicating extract significantly reduced the solid tumor volume induced by DLA cells.\textsuperscript{149}

Kumar et al. Reported antioxidant defense system against induced hepatocarcinogenesis on MECA against hepatocellular carcinoma induced by N-nitrosodiethylamine (NDEA). The MECA was found to be protective against NDEA-induced carcinoma by decreasing the activity of serum enzymes, bilirubin and increase the protein and uric acid levels exhibited significant chemo preventive effects of MECA by suppressing nodules development and enhancing the antioxidants in NDEA carcinogenesis by reducing the formation of free radicals.\textsuperscript{150}

\textbf{O. Acid base indicator}\textsuperscript{151}: Wadkar et al. suggested the use of methanol extract of the leaves of \textit{C. arborea} as an acid base indicator in acid base titrations. This natural indicator is easy to extract as well as easily available Promising results were obtained when it was tested against standard synthetic indicators (phenolphthalein). Titration shows sharp colour change at the equivalence point.
Herbal medicines are products of biological word. Its properties can be studied using skill and knowledge embedded in the natural science like botany and chemistry. There is chemical similarity between molecules that make up plants and human. The medicine and foods derived from plants provide chemical continuity between these two kingdoms. Some of the phytoconstituents reported antiallergic activity is given in Table 2.2.

Table 2.2 Phytoconstituents having reported anti-allergic activity

<table>
<thead>
<tr>
<th>Chemicals</th>
<th>Plant name</th>
<th>Constituents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycosides</td>
<td><em>Cordyceps militaris</em>₁⁵³</td>
<td>isoflavone glycosides</td>
</tr>
<tr>
<td></td>
<td><em>Picrorhiza kurroa</em>₁⁵⁴</td>
<td>iridoid glycoside</td>
</tr>
<tr>
<td></td>
<td><em>Hassaku Citrus</em>₁⁵⁵</td>
<td>flavanone glycosides</td>
</tr>
<tr>
<td></td>
<td><em>Xanthomonas campestris</em>₁⁵⁶</td>
<td>hesperetin Glycosides</td>
</tr>
<tr>
<td></td>
<td><em>Cistanche tubulosa</em>₁⁵⁷</td>
<td>Acteoside</td>
</tr>
<tr>
<td></td>
<td><em>Prunus persica</em>₁⁵⁸</td>
<td>cyanogenic glycosides</td>
</tr>
<tr>
<td></td>
<td><em>Zingiber officinale</em>₁⁵⁹</td>
<td>Phenolic</td>
</tr>
<tr>
<td></td>
<td><em>Lindera obtusiloba</em>₁⁶⁰</td>
<td>Phenolic glycosides</td>
</tr>
<tr>
<td></td>
<td><em>Prunus persica</em>₁⁶¹</td>
<td>phenolic glycosides</td>
</tr>
<tr>
<td></td>
<td><em>viscum album</em>₁⁶²</td>
<td>Flavonoids</td>
</tr>
<tr>
<td></td>
<td><em>Kaempferia parviflora</em>₁⁶³</td>
<td>Phenolic</td>
</tr>
<tr>
<td></td>
<td><em>gossypin</em>₁⁶⁴</td>
<td>Biflavonoid</td>
</tr>
<tr>
<td>Alkaloids</td>
<td><em>Cissampelos sympodialis</em>₁⁶⁵</td>
<td>alkaloid warifteine</td>
</tr>
<tr>
<td></td>
<td><em>Rauwolfia serpentina</em>₁⁶⁶</td>
<td>Alkaloid</td>
</tr>
<tr>
<td></td>
<td><em>Plumeria acutifolia</em>₁⁶⁷</td>
<td>Plumerianine</td>
</tr>
<tr>
<td>Terpenoids</td>
<td><em>Cyperus rotundus</em>₁⁶⁸</td>
<td>Terpenoids</td>
</tr>
<tr>
<td></td>
<td><em>Alismatis Rhizoma</em>₁⁶⁹</td>
<td>Terpene</td>
</tr>
<tr>
<td></td>
<td><em>Bupleurum falcatum</em>₁⁷⁰</td>
<td>Triterpenoid</td>
</tr>
<tr>
<td></td>
<td><em>Glycyrrhiza glabra</em>₁⁷¹</td>
<td>Triterpenoid</td>
</tr>
<tr>
<td></td>
<td><em>Gymnema sylvestre</em>₁⁷²</td>
<td>gymnemic acid</td>
</tr>
<tr>
<td></td>
<td><em>Prunella vulgaris</em>₁⁷³</td>
<td>Triterpenes</td>
</tr>
<tr>
<td></td>
<td><em>Camellia sasanqua</em>₁⁷⁴</td>
<td>triterpene saponins</td>
</tr>
<tr>
<td>Steroid</td>
<td><em>Tylophora sylvatica</em>₁⁷⁵</td>
<td>Steroid</td>
</tr>
<tr>
<td></td>
<td><em>Dioscorea membranacea</em>₁⁷⁶</td>
<td>Steroid</td>
</tr>
<tr>
<td>Saccharides</td>
<td><em>Sweet Potato</em>₁⁷⁷</td>
<td>Oligosaccharides</td>
</tr>
<tr>
<td></td>
<td><em>Algae</em>₁⁷⁸</td>
<td>Polysaccharides</td>
</tr>
</tbody>
</table>
2.3 References

4. Khare CP. Indian herbal remedies: rational Western therapy, ayurvedic, and other traditional usage, botany. Springer, 2004; 236-37


25. http://www.bsienvis.nic.in/medi.htm#Gmelina%20arborea


41. http://www.bsienvis.nic.in/medi.htm#Gmelina%20arborea


50. Vijay T, Rajan MSD, Sarumathy K, Palani S and Sakthivel K. Cardioprotective, antioxidant activities and Phytochemical analysis by GC-MS of \textit{Gmelina arborea} (GA) in Doxorubicin-induced myocardial necrosis in \textit{Albino} rats. Journal of Applied Pharmaceutical Science 01 (05); 2011: 198-204.

51. Wansi SL, Nyadjeu P, Nguelefack TB, Fodouop SF, Donatien AA, Kamanyi A. In vivo antioxidant and vasodilating activities of \textit{Gmelina arborea} (Verbenaceae) leaves hexane extract. \textit{J Compl and Integr Med}. 2012; 9(1). ISSN (Online) 1553-3840,


HNGU Ph.D Thesis
CHAPTER: 2
LITERATURE REVIEW


64. Gangwar A, Ghosh AK, Hoque M, Saxena V. Analgesic Activity of *Gmelina arborea* Roxb in Colony Bred Swiss Mice and Wister Rats. *Inter J Pharmacog and Phytochem Res*. 2013; 5(1); 66-67


92. http://www.ars-grin.gov/cgi-bin/duke/ethnobot.pl


94. Pandey CN. Medicinal plants of Gujarat, Gujarat Ecological Education and Research Foundation, Gujarat (India), 2005:146.


