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Review Article

REVIEW ARTICLE ON GAMBHARI (*GMELINA ARBOREA LINN*)

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ABSTRACT

Gmelina arborea an important medicinal plant is one of the most widely cultivated species of the family *Verbenaceae*. It is commonly known as “Gamhar” is a beautiful fast growing tree throughout in India and one of the herbs mentioned in all ancient scriptures of Ayurveda. It is known to have been used in traditional Indian medicine having important source of chemicals of immense medicinal and pharmaceutical importance. It is highly valued from time immemorial because of its vast medicinal properties. Gambhari, an essential component of Dashamula dravya is termed to be Rasayana dravya, medhya activity has been related to its fruits, which are edible in nature. It is extensively used traditionally as anthelmintic, antimicrobial, antidiabetic, diuretic, hepatoprotective and antiepileptic agent. The present article provides all necessary information regarding its classical literature.

Keywords: Dashamula, Gambhari, *Gmelina arborea*, *Verbenaceae*.

INTRODUCTION

In the last few decades there has been an exponential growth in the field of herbal medicine. It is getting popularized in developing and developed countries owing to its natural origin and lesser side effects¹. Nature has provided a complete storehouse of remedies to cure all ailments of mankind. About 80% of the world population depending on herbal based alternative system of medicine. Herbal drugs have played a vital role in curing diseases throughout history of mankind. Despite the major advances in the modern medicine, the development of new drugs from natural products is still considered important. An estimated 70,000 plants are used medicinally. Ayurveda utilizes about 2000 plants to cure different ailments. There are very few medicinal herbs of commercial importance, which are not cultivated in our country. Approximately 1250 Indian medicinal plants are used in formulating therapeutic preparations, according to Ayurveda and other traditional systems of medicine². The evaluation of various plant products according to their traditional uses and medicinal value based on their therapeutic efficacy leads to the discovery of newer and recent drugs for treating various ailments. This fact forms the basis for the development of new drugs from various plant sources. One of such plants of medicinal value is *Gmelina arborea*, belonging to the family *Verbenaceae*, commonly known as ‘Gamhar’. *Gmelina* is one of the important genera of the family, consisting of about 33 species. It is a beautiful fast growing

deciduous tree, which is a vital ingredient of the “*dasamula*”³. It is a popular commercial timber grows naturally in the warm temperate regions of Mediterranean and South Asia. The plant is commonly found in abundance on the hills and in the Andaman Islands of India.

CLASSICAL REVIEW OF GAMBHARI

Historical aspect of the drug⁴

In ancient Indian literature like Vedas the synonyms of Gambhari like Rohini, Kashmarya, Sriparni etc have been described. For the first time the name Rohini was mentioned in Atharva veda, where it is considered as Asthisansthapaka and Keetanunashaka. The name kashmarya is given in Shatapatha Bramhan, where it is explained as disinfectant. But the properties of which do not correlate with the Gambhari. There is no reference that Rohini and Gambhari are same.

Samhita Kala: The exhaustive information of Gambhari is available in this period.

Charaka samhita: Reference of Gambhari is found at 57 different places. In Charaka samhita Gambhari is explained by the name Kashmari and mentioned its synonyms as Kashmarya and sriparni, other synonyms are Madhuparni, Bhadrarni, Krishna Madhuras and Rohini. As Madhuparni and Kashmari are included in Madhura skanda both are seems to be different drug.

According to Chakrapani madhuparni is madhuyasti. charaka included Gambhari in virechanopaga, dahaprasamana, shwayathuhara, madhura skanda, vataghna gana. 13

formulations of this drug is mentioned in the management of 20 Rogas.

Sushruta samhita: Compared to charaka samhita no much information available in sushruta samhita. But mentioned different names – Kasmari, Kasmarya, Sriparni etc. Sushruta has explained this drug in 37 different contexts, particularly in Panchamoola and sarivadi gana. It is also mentioned in Shalya karma.

Sangraha Grantha: The drug has been mentioned at 15 different contexts by the name Kashmarya and Gambhari. No much information is available to its formulations and indications.

Nigantu Kala: During this period we come across detail description of Gambhari, all nighantu we find similar kind of information.

Table 1: Gana and Varga According to Different Authors

Samhita/ Nighantu	Gana/ Varga	Samhita/ Nighantu	Gana/ Varga
Charaka samhita	shothahara, Dhaprashamana, Virechnopga, Phalavarga, Madhura skanda	Sushruta samhita	Sarivadi, Dashamula, Phalavarga, Madhura gana, Brihat panchamula,
Abhidhana ratnamala	Chaturtha shkanda/Tikta dravya skanda	Mahaoushadhi nighantu	Bilvadi Varga
Ashtanga hridaya	Sarivadi, Brihat panchamula, Madhura varga	Dravyaguna sangraha	Phala varga
Bhavaprakasha nighantu	Guduchyadi Varga	Gunaratnamala	Amradi vargaï
Kaiyadeva nighantu	Oushadhi varga	Chakradatta	Brihat panchamula, Dashamula
Raja nighantu	Prabahadradi varga	Shaligrama nighantu	Guduchyadi Varga
Dhanvantari nighantu	Guduchyadi Varga	Mahaoushadhi nighantu	Bilvadi Varga
Madanapala nighantu	Abhayadi Varga	Dravyaguna sangraha	Phala varga

PARYAYA AND ITS MEANING^{5,6}

- **Gambhari:** It possesses plenty of water. Gambhari is a beautiful tree
- **Kashmari:** It is famous because of its good qualities. like kumbhi, grows fastly
- **Kashmiri:** Found in Kashmir
- **Krishnavrinta:** Blackish petiole
- **Peetarohini:** It bears yellow flowers. Yellowish bark
- **Bhadraparni:** Leaves are beautiful
- **Shreeparni:** It leaves are very beautiful.
- **Mahakumbhi:** Inflorescence is long
- **Mahakusumaka :** Inflorescence is long
- **Vatahruta:** It is a good remedy for vatika disorders
- **Sarvatobhadra:** Each part of this tree has medicinal values. Useful in many ways
- **Suphala:** fruits are wholesome
- **Sthulatwacha:** Bark is thick
- **Heera:** Used as rasayana
- **Madhuparni:** Its leaves are as sweet as honey. Its leaves are glabrous (shining like honey)

Vividha basha nama (Vernacular names) ⁷

1. **Assam** : Gomari
2. **Bengal** : Gamari, Gumar, Gumbar
3. **Bhi** : Chimman, Sag
4. **Bombay** : Kashmari, Shewan
5. **Burma** : Kynboc, Kywonpho, Yamanai, Yemene
6. **Cachar** : Gumai
7. **Canarese** : Bachanige, Gupsi, Kashmiri, Kule, Kumbudi, Kumule, Shivani, Triparni
8. **Central Provinces:** Gumghar, Shiwun
9. **English** : Candhar Tree, Cashmere Tree, Coomb Teak, White Teak – Garo Bolkobak
10. **Gond** : Kurse
11. **Gujerati** : Savan, Shivan, Sivan
12. **Hasada** : Kasom bardaru

13. **Hazara** : Sewan
14. **Hindi** : Gamari, Gambhari, Gambhar, Gamhar, Gumbhar, Kambar, Kambhar, Khambhari, Khammara, Kumar, Kumbhar, Sewan, Shewan, Shiwan –
15. **Kadir** : Kumala
16. **Kolami** : Gumher, Kasamar
17. **Konkani** : Niuvon, Sivony
18. **Koya** : Gumudu – Kumanon Khamara, Kumhar
19. **Kurku** : Kassamar
20. **Lambadi** : Gupsiro
21. **Lepcha** : Numbon
22. **Magahi** : Ramani
23. **Malayalam** : Naguri: Kasmardaru
24. **Nepal** : Gambari, Khamari
25. **Punjab** : Gumhar, Kumhar
26. **Rajputana:** Sewan
27. **Sanskrit** : Ashveta, gbhadra, bhadraparni, Gambhari, Gandhari, Gandharya, Gopabhadrika, Grishti, Hira, Kakodumbhari, Kambharika, Kashmari, Kashmaryya, Kataphala, Krishna, Krishnaphala, Krishnavrintika, Kshirini, Kumuda, Madhubhadra, madhumati, madhuparanika, madhu rasa, Mahabhadra, Mahakumuda, Modini, Pitaphala, Pitarohini Rohini. Sadabhadra, Sarvatobhadra, Sarvotobhadrika, Shriparni, Snigdhaparni, Sthulatvacha, Subhadra, Sudrihatvacha, Suphala, Svarubhadra, Vataha, Vidari, Vidari, Vidarini
28. **Santali** : Kasmar
29. **Sinhalese** : Atdemmata
30. **Tamil** : Arisa, kalarbadi, Kattanam, kumil, Kumbal, Perungumil, Pulirgumil, Umitekku
31. **Telugu** : Adavigum mudu, Challagummudu, Gummadi, Gummudu, Gummudu, Gumuduteku, Gumeteku, kasmari, kasmaryamu, Peddagumudu, Peddagumudutekku, Teggummudu
32. **Uriya** : Bhodroporni, Gombhari, kashmori

Table 2: Gunas (Properties) of Fruit According to Different Authors

Sl. No	Gunas	C.S ⁸	S.S ⁹	A.H ¹⁰	BP N ¹¹	K.N ¹²	R.N ¹³	D.N ¹⁴	M.N ¹⁵	MA.N ¹⁶	M.D ¹⁷	G R M ¹⁸
Rasa												
1	Madhura	+	+	+	+	+	-	-	-	+	+	+
2	Kashaya	+	-	-	+	+	-	-	-	+	+	+
3	Tikta	-	+	+	+	-	+	+	-	+	+	-
4	Amla	+	-	-	+	+	-	-	-	-	-	+
5	Katu	-	-	-	-	-	+	-	-	-	-	-
Guna												
1	Guru	+	+	+	+	+	+	+	-	+	-	+
2	Snigdha	-	-	-	+	+	-	-	-	-	-	+
Veerya												
1.	Sheeta	+	+	+	+	+	-	-	-	-	-	+
Vipaka												
1.	Madhura	+	+	+	+	+	-	-	-	-	-	+
Doshagnata												
1	Vatapitta	-	-	-	+	-	-	-	+	-	-	+
2	Kaphapitta	-	-	-	-	+	-	-	-	-	-	-
3	Kaphavata	-	-	-	-	-	-	-	-	-	+	-
4	Tridosha	-	-	-	-	+	+	-	-	-	-	-

Table 3: Gunas (Properties) of Different Parts of Plant According to Different Authors

Author/Text	Part	Rasa	Guna	Veerya	Vipaka	Doshagnata
Mahoushadhi nighantu	Moola twak	Kashaya, Tikta, Madhura	Guru	Ushna	-	-
Madanapala nighantu	Moola twak	Madhura	Guru	Ushna	-	-
Kaiyadeva nighantu	Moola twak	Madhura, Tikta, Kashaya	Guru	Ushna	-	-
	Pushpa	Madhura, Tikta, Kashaya	Sheeta	Sheeta	Madhura	-
Raja nighantu	Moola Twak, Patra, Pushpa	Katu, Tikta	Guru	Ushna	-	Kapha
Dhanvantari nighantu	Moola twak	Tikta	Guru	Ushna	-	Tridosha
Bhavaprakasha nighantu	Moola twak	Madhura, Kashaya, Tikta	Guru	Ushna	-	-

KARMA (ACTIONS) ACCORDING TO DIFFERENT AUTHORS

Sheetala, Snehana, Medhya, Keshya, vedanasthapana, Trishnashamaka, Deepana, Anulomana, Raktapittashamaka, Raktarodhaka, Shothahara, Sandhaneeya, balya, Mootrajanana, Garbhashthapana, Stanyajanana, Vrishya, Jwaraghna, Dahaprashamana, Katupaushitaka, Brumhana, Rasayana, Vishaghna.

PRAYOGA (THERAPEUTIC USES) ACCORDING TO DIFFERENT AUTHORS

Shirashoola, Bhrama, Mastishkadaurbalya, Palita, vatarakta, Vatavikara, Agnimandya, Vibandha, Arsha, Trishna, Raktatisara, Shotha, Hridroga, Raktapitta, Sheetapitta, Urakshata, Kshaya, Raktakshya, Mootrakrichra, Pooyameha, Vastishotha, Shukradaurbalya, Garbhapata, Sutikaroga, jwara, Daha, samanya dourbalya, Jwarrottara dourbalya, Anguliveshta, Sarpa visha, Virishchika visha.

Table 4: Prayojya Anga (Useful Part) According to Different Authors

Sl No	Prayojya anga	C.S ¹⁹	S.S ²⁰	A.H ²¹	Bp N ²²	K.N ²³	R.N ²⁴	D.N ²⁵	N.A ²⁶	Ma.N ²⁷	M.D ²⁸	G R M ²⁹
1	Phala	+	+	+	+	+	+	+	+	+	-	+
2	Pushpa	+	-	-	-	+	+	-	-	+	-	-
3	Twak	+	+	+	-	+	+	-	-	+	+	-
4	Patra	+	-	-	-	-	+	-	-	+	-	-
5	Mula	+	+	+	+	-	-	+	-	+	-	-
6	Phalamajja	+	+	+	-	-	-	-	-	-	-	-

Table 5: Matra (Dose) According to Different Authors

Sl No	Matra	Bp N ³⁰	R.N ³¹	Ma.N ³²
1	Mulachurna	3-6 Masha	-	3-6 Masha
2	Phala	1-3 Masha	10-20 gms	1-3 Masha
3	Phala twak kwatha	-	5-10 gms	-
4	Pushpa churna	-	4-10 gms	-

ACTIONS AND USES³³

- ❖ The root is acrid, bitter, sweet, stomachic, tonic, laxative, galactagogue and anthelmintic. It is useful in hallucination, fever, dyspepsia, hyperdipsia, haemorrhoids, gastralgia, anasarca and burning sensation.
- ❖ Bark is bitter, tonic and stomachic and is useful in fever and dyspepsia.
- ❖ Leaf paste is good for cephalalgia and leaf juice is useful in gonorrhoea, catarrh of bladder and is a good wash for foul ulcers.
- ❖ The flowers are sweet, refrigerant, bitter, astringent and acrid and are used in treating leprosy and skin diseases,
- ❖ Fruits are acrid, sour, sweet, bitter, refrigerant, diuretic, astringent, aphrodisiac, trichogenous, alternant and tonic. They are used for promoting the growth of hair and for anaemia, leprosy, ulcers, constipation, strangury, leucorrhoea, intrinsic haemorrhage, fever and bilious affections.

ACTION AND USES IN UNANI³⁴

In Unani system of medicine this vanaspathi is used in pittaraktha vikara and kshaya roga. it is viryavardaka, kamottejaka, dhatuparivarthaka & mutrala.

Its leaves are used as antihelmenthic. Its roots are appetizer, strengthening and useful in kapha, sandhivata, jwara & ajeerna, The branches of Gambhari are used in making artificial body parts.

According to Brihatraja it is used as Vishaghna in snake and scorpion bite. According to Roberts the decoction of Root & bark of Gambhari is beneficial in snake bite According to kes and maskar each and every useful part of Gambhari is beneficial in snake and scorpion bite. According to kernel chopra, Gambhari is katu rasa, poustika, Agni vardhaka, virechaka and is beneficial in snake bite and scorpion bite.

Mode of use in different conditions:

- 1) **Mootrakricchra** : In burning micturition the tender leaves juice is used.
- 2) **Krimi Roga** : The root decoction is used in intestinal worms.
- 3) **Kasa** : Gambhari and vasa patra swarasa is beneficial in expectoration and cough.
- 4) **Sheetapitta** : Dry fruit cooked with milk and used.
- 5) **Kshatha** : The kalka of tender leaves is used in Nakha-kshatha.
- 6) **Pitta jwara** : Phala kwatha is beneficial
- 7) **Dugd vridhi** : The Roots of Gambhari is mixed with yastimadhu, sugar and madhu and licked.
- 8) **Amlapitta** : Patra choorna of Gambhari, Roots of Apamarga is mixed with cow milk and given for 14 days cures Amlapitta.
- 9) **Raktha pitta** : By eating ripe fruit of Gambhari 1 or 2 every day cures Rakthapitta.

FORMULATIONS AND PREPARATIONS³⁵

- Dashamoolarishta
- Dashamoolaharitaki
- Dashamoola ghrita
- Dashamoola shatapalaka ghrita
- Arvindasava
- Drakshadi kvatha churna
- Shriparnyadi kvatha
- Shriparni taila
- Brihat panchamoolyadi kvatha
- Kashmarya kvatha
- Kashmaryadi sheeta kashya
- Mooshakadya taila
- Vayuchchhaya surendra taila
- Mritasanjivani sura
- Dashamoola kvatha churna
- Indukanta ghrita
- Dhanvantara ghrita

CONCLUSION

In a nutshell, the present review is indicative of multiple uses of Gambhari in clinical conditions, however the exact mechanism of drug action and possible toxicity effects needs to be evaluated in further animal and clinical studies.

REFERENCES

1. U N Brahmachari. Current science, 2001,81(1), 15-16
2. Daniel M .Medicinal plants: Chemistry and properties: Science publishers; 2006.
3. Bhagwan D V , Fundamentals of Ayurvedic medicine. Delhi: Bansal and Co;1978.
4. Kapila deva Dwivedi, Vedome Ayurveda, Vedome nirdishta vanaspathi. Varanasi: vishwa bharti anusandhana parishad; 2001. P.247
5. Sharma PV, Namarupa vignanam, 1st edition, Varanasi; Satya priya prakashana:2000.P.71-72
6. Dr. J. L. N. Shastri, Aoushadhi nirukta mala, 1st ed. Varanasi: Chaukhambha Orientalia, 2001, p.
7. Kirtikar KR, Basu BD, Indian Medicinal Plants Vol.-III. 2nd ed. Dehra Dun: International Book Distributors; 1999. P 1931-1935.
8. Agnivesha, Charaka Samhita, chikitsa sthana, Dr.Brahmanand Tripathi editor, Uttaradha, Chapter 12th, Sloka 67, Chapter 29th, Sloka 85, Varanasi; Choukamba Samskrit Pratishthana, reprint 2001, P 455 and P.997
9. Sushruta, Sushruta Samhita, Uttaratantira, chapter 39 Sloka 179. chikitsa sthana, chapter 27 Sloka 9. Prof. -Kaviraj Ambikadatta shastri editor. 2nd ed. Varanasi:

- Chaukhamba samskrit samsthana; reprint 2005 .P 195 and P.122
10. Vagbhata, Astanga hridaya, chikitsa sthana, chapter 9 sloka 85. chapter 16 sloka 6. kaviraj atrideva gupta editor. Reprint. Varnasi: Chaukhamba Sanskrit sansthana: 2005. P 358 and P.366
 11. Bhavamisra, Bhavaprakash Nighantu, Guducchyadi varga sloka 14-18. G.S. Pandey editor. 7th ed. reprint. Varanasi: Chaukhamba Bharati Academy; 2004. P 276-278.
 12. Kaiyadeva, Kaiyadeva Nighantu Oushadha varga, sloka 32. P.V. Sharma editor. 1st edition. Varanasi: Chaukhamba Orientalia; 1979. P. 9
 13. Pandit Narahari, Raj Nighantu, Prabhadradi varga, Sloka 35 –38,, Dr.Indradev Tripathi editor, 3rd ed. Varanasi; Choukamba Krishnadas Academy, 2003. P 270-271
 14. Dhanvantari, Dhanvantari Nighantu, Guducchyadi varga, sloka 114-115. P.V. Sharma editor. 3rd ed. Varanasi: Chaukhamba Orientalia; 2002. P 36-37.
 15. Madanapala, Madanapala Nighantu Abhayadi varga, sloka 50-52, 28. Ramprasad patiyala editor. 1st ed. Bombay: Khemaraj Shrikrishnadas Prakashan; 1998. P 11.
 16. Indradeva Tripathi, Mahoushadha nighantu, Bilvadi varga, sloka 3-4,Varanasi: Chaukhamba Vidya bhavana:1971.P.98-100
 17. Madhava, Madhava dravyagunah (Bhavaswabhava vada), Phala varga, sloka 56. P.V. Sharma editor. 1st edition. Varanasi; Chaukhamba Vidyabhavan; 1973. P.50.
 18. Dr.Kailash Pati Pandey and Dr. Augraha Narain Singh, Gunaratnamala of Bhavamishra, Amradi varga,1st edition. Varanasi: Chaukhamba Sanskrit Bhavana; 2006.P.360
 19. Agnivesha, Charaka Samhita, chikitas sthana, Dr.Brahmanand Tripathi editor, Uttaradha, Chapter 12th, Sloka 67, Chapter 29th, Sloka 85, Varanasi; Choukamba Samskrit Pratishtana, reprint 2001, P 455 and P.997
 20. Sushruta, Sushruta Samhita, Uttarantra, chapter 39 Sloka 179. chikitsa sthana, chapter 27 Sloka 9. Prof. –Kaviraj Ambikadatta shastri editor. 2nd ed. Varanasi: Chaukhamba samskrit samsthana; reprint 2005 .P 195 and P.122
 21. Vagbhata, Astanga hridaya, chikitsa sthana, chapter 9 sloka 85. chapter 16 sloka 6. kaviraj atrideva gupta editor. Reprint. Varnasi: Chaukhamba Sanskrit sansthana: 2005. P 358 and P.366
 22. Bhavamisra, Bhavaprakash Nighantu, Guducchyadi varga sloka 14-18. G.S. Pandey editor. 7th ed. reprint. Varanasi: Chaukhamba Bharati Academy; 2004. P 276-278.
 23. Kaiyadeva, Kaiyadeva Nighantu Oushadha varga, sloka 32. P.V. Sharma editor. 1st edition. Varanasi: Chaukhamba Orientalia; 1979. P. 9
 24. Pandit Narahari, Raj Nighantu, Prabhadradi varga, Sloka 35 –38, Dr.Indradev Tripathi editor, 3rd ed. Varanasi; Choukamba Krishnadas Academy, 2003. P 270-271
 25. Dhanvantari, Dhanvantari Nighantu, Guducchyadi varga, sloka 114-115. P.V. Sharma editor. 3rd ed. Varanasi: Chaukhamba Orientalia; 2002. P 36-37.
 26. Bhapala G. Vaidya, Nighantu Adarsa, uttarardha, Nirgundyadi varga . 1sted. Varanasi; Chaukhamba Bharati academy; 1985. P 247.
 27. Indradeva Tripathi, Mahoushadha nighantu, Bilvadi varga, sloka 3-4,Varanasi: Chaukhamba Vidya bhavana:1971.P.98-100
 28. Madhava, Madhava dravyagunah (Bhavaswabhava vada), Phala varga, sloka 56. P.V. Sharma editor. 1st edition. Varanasi; Chaukhamba Vidyabhavan; 1973. P.50.
 29. Dr.Kailash Pati Pandey and Dr. Augraha Narain Singh, Gunaratnamala of Bhavamishra, Amradi varga,1st edition. Varanasi: Chaukhamba Sanskrit Bhavana; 2006.P.360
 30. Bhavamisra, Bhavaprakash Nighantu, Guducchyadi varga sloka 14-18. G.S. Pandey editor. 7th ed. reprint. Varanasi: Chaukhamba Bharati Academy; 2004. P 276-278.
 31. Pandit Narahari, Raj Nighantu, Prabhadradi varga, Sloka 35 –38, Dr.Indradev Tripathi editor, 3rd ed. Varanasi; Choukamba Krishnadas Academy, 2003. P 270-271
 32. Indradeva Tripathi, Mahoushadha nighantu, Bilvadi varga, sloka 3-4,Varanasi: Chaukhamba Vidya bhavana:1971.P.98-100
 33. Gyanendra Pandey, Dravyaguna vignana, volume 1, Varanasi; Choukhamba Krishnadas Academy, Reprint 2004, P 663-671
 34. Vaidyaratna hakeem Daljit Simha, Yunani Dravyagunaadarsha vol-II, 1st ed Luknow: Ayurvedic and Tibbi academy; 1984,
 35. Data base on medicinal plants used in Ayurveda, Vol 3, Reprint, New Delhi, CCRAS, dept of ISM & H, 2005, P.217-228

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