



Review Article

A REVIEW ON PHARMACOLOGICAL AND THERAPEUTIC ASPECT OF *SHIRISHADI AGADA*
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ABSTRACT

In *Agadtantra* many *Jangam* (animal poison) and *Sthawar visha* (plant poisoning) are described and in treatment of *Visha* many *Agada* are described. *Agad* means drug or formulation of drug which act against poisons or neutralize the poisoning effects. *Keet visha* (insect bite) is one of the common poisoning in *Jangam visha*. In Ayurvedic *Samhitas* many *Agada* formulations are described in treatment of *Keet visha*. *Shirishadi Agada* is mentioned in treatment of *Keet visha* (insect bite), *Sarp* (snake bite), *Luta* (spider), *Mushak* (rat poison) and *Vruschik visha* (scorpion bite) in *Ashtang hridayam* in *Uttarsthana*. *Shirishadi Agad* is herbal formulation contains *Shirish*, *Pippali* and *Arka*. This review is for collective information about therapeutic and pharmacological action of *Shirishadi Agada*.

INTRODUCTION

Agadtantra is a branch of Ayurveda that deals signs, symptoms and with the management of various poisons by many formulations. The term *Visha* is derived from the word *Vishad*^[1] (depression of spirit or sorrow). *Visha* are classified into main two types *Sthawar visha* (poison originates from plants) and *Jangam visha* (poison originates from animal)^[2]. *Jangam visha* includes *Sarp visha* (snake bite), *Vruschik visha* (scorpion bite), *Keeta visha* (insect bite), *Luta visha* (spider poisoning), *Mushak visha* (rat poison) and *Alark visha* (rabies)^[3]. *Keeta visha* (insect bite) is very common type of poison next to *Sarp visha* (snake bite poisoning) which we come across in our clinical practice. There are four types of *Keeta visha*^[4]. *Makshika* (bee) is one of the types of *Keeta*. It causes *Kandu* (itching), *Daah* (burning sensation), and *Vedana* (pain)^[5]. *Acharya Vagbhata* mentioned *Shirishadi agada* in *Ashtang hridayam Uttarsthana*. *Shirishadi agad* is herbal formulation contain *Shirish*, *Pippali* and *Arka*. It is mainly use in treatment of *Keet visha* (insect bite), *Sarp* (snake bite), *Luta* (spider), *Mushak* (rat poison) and *Vruschik visha* (scorpion bite)^[6]. *Albizia lebeck* (*Shirisha*) has properties like *Vishaghna* (anti-

poisonous) and also use as medicine in diseases like *Visarpa* (erysipelas), *Hicca* (hiccup), *Shwasa* (breathlessness) and *Kasa* (cough). Recent researches reported that it has anti-inflammatory, anti-histaminic, anti-anaphylactic, anti-asthmatic, anti-microbial properties. *Pippali* (*Piper longam*) use to treat chronic bronchitis, asthma, constipation, gonorrhoea, paralysis of the tongue, diarrhoea, cholera, chronic malaria, viral hepatitis, respiratory infections, stomachache, bronchitis, diseases of the spleen, cough and tumors. According to Ayurveda *Calotropis procera* is used alone or with other medicines as Ayurvedic formulations to treat common diseases such as *Jwara* (fever), *Amvata* (rheumatism), *Aam* (indigestion), *Kas* (cough), *Pratishyay* (cold), *Vicharchika* (eczema), *Shwas* (asthma), *Shlipad* (elephantiasis), *Chardi* (nausea and vomiting), *Atisar* (diarrhoea).

Present article focus on therapeutic properties and pharmacological action of *Shirishadi agad* described in Ayurvedic *samhitas* and related text books and different research articles available on internet.

AIM

To study pharmacological and therapeutic aspect of *Shirishadi Agada*.

OBJECTIVES

1. To study therapeutic and pharmacological action of each ingredient of *Shirishadi Agad*.
2. To study pharmacological and therapeutic action of *Shirishadi Agad*.

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MATERIALS AND METHODS

Literature collected from Ayurvedic Samhitas, textbooks and published articles on internet.

Review of Literature

Method of preparation of *Shirishadi Agad*^[6]

Shirish beej (seeds) and *Pippali churna* (powder) are grind with milk extract of *Arka* i.e. three *bhavana* of milk extract of *Arka* is given and small tablets are prepared.

Table 1: Raspanchaka of ingredients of Shirishadi Agad ^[7-9]

S.no.	Name	Latin Name	Ras	Virya	Vipak	Guna	Karma
1.	<i>Shirish</i>	<i>Albizia lebbek</i>	<i>Kashaya, Tikta, Madhura</i>	<i>Ushna</i>	<i>Katu</i>	<i>Laghu</i>	<i>Shothhara, Visarpaghna, Vranahara, Kushtaghna</i>
2.	<i>Pippali</i>	<i>Piper Longum</i>	<i>Katu</i>	<i>Ushna</i>	<i>Madhur</i>	<i>Laghu, Tikshna</i>	<i>Deepniya, Asthapanopaga, Shool Prashamana</i>
3.	<i>Arka</i>	<i>Calotropis procera</i>	<i>Arkadugdha-Tikta, Lavan, Multwak-Katu, Tikta</i>	<i>Ushna</i>	-	<i>Snigdha, Laghu</i>	<i>Agnideepan, Rasayan, Balya</i>

Shirish^[10]

Latin name - *Albizia lebbek*

Family - *Fabaceae (Mimosoideae)*

Chemical constituents- Saponin, tannin, protein, amino acids.

Pharmacological Action

- 1. Anti-inflammatory activity**^[11]- The anti-inflammatory activity of *Shirish* studied on rat models induced by carrageenan. The extract of *Shirish* obtained using petroleum ether, chloroform and ethanol were administered at concentrations of 100, 200 and 400mg/kg body weight. The petroleum ether and ethanol extract at 400mg/kg, showed maximum inhibition of inflammation induced by carrageenan. The extract shows marked inhibitory effect on paw edema that means it possesses anti-inflammatory activity and can be use in various inflammatory conditions.
- 2. Anti-asthmatic activity**^[12]- Bark decoction of *Albizia lebbek* administered in the ginea pig (300-400g of either sex) with histamine induced bronchospasm. The action started within 1 hour of drug administration and protection was maximum with dose of 1gm per kg. The decoction of flower also protects ginea pig from histamin induced bronchospasm. It is proved that both bark and flower decoction of *Shirish* has anti-asthmatic property.
- 3. Anti-venom activity**^[13]- In vitro analysis of seed extract (methanolic extract) of *Albezia lebbek* shows demonstrated significant inhibition of ECV proteases, the major enzyme toxin responsible for local toxicity. ALME contained high concentrations of phenolics and flavonoids and ALME neutralizes ECV enzymes that contribute in local tissue damage and haemostatic alteration. The study shows antidotal and antivenom property of *Albezia lebbek*.

4. Antimicrobial activity^[14]- Phytochemical screening of leaves of *Albizia lebbek* showed that it contains alkaloids, glycosides, tannins, saponins, flavonoids, carbohydrates, proteins, and amino acids. Antibacterial activity of leaves of *Albizia lebbek* was studied against *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Bacillus cereus*. Study showed that extract is sensitive for both gram positive and gram negative bacteria with maximum against *Pseudomonas aeruginosa* and minimum against *Escherichia coli*.

5. Analgesic and Antipyretic activity^[15]- In radiant heat tail- flick the crude ethanolic extract produced 77.29% and 95.80% elongation of tail flicking time 15 minutes after oral doses of 200 and 400mg/kg respectively. The crude extract produced maximum analgesic effect after oral doses 200 and 400mg/kg. The antipyretic activity was studied on Brewer's yeast induced rats. Crude ethanolic extract of *Albizia lebbek* leaves reduced shows 6.46% (p<0.05) and 7.20% (p<0.05) of temperature in 180 minutes after oral doses of 200 and 400mg/kg.

Pharmacological Action According to Ayurveda^[16] *Shothahara, Visarpaghna, Kasahara, Vranahara, Vishapaha, Varnya, Kushtaghna, Kandughna.*

Therapeutic action^[17]- *Kushtha, Gandmala, visphot, Visarp, vrana, Shwetpradara.*

Pippali^[18]

Botanical name- *Piper longum* Linn.

Family - *Piperaceae*

Chemical constituents- Essential oil, mono and sesquiterpenes, caryophyllene, piperine, piperlongumine, piperlonguminine, pipernolanine, piperundecalidine, pipericide, sesamin, B-sitosterol, four aristolactum.

Pharmacological action of *Pippali*

- 1. Antimicrobial and antifungal activity^[19]**- In vitro study carried out to study antimicrobial and antifungal activity of *Piper longum* against 13 pathogenic bacteria (5 gram-positive and 8 gram negative) and 6 fungi by the standard disc diffusion method. Study performed with petroleum ether, ethyl acetate, chloroform and methanol extract of root, stem and leaves of *Piper longum* (*Pippali*). Nutrient agar medium was used for antibacterial activity and potato dextrose agar medium was selected for antifungal activity. Result of study showed that ethyl acetate has antibacterial activity against bacteria. Ethyl acetate extract of piper longum shows activity against fusarium species. Petroleum ether extract shows activity against fungus *Aspergillus niger* and *Aspergillus fumigatus*.
- 2. Anti-inflammatory activity^[20]**- *Piper longum* shows anti-inflammatory activity against Carrageenan induced rat model and dextran induced oedema in rats. It shows chronic anti-inflammatory activity in cotton pillet induced granuloma.
- 3. Antiasthmatic and Anti-allergic activity^[21]** - The fruit extract of *Piper longum*, petroleum ether, alcoholic and decoction of fruits of *Piper longum* was studied for anti-histaminic activity. Study was conducted using Guinea pig ileum (in vitro) and in Mice (in vivo). Fruit extract shows significant protection in histamine induced bronchospasm.
- 4. Hepatoprotective activity^[22]** - Ethanolic extract of fruits of *Piper longum* and crude extract was used to study hepatoprotective activity of *Piper longum* in CCL₄ (carbon tetrachloride) induced hepatotoxicity in adult Wistar rats. Ethanolic extract of fruits shows hepatoprotective activity by lowering serum enzymes glutamic oxaloacetic transaminase and glutamic pyruvic transaminase in rats.

Pharmacological Action According to Ayurveda^[23]
Kasahara, Hikkanigrahan, Shirovirechan, Deepniya, Shoolaghna, Yogwahi, Rasayana.

Therapeutic action^[24] - *Aamvata, Urustambha, Kasa, Shwasa, Shool, Gulma, piles, Prameha, Arsha, Pandurog, Shotha, Vishamjwara, Chardi, Vatarakta, Pleeharog.*

Arka

Botanical name - *Calotropis procera*

Family - *Apocynaceae*.

Chemical constituents^[25]

Pharmacological action of *Calotropis procera*

- 1. Anti-inflammatory activity^[26]**- Study has been carried out to find inflammatory activity of methanolic extract of root of *calotropis procera* on rodents. This activity was evaluated using acute inflammatory model like carrageenan induced paw

oedema and chronic model like cotton pillet induced granuloma. Phytochemicals in root bark proved effective in chronic model of cotton pillet induced granuloma, there was significant reduction in granular tissue. The methanolic extract of root of *calotropis procera* proved effective in carrageenan induced paw oedema.

- 2. Hepatoprotective activity^[27]** - Hepatoprotective activity of methanol extract of root bark of *calotropis procera* was evaluated using carbon tetrachloride induced liver injury in rats. Group I and II serves as control group. Group III animals were treated with silymarin. Group IV and V animals were treated with methanol extract of *Calotropis procera*. After 7 days blood was collected and liver extract was send for histopathological examination. The result showed that after treating with methanol extract there was decrease in the values of serum transaminases, alkaline phosphatase and decrease in total and direct bilirubin level, increase in high density lipoprotein. It improves functional status of liver cells, there increase in the level of protein and albumin.
- 3. Antipyretic activity^[28]** - *Calotropis procera* posses anti-inflammatory and antipyretic activity. Study is carried out on Albino rats and fever was induced using yeast. Administration of dry latex of *Calotropis procera* 250mg/kg and 500mg/kg at 4h produced a significant ($p < 0.05$) decline in rectal temperature.
- 4. Anti-ulcer activity^[29]**- Antiulcer activity of methanolic extract of the *Calotropis procera* root was tested in rats, in which gastric ulcerations were experimentally induced by aspirin, alcohol, stress and pylorus ligation. Methanolic extract of the root of *Calotropis procera* was significantly effective in protecting gastric mucosa against aspirin, alcohol, stress at all the dose level studied.
- 5. Antimicrobial activity^[30]**- Antimicrobial activity of crude leaf extract of *Calotropis procera* was studied on *salmonella typhae*, *salmonella paratyphae*, *vibrio cholera* and *klebsiella pneumoniae* using agar well diffusion method. Crude extract in methanol, ethyl acetate, chloroform and hot water added to each well. Among all extracts ethyl acetate extract shows best antimicrobial activity.
- 6. Anti-fungal activity^[34]** - Aqueous and ethanol extract of leaf and latex of *Calotropis procera* was tested for their antifungal activity against seed borne dominant fungi *Culvularia lunata*, *Alternaria Alternata*, *Rhizoctonia solani*, *Fusarium solani*, *Penicillium chrysogenum*, *Aspergillus niger*, *A-flavus*, *A-terrus*, *A-fumigatus* and *Rhizopus sp.* Were determined using agar well deffusion method. The

result revealed that ethanolic extract of both leaf and latex showed inhibition of growth in the test fungi with the widest zone of inhibition.

7. **Antioxidant activity**^[32]- Methanolic extract of *Calotropis procera* flowers exhibited the high radical scavenging property and cytotoxic activity. The effectiveness of flower might be due to the hydroxyl groups existing in the phenolic compounds chemical structure that can provide the necessary component as a radical scavenger. A potent scavenger of free radicals may serve as a possible preventive intervention for the disease. The present study suggests that the flowers of *Calotropis procera* is potential source of natural antioxidants.

Pharmacological action according to the Ayurveda^[33]

Vranaghna (wound healing property), *Kushthagha* (leprosy), *Krimighna* (antihelmintic), *Rakt vikar* (blood disorders), *Jwaraghna* (fever).

Therapeutic action^[34] - *Jeerna Amvaat*, *Kushtha*, *Jwara*, *Arsha*, *Vrana*, ulcers, pruritus and erysipelas, *Shwasrog*, *mutrakrucha*, *shotha*, *Kandu*, *Visarpa*, *Pratishyay*, *Pliha*, *Krumi*, *Gulma*, *Prasek*, *Udar*, *Yakrut*, *Pachak*, *Kas*, *Aruchi*.

Vishaghna (antitoxic) action of Shirish - *Shirish* is used as single drug and in many *Agada* formulations in the treatment of poisoning. It is used in *Adaga* such as *Mritasanjivini Agad*^[35], *Gandhahasti Agad*^[36], *Mahagandahasti Agad*^[37], *Ksharagad*^[38], *Koshatkyadi Agad*^[39], *Mahasugandi Agad*^[40], *Ashtanga Agad*^[41], *Dhomagad*^[42], *Sarvakarmika Agada*^[43], *Parama Agada*^[44], *Pancha Shirisha Agad*^[45], *Amrut ghruta*^[46].

Vishaghna (antitoxic) action of Pippali - *Pippali* is use as single drug and in *Agada* formulations in the treatment of poisoning. It is used in *Dushivishari Agad*^[47], *Chandrodaya Agada*^[48], *Katukadi Agad*^[49], *Bilwadi Agad*^[50], *Dashang Agad*^[51], *Gandhahasti Agad*, *Mahagandahasti Agad*, *Hingwadi yog*^[52], *Ksharagad*, *Pippalyadi anjan* in *netragat Visha*, *Pippali* also use in snake bite (*Sarpa Visha*), *Keeta Visha* (insect bite), *Mushak Visha* (rat bite).

Vishaghna (Antitoxic) action of Arka - *Arka* is use as single drug and in *Agada* formulations in the treatment of poisoning. It is use in *Karviradi Agad*^[53]. It is also use in *Sarpa damsha* (snake bite), *Vrischik damsha* (scorpion bite), *Keet Visha* (insect bite).

DISCUSSION

According to *Acharya Vagbhat Shirishadi Agad* indicated in *Keeta visha*, *Sarpa visha*, *Luta visha*, *Mushak visha* and *Vrischik visha*. It contains three drugs *Shirish beeja*, *Pippali* and *Arka dugdha*. *Shirish* shows anti-inflammatory activity, anti-asthmatic activity, anti-venom activity, anti-microbial activity, anti-pyretic and analgesic activity. It can be used in many

conditions like skin disease, gastrointestinal manifestation, fever, injury, oedema, asthma. *Pippali* possesses anti-antipyretic, antiulcer, hepatoprotective and antioxidant activity. It can be used in various skin diseases, ulcers, injury, bacterial infections, worm manifestation, fungal infections and liver diseases. *Arka* shows anti-inflammatory, antifungal, antimicrobial, anti-asthmatic, anti-allergic and hepatoprotective activity. It can be used in many conditions like cough, asthma, fungal manifestations, in bacterial infections and in skin disease also. *Shirishadi Agad* can be used as *Shothahara*, *Visarpaghna*, *Kasahara*, *Vishapaha*, *Varnya*, *Kushtaghna*, *Kandughna*, *Hikkanigrahan*, *Shirovirechan*, *Deepniya*, *Shoolaghna*, *yogwahi*, *Rasayana*, *Vranaghna* (wound healing property), *Krimighna* (antihelmintic), *Rakt vikar* (blood disorders), *Jwaraghna* (fever).

CONCLUSION

All the contents of *Shirishadi Agad* has very important pharmacological action so that it can be use in skin diseases, inflammatory conditions, gastrointestinal conditions, in wound healing, in case of injury and in worm infection. *Shirishadi Agad* mentioned in the treatment of *Keet visha*, *Sarpa Visha*, *Luta visha*, *Mushak visha* and *Vrischik visha*. *Shirishadi Agad* can be used in clinical practice because of its therapeutic actions but further research and clinical trials are needed. The review of this article is to provide collective information on pharmacological action of *Shirishadi Agad*.

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