Chapter

Impact of Shodhana on *Semecarpus anacardium* Nuts

Pratap Kumar Sahu and Prashant Tiwari

Abstract

Semecarpus anacardium is classified in Ayurveda under the category of toxic plants. However, this toxic plant is reported to possess anti-inflammatory activity, anti-arthritic effect, antioxidant activity, antimicrobial activity, anti- carcinogenic activity, hypoglycemic activity, cardioprotective, hepatoprotective, neuroprotective, and hypolipidemic activity etc. All these activities are attributed to its various constituents like phenolic compounds, flavonoids, carbohydrates, alkaloids, steroids, etc. In Ayurveda, a series of pharmaceutical procedures which converts a poisonous drug into a safe and therapeutically effective medicine is termed as Shodhana. Shodhana improves the yield, decreases the phenolic and flavonoid content; and converts toxic urushiol into nontoxic anacardol derivative thereby reducing toxicity of nuts of *Semecarpus anacardium*. There are reports of alteration in pharmacology and phytochemistry of nuts of *Semecarpus anacardium* due to Shodhana.

Keywords: Shodhana, *Semecarpus anacardium*, nuts, ayurvedic, toxic, urushiol, anacardol

1. Introduction

Ayurveda is proven to be the ancient traditional way of treatment in India, which is fully based on philosophical, experimental and practical concepts. It includes the use of indigenous drugs which have been preferred by many pharmaceutical industries towards a novel strategy for natural drug discovery. Ayurvedic proven concepts signifies more on human health and disease that recommend the use of herbal enriched compounds as special diets. However, some herbal compounds may have toxicity besides their therapeutic potential if used improperly [1].

There are so many plants which are identified as poisonous and semi-poisonous in Ayurveda. Plants like Atsanabha (Aconitum species), nux-vomica, *Acorus calamus*, *Semecarpus anacardium*, Strychnos, *Abrus precatorius* etc., are the most known examples of toxic plants. These plants are known for their hidden medicinal values and broadly accepted by the Indian Ayurvedic system of medicine. These plants are still used in Indian system of development of medicine for treatment. Aconite, strychnine, β–asarone, bhilawanols, abrin are some of the toxic components present in these plants [2].

Shodhana is the purificatory measure used in Ayurveda to purify toxic medicinal plants (*upavishadravyas*), by various pharmaceutical procedures like soaking, rubbing and washing etc. with specific medias like *gomutra* (cow's urine), *godugdha* (cow's milk) etc. Poisonous plants are subjected to *shodhanasanskara* (purification

process), before their therapeutic use. This process reduces toxicity of poisonous plant considerably and keeps it at required optimum level. Physico-chemical changes and reduction of the toxic chemicals from the poisonous plants like strychnine, brucine in *kupilu* and scopolamine in *dhattura* have been reported [3].

Bhallataka (*Semecarpus anacardium* Linn; Anacardiaceae) fruit is one of the *upavishadravyas* (semi poisonous drugs). Its importance and utility is increasing day by day because of its therapeutic significance in many a diseases including cancer. Though the fruits of *Bhallataka* has many therapeutic values, pharmacies are scared to use this drug because of its irritant vesicating nature. If juice of *Bhallataka* (even in traces) comes in contact with body, produces severe *daha* (burning sensation), and *Vrana* (ulcer). When it comes in contact with face, it produces acute burning sensation with *shotha* (inflammation) and *Visarpa* (skin disease). The fruit contains tarry oil which causes contact dermatitis. Medically it is very well recognized as Urushiol induced contact dermatitis because the chemical Urushiol is responsible for dermatitis. If this vesicant nature is removed, the drug could be a good source for pharmaceutical industries in manufacturing many formulations containing *Bhallataka* as an ingredient [2, 4].

Ayurveda advocates *bhallataka* after *shodhana* (purificatory procedures). Though there are different *shodhana* methods mentioned in Ayurveda, the *shodhana* method mentioned in the text *Rasamrutam* was adopted and quoted in (The Ayurvedic Pharmacopeia of India) (API) and the Ayurvedic formularly of India (AFD). The procedure is soaking the fruits in cow's urine, cow's milk and rubbing it in brick powder [5]. It is reported that R_f values change in *shodhita* samples of *Bhallataka* when compared to raw *bhallataka* [3].

2. *Semecarpus anacardium*

This is a native of India. It is known as bhallatak in India and "marking nut" by Europeans. *Semecarpus anacardium* plant (**Figure 1**) is widely available in sub-Himalayan province, tropical and central part of our country India. It is known as a deciduous tree; medium in size. Height of the tree is normally 12–15 m. Leaves are large and simple about 60 cm long and 30 cm wide. The color of bark is deep brown and is quite rough in structure. The flowers are dull greenish in color [6].

Figure 1.
Semecarpus anacardium *plant and its nuts.*

Figure 2.
Semecarpus anacardium *(Bhallatak) nuts.*

Abundantly the plant is found in Odisha, Chittagong, central India and Northern Australia [7]. The color of fruit is black when ripe as well as smooth and shiny in texture (**Figure 2**). The fruit is generally categorized as toxic and the integral part of the fruit i.e. nut is about 1 inch long in size [8].

3. Active principles of *Semecarpus anacardium*

The active principles present in *S. anacardium* Linn. are given in **Table 1** and their structures are presented in **Table 2**. Bhilawanols, phenolic compounds, [9, 10] biflavonoids, sterols and glycosides [11] are proven to be the most significant components of *S. anacardium* Linn. An alkaloid, Bhilawanol, has been identified as isolated from oil and seeds of *S. anacardium*. Bhilawanol is a mixture of cis and trans isomers of urushiol. Bhilawanol is isolated from oil of nuts. It is a mixture of phenolic compounds like 1, 2-dihydroxy-3 (pentadecadienyl-8, 11) benzene and 1, 2- dihydroxy-3 (pentadecadienyl-8′, 11′) –benzene [10]. Bhilawanol on catalytic reduction absorbs one mole of hydrogen to give hydrourushiol (3-pentadecyl-catechol) [12, 13]. When the phenolic compounds are exposed to the air, then they get oxidized to Quinones. When the oil is kept under nitrogenoxidation process can be prevented. Nut shells contain several biflavones [14], jeediflavanone [15, 16], semecarpuflavan and gulluflavone [17–19] (**Table 1**).

4. Uses of *Semecarpus anacardium*

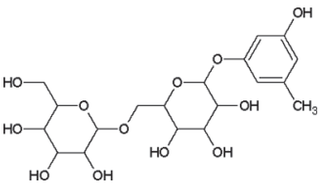
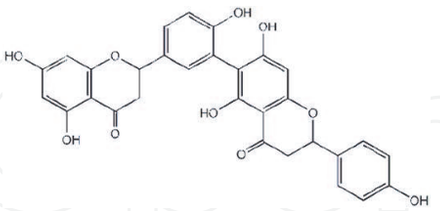
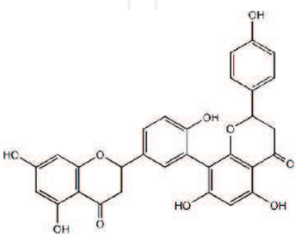
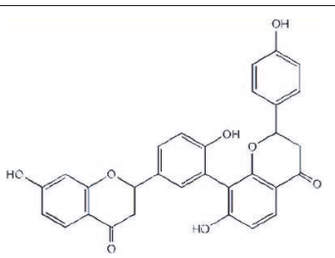
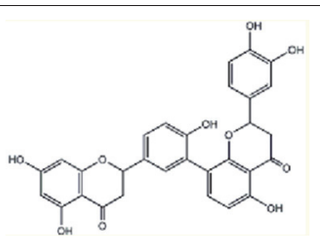
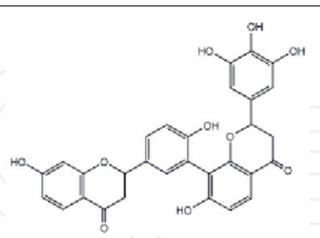
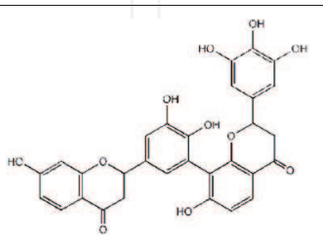
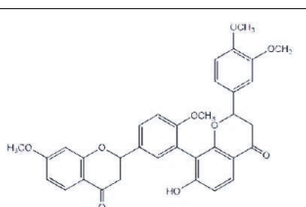
It has been reported for wide arena of ethno-pharmacological activities. Researchers have identified SA nuts extracts for potent pharmacological actions. Most of these studies are pre-clinical studies. Their clinical efficacy is yet to be reported. The list of health disorders against which *Semecarpus anacardium* has a potential to be used is given in **Table 3**. The possible mechanism of action is also described.

4.1 Analgesic and anti-inflammatory effect

There are reports of analgesic [20] and anti-inflammatory [21, 22] activity by *Semecarpus anacardium*. Biflavonoid like tetrahydroamentoflavone (THA) showed significant COX-1 and COX-2 inhibition *in vitro.* THA may be responsible for its

Phytoconstituents	**Name**
Glycoside	Anacardoside
Alkaloid	Bhilawanol/urushiol
	Urshenol
Phenolic compounds	1,2-dihydroxy-3 (penta decadienyl-8, 11) benzene
	1,2-dihydroxy-3 (penta decadienyl-8′, 11′) benzene
	Bhilavanol A (monoenepentadecyl catechol I)
	Bhilavanol B (dienepentadecyl catechol II)
Biflavonoids	Biflavones A, C, A1, A2
	Tetrahydrorobustaflavone
	Tetrahydromentoflavone
	Jeediflavanone
	Semicarpuflavonone
	Galluflavone
	Nallaflavanone
	Semicarpetin
	Anacarduflavanone
	O-trimethylbiflavanone A1
	O-trimethylbiflavanone A2
	O-tetramethylbiflavanone A1
	O-hexamethylbichaleone A
	O-dimethyl biflavanone B
	O-heptamethylbichaleone B1
	O-hexamethylbichaleone B2
	O-tetramethylbiflavanone C
Other components	Anacardic acid
	Cardol
	Catechol
	Fixed oil
	Anacardol
	Anacardoside
	Semecarpol
	Oleic acid
	Linoleic acid
	Palmitic acid
	Stearic acid
	Arachidic acid

Table 1.
Phytoconstituents present in Semecarpus anacardium.

Active compounds	Chemical formulae
Anacardoside	
Tetrahydrorobustaflavone	
Tetrahydromentoflavone	
Biflavanone C	
Biflavanone A	
Semicarpuflavonone	
Galluflavone	
Semicarpetin	

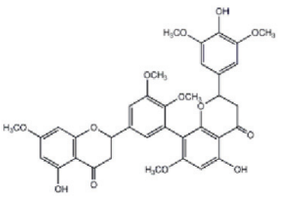
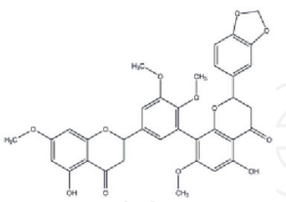
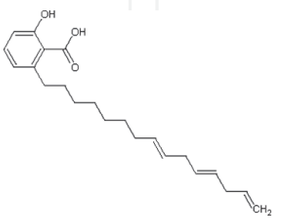
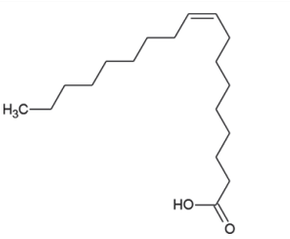
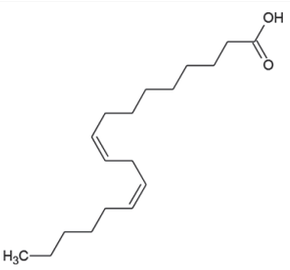
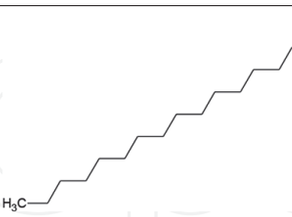
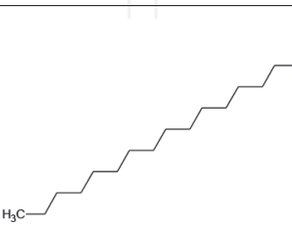
Active compounds	Chemical formulae
Nallaflavanone	
Anacarduflavanone	
Anacardic acid	
Oleic acid	
Linoleic acid	
Palmitic acid	
Stearic acid	

Table 2.
Chemical formulae of the active principles of Semecarpus anacardium.

analgesic and anti-inflammatory activity [23]. SA extracts were studied for their anti-inflammatory activities *in vitro* using synovial fluid and blood of healthy individuals and rheumatoid arthritis patients. SA inhibited proinflammatory cytokine production like IL-1 beta and IL-12P40 without affecting IL-6 and TNF-alpha production [24].

Potential use/activity	Efficacy proved in	Possible mechanism of action
Analgesic, anti-inflammatory, anti-arthritic	Animal models (pre-clinical)	Inhibition of cyclooxygenase (COX 1 and COX 2), inhibit pro-inflammatory cytokine production
Anti-cancer (breast cancer, hepato cellular carcinoma, leukemia)	Cell lines and animal models (pre-clinical)	Cytotoxicity by inducing apoptosis following caspase 3 pathway
Cardioprotective (anti atherogenic, lipid lowering)	Animal models (pre-clinical)	Anti-oxidant, decrease cholesterol, increase HDL
Nootropic (memory enhancer)	Animal models (pre-clinical)	Inhibit acetylcholine esterase, increase cholinergic activity
Hepatoprotective	Animal models (pre-clinical)	Anti-oxidant
Anti-fungal and Anti-bacterial (Gram +ve, Gram −ve, tuberculosis)	Microbial culture (in-vitro)	Inhibit microbial growth
Aphrodisiac (increase sex desire) in male but spermicidal	Animal models (pre-clinical)	Increase mounting and mating performance, cause spermatogenic arrest (decrease motility and density of sperm)
Anthelmintic	Indian earthworm (*Pheretima posthuma*)	Muscle paralysis

Table 3.
Potential uses of Semecarpus anacardium *with possible mechanism of action.*

4.2 Anticancer activity

Nut extracts of *Semecarpus anacardium* showed efficacy against human breast cancer cell line (T47D) [25] and mammary carcinoma in rats [26]. It also showed efficacy against leukemic cells in mice [27]. SA extracts have energy restoration, tumor marker regulation and membrane stabilization effect against hepato-cellular carcinoma [28]. *Semecarpus anacardium* may have a protective as well as therapeutic contribution against Mitomycin-C induced mutagenicity [29]. *Semecarpus anacardium* showed significant cytotoxicity having LC50 29.5 μg in brine shrimp lethality test [30]. The mechanism of cytotoxicity is by inducing apoptosis following caspase 3 pathway [31].

4.3 Cardioprotective effect

S. anacardium nuts prevented isoproterenol (ISO) induced myocardial damage in rats [32]. *S. anacardium* (1 mg/100 g body weight) reduced serum cholesterol levels and raised HDL levels in rats fed with atherogenic diet [33]. The process of atherogenesis triggered by lipid peroxidation can be inhibited by *Semecarpus anacardium* [34].

4.4 Nootropic effect

Semecarpus anacardium effectively inhibits acetyl choline esterase which in turn prolongs the half-life of acetylcholine. Hence, SA has been shown to be useful in improving cognitive ability [35–37].

4.5 Hepatoprotective effect

S. anacardium decreased the levels of the marker enzymes induced by lead acetate in liver [38]. This hepatoprotective action may be attributed to its anti-oxidant action [39].

4.6 Antimicrobial activity

The flavonoid present in *S. anacardium* showed antifungal activity at 400 mg/ml concentration [40]. Furthermore, the oil possessed anti-microbial activity against both Gram positive (*B. subtilis, S. aureus*) and Gram negative (*P. vulgaris, E. coli*) organisms [41]. The petroleum ether and aqueous extracts of SA inhibit the growth of *Staphylococcus aureus* and *Shigella flexneri*. However, chloroform and ethanol extracts showed inhibition against *Bacillus licheniformis* and *Pseudomonas aeruginosa* respectively [42]. The alcoholic extract of SA was found to be bactericidal against Gram positive (*E. coli*, S. Typhi and *P. vulgaris*) and Gram negative (S aureus and C diphtheria) strains [43]. Water extract showed potential with MIC 6.25 μg/ml against M. tuberculosis during in vitro bioassay [44].

4.7 Aphrodisiac and spermicidal activity

Semecarpus anacardium significantly improved both mounting and mating performance of male mice [45]. However, there are reports of spermicidal activity including spermatogenic arrest in male rats. There is also decrease in density and motility of sperms [36, 46, 47].

4.8 Anthelmintic activity

Petroleum ether, chloroform extract of nuts of *S. anacardium* showed anthelmintic activities against adult Indian earthworm (Pheretima posthuma) [48].

4.9 Hypoglycemic effect

Ethanolic extract of SA (100 mg/kg) reduced blood glucose level in normoglycemic rats. However, no effect was observed in case of hyperglycemic rats [49, 50].

5. Toxicity of *Semecarpus anacardium*

Use of Bhallataka needs adequate precaution due to its extreme hot and sharp attributes. It should be kept away from pregnant women, old aged person and also children. Individual persons showing allergic reactions like rash, itching and swelling to it should avoid its use. Furthermore, it is highly recommended to keep away from direct exposure to sunlight, heat and extreme sex during the course of Bhallataka treatment. The oily portion of nut should be removed for its safe use which can lead to nephropathy. Fewer antidotes like coconut oil, coriander leaves pulp and ghee is useful in case of allergic reactions [51]. The traditional way of administration with peanut oil was proven to be safe up to 25 mg/kg/day for 9 day [52].

Bhallataka nut oil extracts in male albino rats is reported to decrease hemoglobin count as well as erythrocytes indicating anemia. It exhibited an alteration in kidney enzyme level leading to nephrotoxicity during acute and subchronic toxicity [53].

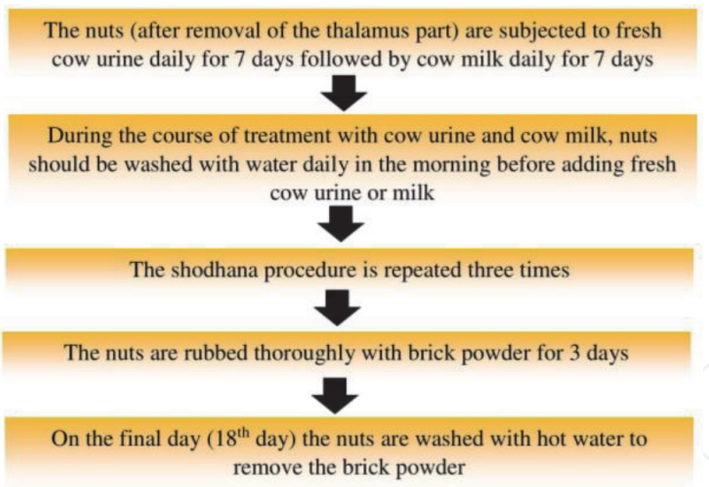


Figure 3.
Flow chart of Shodhana of Semecarpus anacardium *nuts.*

Hence, it is necessary to undertake Shodhana sanskara of Bhallataka with precaution before using it in medicine to avoid toxic effects of Ashuddha (impure) Bhallataka [54].

6. Shodhana of *Semecarpus anacardium* nuts

The process Shodhana, which is also known as detoxification or purification process signifies the conversion of any poisonous drug into beneficial, non-poisonous/nontoxic drug. *Shodhana* process involves sequential steps to purify and reduce the extreme toxicity levels/principles and also sometimes may result in enhancing the therapeutic efficacy. Shodhana is essential because higher concentrated chemicals may contribute towards adverse episodes on human body. There are 2 types of Shodhana i.e. Samanyashodhana and visheshshodhana which purifies toxic drugs. Furthermore, shodhana limits toxicity by removing the visible and invisible impurities, heterogeneous substances and toxic substances [55].

As per Ayurvedic texts shodhana can be done for SA nuts (**Figure 3**). The thalamus part of the fruit is removed with a steel knife. Then, the nuts are subjected to fresh cow urine daily for 7 days followed by cow milk daily for 7 days followed by rubbing thoroughly with brick powder for 3 days. During the treatment with cow urine and cow milk, the nuts are washed with water before adding fresh cow urine or milk. On the final day (18th day), the nuts are washed with hot water to remove the brick powder. This shodhana procedure is repeated three times [35, 56–58].

7. Effect of Shodhana

Shodhana helps in conversion of toxic urushiol into nontoxic anacardol [56]. Our studies on GC-MS which elucidate the presence of anacardol derivative (Anacardol, tetrahydro-; retention time 51.538 in GC-MS) in shodhit extract and urushiol derivative in pre-shodhit extract (1,2-Benzenediol, 3-(8,11,14-pentadecatrienyl)-, (*Z*,*Z*)-, retention time 56.270 in GC-MS) further confirms that shodhana helps in removal of toxic principle urushiol [59].

Shodhana improves the yield in methanolic extract, but decreases the phenolic and flavonoid content [31]. Shodhana decreases cytotoxicity without affecting anticancer activity significantly. The reduction in cytotoxicity may be attributed to reduction in oxidative stress [59]. Shodhana of the nuts reduce nootropic activity

[35]. So shodhana not only reduces toxicity but also alters its pharmacological activities.

8. Conclusion

Semecarpus anacardium is classified in Ayurveda under the category of toxic plants. There are reports of anti-inflammatory activity, anti-arthritic effect, antioxidant activity, antimicrobial activity, anti- carcinogenic activity, hypoglycemic activity, cardioprotective, hepatoprotective, neuroprotective, and hypolipidemic activity etc. shown by *Semecarpus anacardium.* Shodhana of nuts of *Semecarpus anacardium* can be done as per method given in Ayurvedic Pharmacopeia of India. Shodhana improves the yield, decreases the phenolic and flavonoid content; and converts toxic urushiol into nontoxic anacardol derivative thereby reducing toxicity. Shodhana not only reduces toxicity but also alters its pharmacological activities. Shodhana decreases cytotoxicity without affecting anticancer activity significantly. Shodhana also reduces nootropic activity.

9. Future scope

The effect of Shodhana on other pharmacological activities of *Semecarpus anacardium* can be studied in future. This work can also be extended to other poisonous and semi poisonous plants for which shodhana method is described in Ayurvedic Pharmacopeia of India.

Acknowledgements

The authors are grateful to the Siksha O Anusandhan Deemed to be University, Bhubaneswar, India, for providing necessary support and basic infrastructure to make this work successful. The authors also thank Mr. Tapas Ranjan Satapathy for secretarial help.

Conflict of interest

The authors declare that they have no conflict of interest.

Abbreviations

API	The Ayurvedic Pharmacopeia of India
SA	*Semecarpus anacardium*
THA	tetrahydroamentoflavone
COX-1	cyclooxygenase 1
COX-2	cyclooxygenase 2
HDL	high density lipoprotein
MIC	minimum inhibitory concentration
GC-MS	gas chromatography-mass spectrometry

DOI: http://dx.doi.org/10.5772/intechopen.94189

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