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Review Article

Detoxification and Pharmacological Actions of Medicinally Important Herbal Drug Baladur (Semecarpus anacardium L.): A Comprehensive Review

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Abstract

In the traditional system of medicine herbal drugs are reported to be beneficial in treating different nervous diseases. Among them Semecarpus anacardium L., commonly known Baladur, 'Bhallataka' or 'Bhilwa', is one of the herbal drugs that have been used for various ailments of nervous system since antiquity. Tarry oil, a corrosive juice present in the pericarp of the Baladur fruit causes blisters on contact which contain catechol, fixed oil, and anacardol. According to the Unani system of medicine, Baladur (Semecarpus anacardium Linn.) being poisonous drug have the potential to cure many uncurable diseases after detoxification. The main purpose of detoxification is to increase the efficacy and to decrease or to remove the harmful effects from them to make it safe in order to enhance their actions prior to use clinically. Its nuts and fruits contain a variety of biologically active compounds such as biflavonoid, phenolic compounds, bhilawanols, minerals, vitamins and amino acids, which show various medicinal activities like antiatherogenic, anti-inflammatory, antioxidant, antimicrobial, anti-reproductive, Central Nervous System stimulant, hypoglycaemic, anticarcinogenic and hair growth promoter.

We searched different online databases (AYUSH research portal, PubMed, Scopus, Google scholar) using phrases "Semecarpus anacardium OR Baladur", "Detoxification OR Mudabbar", and "Pharmacological actions of Semecarpus anacardium" for searching the pharmacological actions and concept of detoxification of Semecarpus anacardium. Different Unani text books were reviewed for the process of detoxification (Mudabbar.).

The present review article is aimed to explain the process of detoxification of Semecarpus anacardium to make it safe by minimizing its harmful effects and therapeutic potential of detoxified Semecarpus anacardium in various ailments with the reference of Unani concepts and scientific studies. After the process of detoxification Semecarpus anacardium, causes less harmful effect and become suitable for the therapeutic use. In future, research is needed to be carried out on this drug as to elicit that what actual chemical changes has been occurred after detoxification.

Keywords: *Semecarpus anacardium; Baladur; Detoxification; Mudabbar Unani*

Introduction

In the Unani System of Medicine many drugs are reported to be beneficial in treating different nervous diseases along with the thrombolytic diseases. One of such plant based drug of the Unani system - Baladur (*Semecarpus anacardium*) has been used clinically since the ancient time for curing Phlegmatic (balghami), thromboembolic diseases like, Paralysis, Facial palsy, Nerves weakness, Dementia, and many uncurable diseases, because of its actions like, *Mufatteh-i-sudad* (Deobstruent) *Muḥallil-i-Waram* (Anti-inflammatory), *Mulattif* (Demulcent), *Musakhkhin* (Calorificient), *Muqawwī -i- Dimāgh wa A'ṣāb* (Brain and Nervine tonic) [1-6].

The ancient Unani scholars were well aware of toxicity of the drug Baladur and placed drug into fourth degree according to the Mizaj (temperament). The fourth-degree drugs produce strong effects that may disturb the physiological functions of the body; such drugs are also considered to be poisonous and fatal drugs. Different methods of purification have been mentioned for Baladur and always recommended their use after Mudabbar (rectification/detoxification). Otherwise, this drug may destroy the physiological function of the body. After detoxification process the drug become physically and chemically suitable, therapeutically more effective and less toxic [4,5].

So, in this review an attempt has been made to describe the detoxification process as well as the therapeutic potential of detoxified Baladur in various ailments with the reference of Unani concepts and scientific studies.

Methodology

We searched different online databases (AYUSH research portal, PubMed, Scopus, Google scholar) using phrases "*Semecarpus anacardium* OR Baladur", "Detoxification OR Mudabbar", and "Pharmacological actions of *Semecarpus anacardium*" for searching the pharmacological actions and concept of detoxification of *Semecarpus anacardium*. Different Unani text books were reviewed for the process of detoxification (Mudabbar.). Additional efforts made by general google searches. Botanical name is verified by the recent accepted name in - The Plant list- A working list of all plant species. http://www.theplantlist.org.

Figure 1A: *Baladur (semecarpus anacardium) plant.*

Figure 1B: *Baladur (semecarpus anacardium) fruit.*

Detoxification (mudabbar) and its importance in unani medicine

The process of detoxification is called as Tadbeer-e-Advia and the drugs which undergo this process are term as Mudabbar/Maghsool/Musaffa (detoxified). Some natural components present in the drug (plants, animals and metals) are toxic in their properties so, it is necessary to detoxify the drugs in order to overcome their toxicity [7].

Tarry oil, a corrosive juice present in the pericarp of the Baladur fruit causes blisters on contact which contain catechol, fixed oil, and anacardol ($C_{18}H_{13}O_3$.COOH) and the corrosive properties of the juice are due to two phenolic acids $C_{16}H_{15}O_3$.COOH and $C_{14}H_{13}O_3$.COOH. Major chemical constituents of tarry oil are Bhilawanol which is a mixture of phenolic compounds. Bhilawanol A and B are known as Urushiol, and also, anacardic acid is closely related to Urushiol. Urushiol-induced contact dermatitis is the medical name given to allergic rashes produced by the oil Urushiol. It should be use with caution (i.e. after Detoxification only) [8-10].

There are many processes of detoxification of the toxic drugs in Unani System which are safe and effective prior to use clinically. Such detoxification process has been mentioned as follows:

1. Take one Mann (38400 ml) of pure Cow milk start boiling it, then after 5 minutes mix one ser (960 ml) of pure oil of Baladur (extracted from whole fruit) carefully, boil the contents till the preparation be decreased to 1/4th then add one ser (960 ml) of pure Sesame oil in to the preparation and again heat (on low flame) till the whole preparation becomes thick, so that you can prepare round tablets - that indicates that the Baladur extract has become safer, able to eat (Detoxified) by the process of Unani system [11,12].
2. 1 Tola Baladur should be made to fine paste in the mortar and pestle then add 16 tola Til (Sesame) then again make a fine paste [11,12] (1 Tola = 12 gram, 1 Ratti = 125 mg).
3. Baladur, Maghz -e- akhrot and Kunjad/Til Muqasshar (peeled off Sesame) should be taken in equal quantities and make tablets equal to 1 gm [11,12].
4. Baladur oil, Jouzbuaa, and Filfil Saad each - sava 2 tola (2.25 tola), Halela siyah and Aamla each - 13 tola, Filfil daraaz and Anisoon each- 4 tola, Naushadar - 7 Masha and Misri - 225 tola, mix all mentioned drugs and make 360 tablets [11,12] (1 Masha = 1 gram).
5. Take 10 pieces of Baladur fruit and prick them with the needle from all the sides and put them in the 375 gm pukhta Roghan-e-ghee and roast (Tashwia/bhil bhilana) them on slow heat, till they become brown then clean the Roghan-e-ghee [11,12].

Figure 2A-2C: *Detoxification ((Mudabbar) process.*

Brief description of Semecarpus anacardium L.

Kingdom	Plantae
Division	Tracheophyta
Subdivision	Spermatophytina
Class	Magnoliopsida
Order	Sapindales
Family	Anacardiaceae
Genus	*Semecarpus*
Species	*Semecarpus anacardium*

Table 1: *Taxonomic classification [13].*

Vernacular names [14-17]

Farsi- Baladur; Arabic- Hub-ul- Qalb, Hub-ul- Faham, Beladin; Urdu-Baladur, Bhilavan, Billar; Hindi- Bhilawa (Bhilv), Bhela (Bhel), Bhilwa, Belatak; Sanskrit- Bhallataka, Agnimukhi, Bhallatakah, Antasatva, Arusharah, Arushkara, (Arukara), Arzohita, Ballata (Bhallata), Vanhinama, Visasya; English- Indian Marking Nut Tree, Oriental Cashew Nut; French- Anacardier d'Orient; Tamil- Erimugi (Erimuki), Sengottai, Tatamkottai, Kalagam; Gujarati- Bhilamo, Bhilamu; Kannada- Ker beeja, Goddugeru; Marathi- Bibha, Bibwa, Bibu; Malayalam- Chera, Cherkkuru, Kampira, Temprakku; Punjab - Bhilawa, Bhiladar, Bhela; Telugu- Bhallataki, Jidi, Nallajeedi, Bhallatamu, Gudova; Bengal- Bhela, Bhelatuki; Uriya - Bhollia, Bhollatoki, Bonebhalia; Nepal- Bhalaiyo, Bhalai; Russian- Semekarpus Anakardii.

eographical description

The plant grows naturally in tropical and dry climate. It is native to India and is found in abundance in the forests of Andhra Pradesh and other hotter parts of India like Assam, Bihar, Bengal and Orissa, Chittagong and central India. It is also found in other parts of the world including Western Peninsula of East Archipelago, Northern Australia, Malaysia, Myanmar, Singapore, China and Africa [18].

Botanical description

It is a moderate-sized deciduous tree up to 15 - 25m in height with grey bark exfoliating in small irregular flakes. The young branches are rusty, tomentose with milky latex. Leaves are simple alternate, obviate - oblong, about 30 - 60 cm long and 12 - 30 cm broad with rounded apex. The leaves are smooth coriaceous above and more or less pubescent below. Flowers are small and greenish yellow in colour which are borne in terminal pubescent panicles. Calyx is deciduous and consists of five sepals with imbricate aestivation. Corolla consists of five petals with imbricate aestivation. Androecium consists of five stamens which arise from below the disc and easily recognized by large leaves. The actual fruit is a moderate shade bearer, obliquely ovoid or oblong drupe, 2.5 to 3.8 cm long, laterally flattened in shape, longitudinally wrinkled ridged, greenish in unripe condition and turns shining black when ripe. The pericarp of the fruit contains a corrosive resinous juice. Below the true drupaceous fruit, there is false fleshy fruit, hypocarp, which develops from the upper part of the pedicel of the flower. It turns yellowish orange on ripening and can be eaten. Seeds are ovate, oblong or conical, irregularly flattened with occasional twisted edges, having acute apex and rounded base. Seeds are about 12 - 18 mm in width and 3 - 5 mm in thickness with rough surface [15-18].

Hissa-e-Mushtamla **(Parts used):** Oil, Hypocarp, Kernel (Maghz) and gum [1,19].

Zaiqa **(Taste):** Fruit - Slightly sweet, Seed - Bitter [1,19].

Mizaj **(Temperament):**

- Oil- Hār 4 and yābis 4 (Hot 4 and Dry 4) [2,6]
- Maghz- Hār 3 and yābis 1 (Hot 3 and Dry 1) [2]
- Post- Hār 4 and yābis 4 (Hot 4 and dry 4) [4].

***Afāl* (Pharmacological actions):** *Mufattiḥ-i-sudad* (Deobstruent), *Muḥallil-i-Waram* (Anti-inflammatory), *Mulattif* (Demulcent), *Musakhkhin* (Calorificient), *Muqawwī -i- Dimāgh wa A'ṣāb* (Brain and Nervine tonic), *Muqarḥ* (Ulcerative) [2-6].

***Istemal* (Therapeutic uses)- Internal:** *Fālij* (Paralysis), *Laqwā* (Bell's palsy), *Istirkhā'* (Lethargy), *Ra'sha*, (Tremors), *Gathiyā* (Rheumatism), *'Irq al-Nasā* (Sciatica), *Ḍīq al-Nafas* (Asthma) [1-6].

***Istemal* (Therapeutic uses)- External:** *Waja'al-Mafāṣil* (Rheumatoid arthritis), *Juzām* (Leprosy), *Barṣ* (Leukoderma), *Qūbā* (Eczema), *Thālīl* (Wart), *Bawāsīr* (Haemorrhoids) [1-6].

***Muzir* (Side effects):** Muqarrah (Ulcerative), Muharriq-e-khoon, Muarris-e- junoon [1].

***Musleh* (Corrective):** Sesame oil, Raw Coconut/Coconut oil, Walnut/Walnut oil, Ma'ush-shaeer, Fad-e- zahar, Jadwār, Lu-aab -e- Behidana, Ghee, Internal bark of the Imli (Tamarindus indica) tree, curd, Aslussoos, Dhaak bark, Salajeet, milk, Ghee, butter, Maazu, Roghan-e- banafsha and cold items [2,6,12,20].

***Badal* (Substitute):** Fandaq, Balsan [1,2].

***Miqdaar -e- khuraak* (Therapeutic dose):** Oil- 4 ratti, Maghz (Kernel)- 1 Masha [1,6].

***Murakkabat* (Compound formulations):** Jawarish Baladur, Majoon Asl-e-Baladur, Anqardiya-e-Kabeer, Anqardiya-e-sagheer, Anqardiya-e-Sara, Tila-e-khaas [1,5,19].

Chemical constituents

The most significant components present in the *Semecarpus anacardium* Linn. are bhilwanols, phenolic compounds, biflavonoids, sterols and glycosides. Bhilwanol from fruits was shown to be a mixture of cis- and trans isomers of Ursuhenol. This compound consists mainly of 1,2, dihydroxy-3 (pentadecadienyl 8',11') benzene and 1,2, hydroxy-3 (pentadecadienyl 8') benzene. Other components are anacardoside, semecarpetin, nallaflavanone, jeediflavanone, semecarpuflavanone, galluflavanone, anacarduflavone, mono-olefin I, diolefin II, bhilawanol-A, bhilawanol-B, amentoflavone, tetrahydroamentoflavone, semicarpol, anacardic acid, tetrahydrobustaflavone, O-trimethyl biflavanone A1, O-trimethyl biflavanone A2, O-tetramethyl biflavanone A1, O-hexamethyl bichalcone A, Odimethyl biflavanone B, O-heptamethyl bichalcone B1, O-hexamethyl bichalcone B2 and O-tetramethyl biflavanone C [21-29].

Evidence based pharmacological studies

Anti-atherogenic effect

Sharma., *et al*. demonstrated the cardiac activity of *Semecarpus anacardium*, as it generally reduced the tissue and serum hyperlipidaemia by the inhibition of intestinal cholesterol absorption coupled with peripheral disposal thus possessing anti-atherosclerotic activity [30].

Antiarthritic activity

Ramprasath., *et al*. and Prakash., *et al*. evaluated the antiarthritic activity of *Semecarpus anacardium* Linn. nut milk extract in paraffin-induced arthritic rats. The extract showed alterations in the bone by modulating the levels of calcium, phosphorus and the activities of the enzyme such as tartrate resistant acid phosphatase, acid phosphatase and alkaline phosphatase along with decrease in the levels of TNF-alpha and provide significant protection against protein denaturation and RBC membrane damage [31,32].

Anti-inflammatory activity

Salvem., *et al*, Bhitre., *et al*. and Sushma Y investigated that ethanolic, chloroform, ethyl acetate and petroleum ether extracts of Semecarpus anacardium fruits possess significant anti-inflammatory in carrageenan-induced paw edema comparable to ibuprofen and aspirin [33-35].

Antioxidant activity

Sahoo., *et al*. investigated the antioxidant activity of ethyl acetate extract of stem bark of *Semecarpus anacardium*. Ethyl acetate extract showed the stronger antioxidant activity (due to presence of highest total phenolic content of 68.67% measured as pyrocatechol equivalent) compared to the other (hexane, chloroform and methanol) extracts [36].

Antimicrobial activity

Bagewadi., *et al*. and Purushothaman., *et al*. evaluated the antimicrobial activity of *Semecarpus anacardium* nut extract that showed inhibitory activity against *Escherichia coli*, *Micrococcus luteus*, *Salmonella typhi*, *Bacillus subtilis* and *Klebsiella pneumonia*. The petroleum ether extract of *Semecarpus anacardium* nut exhibited antibacterial activity due to petroleum ether extractable compounds against gram-positive and gram-negative bacteria by agar well method [37,38].

Hypoglycaemic activity

Hedaythullah Khan., *et al*. and Ali., *et al*. investigated the antidiabetic activity of nut milk extract of *Semecarpus anacardium* in high-fat diet followed by streptozotocin and alloxan induced diabetic rats that showed, a significant fall in blood glucose levels with lowering TC, TG, LDL level dose dependently, and also decreased the levels of HbA1c as compared of control group [39,40].

Anti-carcinogenic activity

Mathivadhani., *et al*. investigated that *Semecarpus anacardium* nut extract possess inhibitory effect on human breast cancer cells (T47D). These changes are accompanied by decrease in Bcl_2 and increase in Bax, cytochrome c, caspases and PARP cleavage, and ultimately by inter nucleosomal DNA fragmentation [41].

Upreti., *et al*. evaluated the effect of methanolic extract of *Semecarpus anacardium* on N-Nitroso Diethylamine (NDEA) induced Hepatocellular carcinoma in Sprague Dawley rats. The extract at the dose of 200 and 400 mg/kg decreased the elevated levels of SGPT, SGOT, ALP and LDH in a dose dependent manner and at the dose of 400 mg/kg extract showed promising effect in management of primary liver cancer [42].

Acetylcholinesterase (AChE) inhibitory activity

Vinutha., *et al*. investigated the acetylcholinesterase (AChE) inhibitory activity (*in vitro*) of methanolic and water extracts of stem bark of *Semecarpus anacardium*. Methanolic Extracts showed the most potent effect in AChE inhibition and successive water extracts showed very low or no activity [43].

Neuroprotective activity

Vijayakumar., *et al*. evaluated the neuroprotective effect of *Semecarpus anacardium* in ammonium chloride (NH4Cl)-induced hyperammonemic rats. Milk extract of *Semecarpus anacardium* nuts (150 mg/kg body weight) showed significant neuroprotective activity with enhancing the activities of superoxide dismutase (SOD), catalase, glutathione peroxidase (GPx) and glutathione (GSH) and reducing the levels of thiobarbituric acid reactive substances (TBARS) and hydroperoxides (HP) in brain tissues [44]. Farooq., *et al*. evaluated the beneficial effect of nuts milk extract of *Semecarpus anacardium* on CNS, mainly for its locomotor and nootropic activities in different experimental animal models. *Semecarpus anacardium* may indirectly modify Ach concentration and removal of negative influence possibly helped in the manifestation of cholinergic effects resulting in improved cognitive function. The extract tested but a slight CNS depressant effect was noted with only 150 mg/kg of the extract and it was found to possess nootropic activity [45].

Anti-spermatogenic activity

Sharma., *et al.* evaluated the anti-spermatogenic activity of ethanolic extract of *Semecarpus anacardium* fruit in male albino rats at 100, 200 and 300 mg/kg dose level. Ethanolic extract showed marked reduction in the number of primary spermatocytes, secondary spermatocytes and spermatids along with reduced sperm motility and density [46].

Antifertility activity

Sushma., *et al*. evaluated the antifertility activity of *Semecarpus anacardium* in female albino rats at 200, 400, 600, and 800 mg/kg dose level. The aqueous and ethanolic extract of *Semecarpus anacardium* fruit possess highly significant increasing Diestrus index in a dose dependent manner and results in reversible antiovulatory effects [47].

Hepatoprotective activity

Kangralkar., *et al*. evaluated the aqueous and alcoholic extracts of *Semecarpus anacardium* to identify the hepatoprotective activity which revealed that both aqueous and alcoholic extracts showed significant hepatoprotective activity against paracetamol-induced hepatic injury. The alcoholic extract appears to be better than aqueous extract since it significantly elevated total serum protein [48].

Conclusion

Baladur (Semecarpus anacardium) is a plant origin drug. The great Unani scholars had been widely using this Unani drug from the ancient time for the treatment of *Fālij* (Paralysis), *Laqwā* (Bell's palsy), *Istirkhā'* (Lethargy), *Ra'sha* (Tremors), *Gathiyā* (Rheumatism), *'Irq al-Nasā* (Sciatica), *Ḍīq al-Nafas* (Asthma) and skin diseases like Pityriasis, Vitiligo and Tinea. Recent scientific studies showed the anticancerous activity, anti-inflammatory, antimicrobial, antioxidant, hypoglycaemic activity of Detoxified Baladur. Detoxified Baladur exhibit the medicinal properties due the presence of active constituents like Bhilawanol, Semicarpetin, Anacardic acid and Tetrahydrobusta flavone. This review tried to bring many information together which helps better therapeutic utilization of the drug (Detoxified Baladur) in different diseases condition and also helpful to explore the scientific potential of drug in order to generate more scientific data. At the time Baladur even though is a highly toxic drug but after its classic detoxification process has tremendously changed into an effective medicinally important drug which is useful in varied pathological conditions. In this review paper different detoxification process has been mentioned according to Unani literature and it has been seen that these processes lacking in lot of modern analytical prerequisites for its complete understanding and scientific validation. Hence further urge of research is required to elicit that what actual chemical changes has been occurred after detoxification.

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Conflict of Interest

None.

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