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Review Article

CONCEPTUAL STUDY ON ACTION OF *VISHA GUNAS* WITH SNAKE VENOM COMPOUNDS - A COMPARISON

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ABSTRACT

Ayurveda, an *Upaveda* of *Atharvaveda* emphasis on the prevention of disease and yield positive health through proper diet, healthy lifestyle, right thinking with pleasant mind along with use of right choice of drugs, in short, a proper balance between body, mind and senses. Ayurveda deals mainly with eight branches of special units. *Agadatantra* (toxicology) is one among them and a most special wing for the diagnosis and management of different kinds of animate and inanimate poisoning. *Visha* (poison) is a substance imbalance the healthy constitution of the body and destructs the life by its different *Gunas* (properties). The qualities of *Visha* determine the lethality. In ancient Ayurvedic literature different opinion regarding the qualities of *Visha*. Each attribute has different action inside the body. The snake venom is highly toxic and contains more than 20 different compounds mainly include proteins and polypeptides. These mixtures of proteins, enzymes and other co factors determine toxicity and fatality, in correspondence with *Teekshnadi Gunas* of *Visha*. This article made an attempt to compare the *Visha Guna* action with that of snake venom compounds.

INTRODUCTION

Agadatantra is the term first coined by *Acharya Susruta*. It also renowned by the names such as *Vishagaravairodhika prasamana* (Charaka), *Damshtra chikitsa* (Vagbhata), *Jangulividya* (Kautilya) etc. The branch mainly dealt with diagnosis of poisoning and its management. *Visha* is the substance that which cause sadness to the world.[1] From Ayurvedic literatures, came to know that *Visha* mainly possesses 10 qualities *(Teekshnadi gunas).* When *Visha* enters the body vitiates *Dhatu, Tridoshas* with their seats then finally reaches *Hridaya* and turn fatal. The qualities of *Visha* are extremely opposite to *Ojas* so it causes sudden death in persons with *Vata Pitta* bodily constitution.[2] Snake venoms are poisonous substance containing complex mixtures of small molecules and peptides/ proteins, having neurotoxic, cardiotoxic cytotoxic, myotoxic and enzymatic activities.[3]

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In Ayurveda, said that *Visha* which is used properly can act as medicine and a medicine if used improperly may produce fatal results.[4] Similarly on other hand snake venom is highly a proteinaceous substance besides its poisonous nature and has therapeutic action by its anticancer activity, fibrinolytic activity, antimicrobial activity etc. The *Teekshnadi Gunas* of *Visha* determines its lethality, correspondingly the action of snake venom components decides the fatality.

Visha - Nirukthi

The term *Visha* has its origin from the *Sanskrit dhatu "Visham Vyapnutha"*- one which pervades the whole body as per *Amarakosha.*

According to *Sabdakalpadruma- "Visha viprayoge*"- to separate

The word *Visha* is derived from the root *"Vish*" by having *"Ka"* suffix which means to encompass or to get occupied. Thus, the one which pervade the whole body immediately after ingestion is called as *Visha.*

Definitions of *Visha*

1. *Jagad vishannam tam drushta tenasou vishasamnjitha*[5] *(Ashtanga Hrudaya*)- Substance which cause sadness to the world is called *Visha.*
2. *Vishaadam Jananatva cha Visham Ityabhideeyathe*[6] *(Susruta Samhitha*)- Substance which causing grief.

3. In *Caraka Samhitha*, *Visha* is defined as a substance having 10 specific properties *(Dasagunam*), 8 stages *(Vega),* origin from *Jala mahabhootha (Ambusambhavam),* and its action is like *Agnimahabhoota (Pavakopamam)* with 24 modalities of treatment *(Chaturvimsathi upakramam*).[7]

Visha Prabhavam

When *Visha* enters the body, it first vitiates *Raktha Dhatu*, then vitiates *Kapha, Pitta Vata* respectively along with their *Asayas* (seats), then finally reaches in *Hridaya.*[8]

If *Visha* not gets mixed with blood it does not cause any harm to the body, but if get mixed with blood it spreads like oil in water (*Tailam Ambuvat).*[9]

According to *Prayogasamuchaya,* if *Visha* gets mixed with blood it spreads like tamarind in milk.

The *Doshas* vitiated by the *Visha* deranges *Agni* and cause *Kapha kopa* and the *Pranavahasrotas* get blocked by *Kapha.* There by the normal passage of *Vata* gets obstructed and victim falls in to a stage of unconsciousness.[10] Thus the vitiated blood enters in to circulation by the virtue of *Vishatejas* and leads to death.

Visha Gunas* – by various *Acharyas

There are about 10 *Visha Gunas* are mentioned by Susruta, Caraka, Vrudha Vagbhata and Yogaretnakara. *Ashtanga Hridaya* describes 11 *Gunas, Sarngadhara* enumerates 8 *Gunas* and *Bhavaprakasha* quoted 7 *Gunas* for *Visha*. *Ashtangahrdaya* enumerates 11 *Gunas* viz, *Teekshna, Ushna, Rooksha, Visada, Vyavayi, Aasu, Laghu, Vikashi, Sookshma, Avyaktha Rasa, Apaki*. While *Ashtanga Samgraha* mentions these 10 *Gunas* except *Apaki*. *Charaka* quotes 10 *Gunas* same as *Samgraha* by replacing *Avyakta Rasa* to *Anirdesya Rasa*. *Susruta* enumerates 10 *Charakokta Gunas* except *Anirdesya Rasa* but included *Apaki Guna*. *Yogaretnakara* has similar opinion as of *Susrutha. Sarngadhara* told 8 *Gunas* included, *Agneya, Sookshma, Vyavayi, Vikashi, Chedi, Madavahi, Jeevithahara, Yogavahi*.

Table 1: *Visha Gunas* in Samhitas and Nighantus

Gunas	***Ashtanga Hridaya*[11]**	***Ashtanga Samgraha*[12]**	***Charaka*[13]**	***Susruta*[14]**	***Sarngadhara*[15]**
Teekshna	+	+	+	+	_
Ushna	+	+	+	+	_
Rooksha	+	+	+	+	_
Vishada	+	+	+	+	_
Vyavayi	+	+	+	+	+
Aashu	+	+	+	+	_
Laghu	+	+	+	+	_
Vikashi	+	+	+	+	+
Sookshma	+	+	+	+	+
Avyakta Rasa	+	+	_	_	_
Apaki	+	_	_	+	_
Anirdesya Rasa	_	_	+	_	_
Agneya					+
Chedi					+
Madavahi					+
Jeevithahara					+
Yogavahi					+

Table 2: *Visha Guna* Action in different Literatures

Gunas	***Susruta*[16]**	***Charaka*[17]**	***Ashtanga Samgraha*[18]**
Ruksha (Roughness)	*Vata Prakopa*	*Vata Prakopa*	*Vata Prakopa*
Ushna (Hotness)	*Pitta Rakta Prakopa*	*Pitta Kopa*	*Pitta Rakta Prakopa*
Teekshna (Sharpness)	*Mathi, Moha, Marma bandha chinnati* (Destroys vital spots)	*Marmaghna* (Fatal)	*Pitta Rakta Kopa*
Sookshma (Minuteness)	*Sareera Avayava Pravesheth vikarothi* (enters minute	*Asruk Prakopa*	*Dosha dhatu malaadi sareera avayava*

	channels of the body and destructs physiology)		*pravesheth* (enters all over the body tissues)
Aashu (Sudden action)	*Aashu ghnanthi* (Fatal)	*Aashu Vyapnothi* (Quick spread)	*Aashu Vyapadayathi* (Fatal)
Vyavayi (Fast pervading)	*Prakrithim Bhajeth* (Fastly pervasive)	*Kevalam Deham Vyapnothi* (Highly spread throughout the body)	*Dosha dhatu malaadi sareera avayava pravesheth* (enters all over the body tissues)
*Vikas*i (Destruction)	*Dosha Dhatu Malaadin Kshapayeth* (Destroys whole body)	*Pranaghnam* (Fatal)	*Marma Chedanam, Mati* and *Moha* occurs (Fatal)
Vishadha (Clear)	*Atirichyeth* (not adhere to any part of the body)	*Asaktha gati dosham* (not hindered in their path)	*Asakthavegam Prasarathi* (Spread without any obstruction)
Laghu (Lightness)	*Duschikitsyam* (not treatable)	*Durupakramam* (not curable)	*Durnirharam* (couldn't eliminate from the body)
Apaki (Indigestible)	*Durharam* (not assimilated)	-	*Jaram na yathi* (indigestible)
Avyakta Rasa/ Anirdesya Rasa	_	*Kapha Prakopa*	*Kapha Kopa*

Snake Venom

Snakes are the creatures without limb, elongated and body covered with scales. They are mainly classified as venomous and non-venomous snakes. Among 3500 known species of snakes in the world only 350 species are venomous.[19] Among non-venomous snakes, the giant constrictors like rock python of Africa, Anaconda of South America etc belonging to the family Boidae are dangerous to man.[20] Venomous snakes mainly belong to 5 families viz, Colubridae, Atractaspididae, Elapidae (Cobras, Kraits), Viperidae (Russell's viper, Saw scaled viper) and Hydrophidae (Sea snakes).[21] Majority of snakes have four rows of teeth in the upper jaw, and two rows of teeth in the lower jaw. Two of the upper rows are situated along the margins of the jaw and the two are located on the palate called as palate teeth.[22] Lower rows of teeth are situated along the margins of the lower jaw. In addition to normal teeth, the venomous snakes have modified teeth called fangs.[23] Fangs are two in number are located at each side of upper jaw. The fangs are either grooved or canalised and are connected to the venom glands (a pair of modified parotid glands) located on each side of the head, below and behind the eye.[24]

Snake venom is toxic salivary secretion coming from a pair of modified exocrine venom glands. It is a clear, amber coloured fluid. Cobra venom is faint transparent yellow and slightly viscous while Russell's viper venom is white or yellow.[25] Snake venom is the combination of complex mixtures of enzymatic proteins, non-enzymatic proteins, peptides and non-protein components like carbohydrates, metallic cations, lipids, free amino acids, nucleotides and biological amines[26]. There is no data till available about the exact number of proteins and peptides present in snake venom. It is not dangerous to man when ingested. It has acidic ph with specific gravity 1.03[27]. Venom is water and alcohol soluble. The enzymatic components cause local and systemic effects and the nonenzymatic compounds produce lethality[28].

Table 3: Snake venom constituents -an aerial view[29,30]

Constituents	Action
Proteolytic enzymes	• Have two major groups metalloproteases and serine proteases, have action on haemostatic system and causes bleeding, intravascular clotting, oedema, blistering and necrosis. • Destruction of walls of blood vessels with extravasation of blood by releasing histamines from the damaged endothelium. • Shows hypersensitive reaction • Mostly seen in Elapidae and Viperidae families

Hyaluronidases	• Present in all snake venoms • Helps in rapid spreading of venom leading to severe morbidity • Not only helps in the spreading of venom but destroys the tissues in local site. • Increase permeability of cell membrane.
Fibrin ferments	• Enhances coagulation cascade.
Phospholipase A2	• They belong to four groups A1, A2, C & D • Facilitating the hydrolysis of lipids • Changes in the permeability of cell membrane especially in nervous tissues and alters neuromuscular conduction. • Facilitates the penetration of neurotoxin in to the nervous tissue
Protease	• Dissolution of vascular wall
Acetylcholinesterase	• Seen mostly in Elapid venom. • High cholinesterase activity causing impairment of neuromuscular transmissions.
Haemolysins	• Abundantly in Viper venom. • Systemically causing pulmonary congestion with respiratory failure and systemic bleeding causing shock. • Locally causing haemorrhagic oedema.
Cytolysins	• Mostly seen in viper venom • Lysis of blood cells and tissues (cell shrinkage)
Agglutinins	• Agglutination of blood cells
Nucleases (RNase,DNase)	• Present in all snake venoms • Catalyze the hydrolysis of DNA, RNA or any nucleotide chain. • Rapid spread of venom
Ophioxidase	• Helps in autolysis (digestion of cell membranes)
Proteinases	• Cause tissue damage • Coagulant effect
Lecithinase	• Increased permeability of cell membranes and cause fragility
Neurotoxins	• Cause acute neuromuscular paralysis. • Produce presynaptic and postsynaptic neuromuscular blockade. • Pre synaptic toxins have high toxicity and cause respiratory failure. They are identified in Crotalidae, Viperidae, Elapidae and Hydrophidae families. • Post synaptic neurotoxins results death by asphyxiation.
Myotoxins	• Hydrophidae family has myotoxic effect • Acts on skeletal muscles (sarcolemma) and results in haemorrhage and necrosis.
Cardiotoxins	• Particularly seen in cobra venom. • Toxic to heart • Acts on skeletal and smooth muscle membranes also at neuromuscular junction.
L-amino acid oxidase	• Seen in Viperidae and Elapidae venom while abundantly seen in Crotalidae venom. • Cytotoxic activity due to release of hydrogenperoxide.
Biological amines	• Pain at local site • Change in permeability of cell membrane
Peptides and Polypeptides	• Lethal compounds • Cause systemic effects.

Snake venom contains different cations such as sodium, potassium, magnesium, and small amounts of nickel, cobalt, zinc, iron. Sodium is mostly seen. Zinc catalyses the activation of anti-cholinesterase. Calcium is needed for the activation of phospholipase.

Table 4: Action of Snake venom compounds versus *Visha* Action- A Glimpse

Snake venom compounds	**Comparison with *Visha guna***
Proteolytic enzymes	• Liberation of histamines- *Sookshma guna* (Enters minute portions of bodily tissues) • Extravasations of blood- *Teekshna, Ushna, Sookshma guna (Pitta rakta kopa)* • Digestion of tissue proteins and peptides- *Vikashi, Sookshma* (destroys *Dosha, Dhatu, Mala*)
Hyaluronidase	• Rapid spreading of Venom- *Aashu, Vyavayi (Deham vyapnoti), Vishada* (no obstruction in its path), *Yogavahi guna* • Increased morbidity- *Aasu, Jeevithahara, Chedi, Teekshna (Marmaghna), Vikashi (Pranaghna), Laghu (Duschikitsyam), Apaki (Durharam)*- all determines fatality
Fibrin ferments	• Coagulation -*Teekshna, Ushna, Sookshma (Pitta rakta kopa)*
Phospholipase A2	• Changes permeability of cell membranes- *Sookshma* and *Vyavayi guna (Samastha sareera avayava: Anupraveseth)* • Alters neuromuscular conduction- *Rooksha guna (Vata kopa), Madavahi, Teekshna (Mati, Moha*- alters consciousness) • Helps in penetration of neurotoxins in nervous tissue- *Yogavahi* (catalyst), *Sookshma* and *Vyavayi* (penetration of toxins), *Vishada* (no adherence in path)
Protease	• Dissolution of vascular wall- *Sookshma guna (Asrk kopa), Teekshna, Ushna guna (Pitta rakta kopa)*
Acetylcholinesterase	• Impairment of neuromuscular transmission- *Rooksha guna (Vata kopa), Madavahi, Teekshna guna* (alters consciousness)
Haemolysins	• Haemorrhagic oedema- *Teekshna, Ushna guna (Pitta rakta kopa)* • Pulmonary congestion and respiratory failure- *Vyavayi* (spread entire system), *Teekshna (Marmaghna), Vikashi (Pranaghna)*
Cytolysins	• Lysis of blood cells- *Sookshma guna (Asrk kopa)* • Cell shrinkage- *Vikashi* (destruction of *Dosha, Dhatu* and *Mala*)
Agglutins	• Agglutination - *Aagneya, Teekshna, Ushna guna*
Nucleases	• Rapid spread- *Aashu, Vyavayi (Deham vyapnoti) Vishada* (no obstruction in its path) *Guna* • Catalyze the hydrolysis of DNA, RNA- *Yogavahi* (catalyst)
Ophioxidase	• Autolysis- *Vikashi* (Vitiates and destroys *Dosha*, *Dhatu* and *Mala*)
Lecithinase	• Increased permeability of cell membranes- *Sookshma* and *Vyavayi guna (Samastha sareera avayava:anupraveseth*)
Proteinases	• Coagulant effect- *Teekshna, Ushna guna (Pitta Rakta kopa*)
Neurotoxins	• Neuromuscular paralysis- *Rooksha guna (Vata kopa)* • High toxicity cause death- *Aasu, Jeevithahara, Chedi Teekshna (Marmaghna), Vikashi (Pranaghna), Laghu (Duschikitsyam), Apaki (Durharam)*- all determines fatality.
Myotoxins	• Necrosis- *Vikashi guna* (destruction) • Haemorrhage- *Teekshna guna (Rakta kopa)*
Cardiotoxins	• Toxic to heart- *Teekshna (Marmaghna), Vikashi (Pranaghna), Aasu, Jeevithahara, Chedi* • Affect neuromuscular junction- *Rooksha guna (Vata kopa), Madavahi,*

	Teekshna (*Mati, Moha*- alters consciousness)
L-amino acid oxidase	• Damage cellular metabolism (biotransformation)- *Laghu (Duschikitsya/ Durupakrama* due to lightness), *Apaki* (*Durharam* due to Maltransformation)
Biological amines	• Pain at local site – *Rooksha (Vata kopa*) • Change in permeability of cell membranes- *Sookshma* and *Vyavayi guna (Samastha sareera avayava: Anupraveseth)*
Peptides /polypeptides	• Most lethal compounds- *Aasu, Jeevithahara, Chedi Teekshna (Marmaghna), Vikashi (Pranaghna), Laghu (Duschikitsyam), Apaki (Durharam)*- all determines fatality.

DISCUSSION

Visha is a substance that enters the body acts deleteriously and disturbs all body functions and finally results in death. The lethality of *Visha* mainly depends upon its *Guna*. The common *Gunas* described by all *Acharyas* are *Vyavayi, Vikashi, Sookshma, Ushna (Agneya*). The fatality of *Visha* is determined by the *Gunas* like *Teekshna, Vikashi, Laghu, Apaki, Aashu, Chedi*, and *Jeevithahara*. The *Teekshna guna* cause disturbances to the vital spots. Due to the extreme lightness of *Visha* by its *Laghu guna* makes it difficult to treat and *Apaki guna* causes disturbances in metabolism because of its indigestion. *Aashu, Chedi, Jeevithahara* meant about sudden death. The remaining *Gunas* manifests local and systemic effect like aggravation of *Vata* by *Rooksha; Guna*, *Pitta - Rakta Kopa* by *Ushna (Aagneya), Teekshna guna*; Destruction of tissues by *Vikashi guna*, altering consciousness or intellect by *Teekshna, Madavahi, Chedi,* and *Vikashi gunas*. *Aashu, Vyavayi* and *Sookshma gunas* facilitates the spread of *Visha* over the entire body even in the minute channels and causing *Vikaras*. *Yogavahi guna* acts as a catalyst for the penetration of *Visha* and enhances its spreading nature everywhere over the body. The Snake venom is a lethal compound with mixture of enzymatic and non- enzymatic proteins, carbohydrates, amino acids, lipids, nucleic acids, biological amines, some metallic ions and polypeptides. The fatality is caused by cardiotoxins, neurotoxins, hyaluronidase and especially peptides and polypeptides. The action of these compounds can be correlated with action of *Teekshna, Vikashi, Laghu, Apaki, Aashu, Chedi,* and *Jeevithahara gunas* of *Visha.* The enzymatic components in snake venom causes local and systemic effects like pain and neuromuscular paralysis by *Rooksha guna*; changes in the permeability of cell membranes and penetration of venom in deeper structures by *Sookshma* and *Vyavayi guna*, rapid spreading of venom by *Aashu, vyavayi* and *Yogavahi guna*; haemorrhage and coagulation by *Teekshna* and *Ushna guna*; destruction of cells by *Vikashi guna*; conduction of venom without any obstruction by *Vishada guna* etc and so on.

CONCLUSION

Venom composition has remarkable variability among different genus, species, geographical region, evolution history, diet etc. Generally, the accurate number of components in snake venom may not be able to calculate because of these diversities. According to Ayurvedic literatures, the character of a drug is evolved from the attributes present within. *Visha*, a substance indigenously possesses ten qualities and those *Gunas* perform a *Karma*/action in the body while it enters. The Ayurveda science established that the proper dosage of *Visha* can act as nectar and vice versa. The contemporary science proved that, even though the snake venom is lethal it can be used in various maladies because of its anti-cancerous property, fibrinolytic action, immunomodulatory function etc. Concisely can say that the local and systemic symptoms and the fatality caused by *Visha* determined from action of ten peculiar properties contains with it. Simultaneously the lethality of snake venom depends upon the action of different compounds present in it and which has a strong juxtaposition with *Vishakarma.*

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