Ajita Agada for Poisoning Conditions and Interpret its Mode of Actions

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Abstract

Poisonings have been identified as critical conditions in Ayurveda since centuries. *Agada tantra* is the specialized clinical branch where the therapeutic roots for poison management lie. *Agada* are given a significance as anti-poisonous formulations in various Ayurveda treatises. *Ajita agada* is the main concern in this study which the references were found on Susruta Samhita *Kalpasthana*, Aṣhṭanga Samgraha *Uttarasthana* and Bhaisajjaratnavali. This herbo-mineral anti-poisonous formulation is consisted of 17 ingredients and bee honey as its dipping material. *Ajita agada* is prescribed mainly for snake bites (*Sarpa visha*) and also for all the other kinds of animate (*Jangama*) and inanimate (*Sthavara*) poisons. Still, any organized management procedure in critical care for poisonings from Ayurveda perspective hasn't observed included in national health care system of Sri Lanka. This study is aimed at fulfilling this lacuna by means of finding a strategy for critical care of poisonings through *Ajita agada*. Upon Ayurveda pharmacodynamics are concerned, it's observed that *Kaṭu* (76.47%), *Tikta* (35.29%) and *Kashaya rasa* (29.41%) are prominent *Rasa, Laghu* (94.11%), *Tikshṇa* (58.82%) and *Ruksha guna* (35.29%) are prominent *Guna, Ushṇa* (82.35%) and *Katu* (23.52%) as the prominent *Virya* and *Vipaka*. By virtue of pharmacodynamics, *Ajita agada* shows a similarity with poison itself. This is very remarkable in collective understanding the therapeutic action of *Ajita agada* in management of poisonings. Further, chemical and clinical studies should be conducted with this regard.

Keywords: *Ajita agada,* Anti-toxicity, *Visha, Visha upakrama.*

Introduction

Ayurveda is an organized medical system with a ruler strong foundation of eight clinical branches, namely *Ashṭanga* Ayurveda[1]. Among these eight clinical branches, *Agada tantra* broadly elaborates Ayurvedic perspective of toxicology. In present circumstances, toxicology is practiced as a medical sub speciality to diagnose, manage, treat and prevent poisoning conditions. Similarly, all these concepts practiced in present scenario are vividly denoted in *Agada tantra*. References are found for sources, modes of administration, classifications, management, treatment procedures and prognosis for various kinds of poisonings from ancient Ayurveda authentic texts. This well depicts the fact that ancient *Acharyas* had identified the critical need of management of poisoning conditions.

As Ayurveda is a medical system based on natural substances, a line of treatment from medicines comprised of natural herbals and minerals for the management of poisonings are compiled on ancient Ayurveda treatises. These anti-poisonous formulations are given the name, "*Agada*" which are naturally prepared herbal or herbo-mineral drug combinations. In references, preparatory methods, addressable poisoning conditions, other clinical indications, mode of administration, dosage form and vehicles are provided with these formulations.

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In present scenario, poisonings have become a critical condition that is to be managed immediately. Mortality rates attributed to unintentional poisonings in males and females in the year 2019 are 0.7 and 0.2 respectively in Sri Lanka[2]. These rates are identified remaining relatively high in low economy countries[2]. Snakebites are one of the common unintentional poisonings and the annual snakebite incidence in Sri Lanka is about 400 per 100,000 people corresponding to 80,000 snakebites in 20 million population[3].

Agada tantra describes these poisoning conditions as manifestations of features of poisonings (*Visha lakshana*) as the result of intaking poisonous substances (*Viha dravya*) in excessive quantities (*Atimatra*), ignorant ingesting/inhaling (*Mityayoga*), impurified conditions (*Ashodhana*) and excessive duration of exposure (*Adhika kala*) [4].

Ajita agada is such an anti-poisonous preparation in which the references were found on Susruta Samhita *Kalpasthana*, Aṣṭangasamgraha *Uttarasthana* and Bhaisajjaratnavali. This herbo-mineral anti-poisonous preparation is consisted of 17 ingredients and bee honey as its dipping material and the storage medium. *Ajita agada* is prescribed for all kinds of animate (*Jangama*) and inanimate (*Sthavara*) poisons, providing a justification for its literal meaning – conquering, being invisible[5] besides mainly indicated for snake bites.

Modern toxicology emphasizes the utility of antidotes. This concept was being molded along with the progression of understanding the mechanism of poisons[6]. Antidotes are understood as agents which nullify the toxic effects[7]. Antidote action is mediated in major two ways, either preventing the absorption of the toxin by binding with it or inhibiting the metabolism of toxins into more toxic metabolites inside the body[7].

Still, any organized management procedure in critical care for poisonings from Ayurveda perspective hasn't observed included in natural health care system of Sri Lanka. This study aimed at reviewing *Ajita agada* which is indicated for all kinds of poisons and consisted of easily available ingredients and a simple preparatory method to find out a strategy for addressing the critical care of poisonings. And also this study was aimed to review on *Ajita agada* for poisoning conditions and analyze the pharmacodynamic properties and interpret the mode of its action and discussed on preparation of *Ajita agada* as per Ayurveda authentic texts.

Materials and Methods

Data required for the review was collected from relevant published review articles and available Ayurveda authentic texts and associated books. Credible web search engines such as ResearchGate, Google Scholar and PubMed were utilized during the study.

Available Ayurveda authentic texts: Susruta Samhita, Charaka Samhita, Aṣṭanga Saṃgraha, Bhaisajjaratna-vali were used. And other relevant books used: The Ayurvedic Pharmacopoeia of India-Part 1 (Volume i-iv), Dravyaguna Vijnana (Materia medica-Vegetable, drugs) by Prof. G. Pandey (Volume 1-3).

Table 1 shows the authenticated ingredients of *Ajita agada*. Among all 17 ingredients, 12 ingredients are of herbal origin and the rest is of mineral origin. Five varieties of salts (*Lavana*) are the mineral origin ingredients of the preparation. Bee's honey (*Madhu*) is the storage medium used in the preparation process.

Method of Preparation

Authenticated raw materials were spread out in a thin layer in trays and the foreign matters were detected by inspection with the naked eye and by the use of a magnifying lens (6x). Washing and drying of herbal raw materials were undertaken; washed in tap water and shade dried on trays (to avoid destroy of aromatic compounds). Relevant purification methods were followed for *Hingu* and *Lavana varga* (salt varieties). *Hingu* was emulsified in sufficient quantity of water and each salt variety was filtered and evaporated. Dried raw materials were ground separately in a grinding machine and passed through the No 180 sieve and a fine powder was obtained (Figure 1).

Table 1: Ingredients of *Ajita agada*

Ingredient	Scientific name	Family	Used part	Quantity
Viḍanga	*E. ribes*	MYRSINACEAE	Fruit	50 grams
Paṭa	*C. pareira*	MENISPERMACEAE	Roots	50 grams
Haritaki	*Terminalia chebula* Retz.	COMBRETACEAE	Fruit	50 grams
Amalaki	*Embellica officinalis* Gaertn	EUPHORBIACEAE	Fruit	50 grams
Vibhitaki	*Terminalia belerica* Roxb.	COMBRETACEAE	Fruit	50 grams
Shunṭi	*Zingiber offficinale* Roscoe	ZINGIBERACEAE	Rhizome	50 grams
Maricha	*Piper nigrum* L.	PIPERACEAE	Fruit	50 grams
Pippali	*Piper longum* L.	PIPERACEAE	Fruit	50 grams
Hingu	*Ferula asafoetida* L.	UMBELLIFERAE	Resin	50 grams
Ajamoda	*Trachyspermum ammi* L.	UMBELLIFERAE	Seed	50 grams
Citraka	*Plumbago zeylanica* L.	PLUMBAGINACEAE	Roots	50 grams
Tagara	*Valeriana walichi* DC	VALERIANACEAE	Roots	50 grams
Saindhava lavana	-	-	-	50 grams
Sauvarcal lavana	-	-	-	50 grams
Samudra lavana	-	-	-	50 grams
Vid lavana	-	-	-	50 grams
Romaka lavana	-	-	-	50 grams
Bee's honey	Apis cerana Fabricius	APIDAE	-	As necessary

Figure 1: Separately obtained powders from all ingredients

Figure 2: Final homogenous powder mixture

Figure 3: The final homogenous powder mixture with bee's honey added in an adequate amount

Figure 4: Preparation ready for storage inside the cow's horn containing bee's honey

The final homogenous powder was obtained by mixing all the fine powders (Figure 2) and dipped in an adequate amount of bee's honey (Figure 3).

Finally, the paste (*Kalka*) form obtained after the process of dipping was stored in a cow's horn with a lid made of the same material for two weeks (Figure 4).

Results

Three sources were found consisting references for *Ajita agada*: *Sloka* 63(ii)-65(i) of Chapter 5 of Susrutasamhita *Kalpasthana, Sloka* 101 of chapter 40 of, Aṣṭanga Samgraha *Uttarasthana* and *Sloka* 41-42 of chapter 72 of Bhaisajjaratnavali.

All the references were comprised of the ingredients, preparation method, and indications of the preparation. Being a herbo-mineral preparation according to the given recipes, *Ajita agada* was composed of twelve herbal materials and five varieties of salts (*Lavana*) were of mineral origin. Bee's honey which is of animal origin was the grinding material. A specific storage method by using a cow's horn was mentioned in the references from Susrutasamhita [9] and Bhaisajjaratnavali[10].

The pharmacodynamic (*Rasadi panchaka*) analysis which was done during the study is given in table 2. Taste (*Rasa*), attributes (*Guna*), potency (*Virya*), post-digestive effect (*Vipaka*) and effects on three humors (*Dosha karma*) were considered under the pharmacodynamic analysis.

When *Ayurveda* pharmacodynamics are concerned, it's observed that pungent taste (*Kaṭu rasa*) which was 76.47%, bitter taste (*Tikta rasa*) which was 35.29% and astringent taste (*Kasaya rasa*) which was 29.41% were the prominent *Rasa* of the preparation. Lightness *(Laghu*) which was 94.11%, Sharpness (*Tikshṇa*) which was 58.82% *and* Roughness (*Ruksha*) which was 35.29% were the prominent *Guna.* Among *Virya,* hot potency (*Ushṇa virya*) which was 82.35% and among *Vipaka.* Pungent (*Katu vipaka*) which was 23.52% were observed as the prominent. Pacification of both *Kapha* and *Vata* (*Kapha-vata shamaka*) which was 55.56% was the prominent *Dosha karma* of the ingredients of *Ajita agada.*

Table 3 depicts the reported modern pharmacological actions of herbal ingredients in *Ajita agada*. Antioxidant, anti-inflammatory, analgesic, cardioprotective and hepatoprotective were the prominently identified pharmacological actions.

Anti-inflammatory action was found in bee's honey[37] and *Saindhava lavana*[38] Further immunomodulatory actions were found in *Plumbago zeylanica*[39], *Trikatu*[40], and *Triphala*[41] in-vivo experimental studies.

As far as the *Ajita agada* is concerned, the special reference from Susruta Samhita *Kalpasthana* chapter five which is *Sarpadastavisha chikitsa kalpa* by name and dedicated for treatments for snake bites, immunomodulatory action of the ingredients of *Ajita agada* is very remarkable.

Also, it's observed anti-venoms are utilized as a special treatment to manage this critical condition immediately. Anti-venoms act by inducing immunity by binding with the venom for neutralization[42]. Versions of anti-venoms are available for spider bites, snake bites, fish stings and scorpion stings[43].

Though the antivenoms are promised with lowering the mortality from snake bites and highly answerable for the critical management of such conditions, some adverse effects are also been identified. Blood-clotting problems, muscle injury, hypotension leading to shock, kidney damage, neurology problems, severe allergic conditions, swelling and serum sickness are such adverse effects[44]. Also, production of anti-venom is highly cost and lacuna of suitable animal models may be occurred[6].

Table 2: Pharmacodynamic properties of the ingredients of *Ajita agada* according to Ayurveda[11.12]

Ingredient	*Rasa*	*Guna*	*Virya*	*Vipaka*	*Dosha karma*
Vidanga	*Kaṭu* *Kashaya*	*Laghu, Rukṣha,* *Tikṣṇa, Sara*	*Ushna*	*Katu*	*Kapha-vata shamaka*
Paṭha	*Tikta*	*Laghu* *Tikṣṇa*	*Ushna*	*Katu*	*Kapha-vata shamaka*
Haritaki	*Madhura* *Amla, Kaṭu* *Tikta, Kaṣhaya*	*Ruksha* *Laghu* *Sara*	*Ushna*	*Madhura*	*Tridoshaghna* *Vatashamaka*
Vibhitaki	*Kashaya*	*Laghu* *Ruksha*	*Ushna*	*Madhura*	*Tridoshaghna* *Kaphaghna*
Amalaki	*Madhura* *Amla, Kaṭu* *Tikta, Kashaya*	*Ruksha* *Sara* *Guru*	*Sita*	*Madhura*	*Tridoshaghna* *Pittahamaka*
Shunti	*Katu*	*Laghu, Snigdha*	*Ushna*	*Madhura*	*Kapha-vata shamaka*
Marica	*Kaṭu*	*Laghu, Ruksha* *Tikshṇa*	*Ushna*	*Katu*	*Kapha-vata shamaka*
Pippali	*Kaṭu* *Madhura*	*Laghu, Snigdha*	*Anushna*	*Madhura*	*Kapha-vata shamaka*
Ajamoda	*Katu* *Tikta*	*Laghu, Ruksha* *Tikshṇa*	*Ushna*	*Kaṭu*	*Kapha-vata shamaka,* *Pittavardhaka*
Hingu	*Katu*	*Laghu* *Rukhṣa* *Tikshṇa*	*Ushna*	*Kaṭu*	*Kapha-vata shamaka*
Citraka	*Kaṭu*	*Laghu, Ruksha* *Tikshṇa*	*Ushna*	*Kaṭu*	*Kapha-vata shamaka*
Tagara	*Tikta, Katu,* *Kaṣhaya*	*Laghu* *Snigdha*	*Ushna*	*Kaṭu*	*Kapha-vata shamaka*
Madhu	*Madhura Kaṣāya*	*Laghu, Ruksha* *Yogavahi*	*Sita*	*Kaṭu*	*Kaphaghna*
Saindhava lavana	*Lavana* *Madhura*	*Laghu, Snigdha* *Tikshṇa*	*Sita*		*Tridoshaghna*
Sauvarchal lavana	*Lavana* *Kaṭu*	*Laghu, Snigdha* *Sukshma*	*Ushna*	*Katu*	*Vatahamaka*
Samudra lavana	*Lavana* *Madhura* *Tikta, Kaṭu*	*Guru, Snigdha* *Tikshna*	*Ushna*	*Madhura*	*Vatashamaka*
Vid lavana	*Lavana*	*Tiḳshna, Vyavai* *Laghu*	*Ushna*	*Madhura*	*Vatashamaka*
Romaka lavana	*Katu, Tikta* *Katu*	*Laghu, Thikshna* *Sukshma, Vyavai*	*Ushna*	*Katu*	*Kapha-vata shamaka*

Table 3: Reported modern pharmacological actions of the ingredients of *Ajita agada*

Latin name	Biological activity	References
Embelia ribes Burm.f.	Antioxidant, Anti-inflammatory, Cardioprotective, Hepatoprotective	13, 14
Cissampelos pareira L.	Antioxidant, Anti-inflammatory, Cardioprotective, Hepatoprotective	15,16
Terminalia chebula Retz.	Antioxidant, Anti-inflammatory, Cardioprotective, Hepatoprotective	17,18
Embellica officinalis Gaertn	Antioxidant, Anti-inflammatory, Cardioprotective, Hepatoprotective	19,20
Terminalia belerica Roxb.	Antioxidant, Anti-inflammatory, Cardioprotective, Hepatoprotective	21,22
Zingiber offficinale Roscoe	Antioxidant, Anti-inflammatory, Cardioprotective, Hepatoprotective	23,24
Piper nigrum L.	Antioxidant, Anti-inflammatory, Cardioprotective, Hepatoprotective	25,26
Piper longum L.	Antioxidant, Anti-inflammatory, Cardioprotective, Hepatoprotective	27,28
Ferula asafoetida L.	Antioxidant, Anti-inflammatory, Cardioprotective, Hepatoprotective	29,30
Trachyspermum ammi L.	Antioxidant, Anti-inflammatory, Cardioprotective, Hepatoprotective	31,32
Plumbago zeylanica L.	Antioxidant, Anti-inflammatory, Cardioprotective, Hepatoprotective	33,34
Valeriana walichi DC	Antioxidant, Anti-inflammatory, Cardioprotective, Hepatoprotective	35,36

Discussion

Ajita agada is a very simplified herbo-mineral preparation according to its references. Ingredients, preparatory method and indications were mentioned same in all three references whereas the storage method was only found in Susruta Samhita and Bhaisajjaratnavali.

Storing of the final *Kalka* inside a cow's horn with an excessive amount of bee's honey, has been mentioned as the preparatory method. A defined mode of administration, dosage form and an *Anupana* (Vehicle) for the preparation were not available in referred texts. But Venkatro, 2015 mentions *Ajita agada* can be administered internally in the treatments and complications of *Visha*. Also, according to an online resource, *Ajita agada* 12-24 grams to be taken with 100 to 250 ml. of milk twice a day mentioned as a general treatment for all types of *Viṣha*. *Ajita agada* is capable of administering in general *Kalkamatra* (one *Karsha*) and the *Anupana* should be decided upon the condition by the physician.

When Ayurveda pharmacodynamics are concerned, it's observed that *Kaṭu* (76.47%), *Tikta* (35.29%) and *Kaṣhaya rasa* (29.41%) are prominent *Rasa*, *Laghu* (94.11%), *Tikshṇa* (58.82%) and *Ruksha guna* (35.29%) are prominent *Guna*, *Ushṇa* (82.35%) and *Katu* (23.52%) as the prominent *Virya* and *Vipaka*. Almost all the attributes of *Visha* are observed in pharmacodynamics of the ingredients in *Ajita agada*. It is contradicted with the antagonistic properties to *Visha* observed in a typical anti-poisonous drug. Belvadi, 2019 states the availability of certain *Kashta aushada* providing *Viṣhokta lakshana* and simultaneously pacify *Visha*.

Dilipkumar, 2015 mentions being equally potent to *Visha*, possessing *Vyavai guna* to act vigorously on *Vishapiḍita* patient and having the same affinity for the system on which poison has affected are some of criteria of Acharyas elaborated to put forth a *Dravya* as a *Prativisha* (antidote). As Ayurveda pharmacodynamic properties (*Rasadi panchaka*), pharmacological properties (*Karma*), therapeutic indications (*Prayoga*) and also, the reported modern pharmacological actions being tallied above mentioned criteria, *Ajita agada* can be understood as an anti-poisonous preparation with some characteristics of *Prativisha* (antidote).

Being indicated for *Sthavara* (Inanimate) and *Jangama* (Animate) *Visha* is a special remark of *Ajita agada*. Pharmacological properties on both Ayurveda and modern perspectives are contributed in the management of general signs and symptoms of *Sthavara* (inanimate) and *Jangama* (animate) Viṣa, for which the *Ajita agada* is indicated.

Also, the availability of varieties of antivenom for different kinds of animal poisoning conditions such as fish sting, bee sting etc. tallies with one of the authenticated indications of *Ajita agada* for all kinds of inanimate poisons (*Jangama visha*).

Complications and organ damage due to chronic toxicity according to modern toxicology, are answerable from *Ajita agada* due to the reported pharmacological findings observed in its ingredients. Antioxidant, anti-inflammatory, cardio-protective, neuro-protective, hepato-protective and analgesic are some of modern pharmacological actions found on the ingredients in overcoming complications and organ damages. Remarkably these pharmacodynamic properties are capable of overcoming the adverse effects resulted by artificial anti-venom antidotes which were mentioned beforehand.

Pharmacokinetics of the *Ajita agada* can be understood on basis of its pharmacodynamics. Finely powdered ingredients provide a good absorption as the particle size is reduced. Majority of *Guna* such as *Laghu*, *Tikshṇa* and *Ruksha* aided in penetrating into subtle levels of *Srotas* (body channels) and resulting a good distribution. Also, *Yogavahi guna* in bee's honey is contributed in good distribution. The prominent *Katu vipaka* results in good drug metabolism. *Lavana varga* in the preparation help in elimination of the poison as well as the drug.

As per antidote studies in modern toxicology, the action of *Ajita agada* can be conceptually understood as blocking the site of toxin by preventing the further spread of the toxin.

Conclusion

Considering the mode of actions, being similar with *Visha* property wise, the preparation is capable of providing an antagonist effect by blocking the rapid distribution and onset of *Visha*. Also, the actions of *Ajita agada* would be an approach to the management of complications and organ damage due to chronic toxicity on the basis of reported modern pharmacological actions of its ingredients.

Further, chemical studies should be scoped with this regard to understand the mechanism of action of this anti-poisonous formulation. The strategy of developing *Ajita agada* into a cost reductive and side effects minimal pharmaceutical dosage form for management of poisonings from Ayurvedic perspective would be a new milestone.

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