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Review Article

A CRITICAL REVIEW ON *DOOSHIVISHARI AGADA*: A HERBO MINERAL FORMULATION

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ABSTRACT

Dooshivisha (cumulative toxicity) is a type of *Kritrima visha* (artificial poison). It is a transformed state of other types of poison if not eliminated, get collected in small doses leads to this type of poisoning. It is a unique concept of Ayurveda and is the cause of the majority of the health issues in the present era. *Acharyas* have said different treatment principles for the management of *Dooshivisha* (cumulative toxicity). *Dooshivishari agada* is the formulation of choice for its treatment, which is a herbo-mineral formulation comprised of twelve ingredients that are taken in equal amounts for the preparation. Many *Acharyas* such as *Sushruta, Vagbhata,* and *Bhavaprakasha* have explained it in their classical texts. Along with *Dooshivisha* (cumulative toxicity), it can also be used in its complications, and also for the treatment of all types of poisoning and other associated signs and symptoms.

INTRODUCTION

The term *Dooshivisha* (cumulative toxicity) is a combination of two words – '*Dooshi'* and *'Visha'. Dooshi* means denatured, latent, or attenuated, and *Visha* means poison. Thus *Dooshivisha* (cumulative toxicity) means denatured or latent poison. *Acharya Sushruta* and *Vagbhata* described *Dooshivisha* (cumulative toxicity) as any type of poison originating from any animate or inanimate or artificial poison retained in the body after partial elimination or which has previously undergone detoxification by the anti-poisonous drugs. It gets dried due to forest fires, and wind and stays in the body for a long duration without producing any symptoms.[1]

Any poison that is devoid of the natural ten properties of *Visha* (poison), and is incapable to produce acute symptoms of poisoning can be termed as *Dooshivisha* (cumulative toxicity). Low potency of all ten qualities is said to be responsible for delayed action. Due to the low potency of poison and *Avarana* (enveloping) action by *Kapha* (phlegm), these poisons remain in the body for a long duration without producing any fatal symptoms.[2]

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In the current era, there are so many poisonous materials get accumulated in the body of a person in their daily activities, that they will be continued for a prolonged period. Metals, metallic compounds, radiations, pesticides, chemicals, food additives, etc, have found the nature of accumulation within the living body. Over one billion humans have been exposed to elevated levels of toxic metals and metalloids in the environment.[3]

There are different treatment protocol are explained in classical texts for the management of *Dooshivisha* (cumulative toxicity). *Dooshivishari agada* is one such formulation told chiefly for the management of *Dooshivisha* (cumulative toxicity) and also for other poisonous conditions.[4]

Table 1: Ingredients of *Dooshivishari Agada* with Properties and Indication as per *Ashtanga Hrudaya* [5]

S.No	***Dravya* (Drug)**	***Rasa* (Taste)**	***Guna* (Property)**	***Veerya* (Potency)**	***Vipaka* (Metabolic property)**	***Doshagnata***
1	*Pippali[6]* (*Piper longum* Linn.)	*Katu* (pungent)	*Laghu* (light) *Snigdha* (unctuous) *Tikshna* (sharp)	*Ushna* (Hot)	*Madhura* (Sweet)	*Kapha Vatahara* (alleviates *Vata* and *Kapha*)
2	*Dhyamaka[7]* (*Cymbopogon martini(*Roxb.)	*Katu* (pungent) *Tikta* (bitter)	*Laghu*(light) *Ruksha* (dry)	*Ushna* (hot)	*Katu* (pungent)	*Kapha Vatahara* (Alleviates *Kapha* and *Vata*)
3	*Jatamansi[8]* (*Nardostachys jatamansi* (D.Don) DC.)	*Tikta* (bitter) *Kashaya* (astringent) *Madhura* (sweet)	*Laghu* (light) *Snigdha* (unctuous)	*Sheeta* (cold)	*Katu* (pungent)	*Tridoshahara* (alleviates all the *doshas*)
4	*Lodhra[9]* (*Symplocos racemosa)*	*Kashaya* (astringent) *Tikta* (bitter)	*Laghu* (light) *Ruksha* (dry)	*Sheeta* (cold)	*Katu* (pungent)	*Kapha pittahara* (Alleviates *Kapha* and *pitta*)
5	*Ela[10]* *(Elettaria cardamomum)* (L.) Maton.	*Katu* (pungent) *Madhura* (sweet)	*Laghu* (light) *Ruksha* (dry)	*Sheeta* (cold)	*Katu* (pungent)	*Kapha Vatahara* (Alleviates *Kapha* and *Vata*)
6	*Suvarchika[11]* (*Tribulus terrestris* Linn.)	*Madhura* (sweet)	*Guru* (heavy) *Snigdha* (unctuous)	*Sheeta* (cold)	*Madhura* (sweet)	*Vata pittahara* (Alleviates *Vata* and *Pitta*)
7	*Kutannata[12]* (*Oroxylum indicum* (L.) Kurz)	*Madhura* (sweet) *Tikta* (bitter) *Kashaya* (astringent)	*Laghu* (light) *Ruksha* (dry)	*Ushna* (hot)	*Katu* (pungent)	*Kapha Vatahara* (Alleviates *Kapha* and *Vata*)
8	*Tagara[13]* (*Valeriana wallichii* DC.)	*Tikta* (bitter) *Katu* (pungent) Kashaya (astringent)	*Laghu* (light) *Snigdha* (Unctuous)	*Ushna* (hot)	*Katu* (pungent)	*Kapha Vatahara* (alleviates *Kapha* and *Vata*)
9	*Kushta[14]* (*Saussurea lappa* Clarke.)	*Tikta* (bitter) *Katu* (pungent) *Madhura* (sweet)	*Laghu* (light) *Ruksha* (dry) *Tikshna* (sharp)	*Ushna* (hot)	*Katu* (pungent)	*Kapha Vatahara* (alleviates *Vata* and *Kapha*)
10	*Yashtimadhu[15]* (*Glycyrrhiza glabra* Linn.)	*Madhura* (sweet)	*Guru* (heavy) *Snigdha* (unctuous)	*Sheeta* (cold)	*Madhura* (sweet)	*Tridoshahara* (Alleviates all the *Doshas*)
11	*Chandana[16]* (*Santalum album* Linn.)	*Tikta* (bitter) *Madhura* (sweet)	*Guru* (heavy) *Ruksha* (dry)	*Sheeta* (cold)	*Katu* (pungent)	*Kapha pittahara* (alleviates *Kapha* and *Pitta*)
12	*Gairika[17]* (Red ochre)	*Madhura* (sweet) Kashaya (astringent)	*Snigdha* (Unctuous)	*Sheeta* (Cold)	*Madhura* (sweet)	*Kapha pittahara* (alleviates *Pitta* and *Kapha*)

Table 2: Ingredients of *Dooshivishari Agada* with Therapeutic Indication as per *Ashtanga Hrudaya*

Sl.No.	*Dravya* (Drugs)	*Karma* (Action)	*Rogaghnata* (Therapeutic indications)
1	*Pippali*[6] (*Piper longum* Linn.)	*Rasayana* (Rejuvenation of body) *Deepana* (Gastro stimulant) *Vrishya* (Aphrodisiac)	*Udara* (Abdominal disorders) *Pliharoga* (disease of the spleen) *Jwara* (fever) *Kushta* (skin disease) *Prameha* (diabetes) *Gulma* (tumours) *Amavata* (rheumatoid arthritis) *Shula* (pain) *Arshas* (piles)
2	*Dhyamaka*[7] (*Cymbopogon martini* (Roxb.)	*Sthanya janana* (Galactogogues)	*Jwara* (fever) *Daha* (burning sensation) *Trishna* (excessive thirst) *Chardi* (emesis) *Kasa* (cough) *Swasa* (difficulty in breathing) *Krimi* (microbial disorder) *Arshas* (piles)
3	*Jatamansi*[8] (*Nardostachys jatamansi* (D.Don) DC.)	*Medhya* (enhances memory power) *Kustagna* (skin disease alleviating property) *Balya* (strengthens the body)	*Kusta* (skin disease) *Kandu* (pruritis) *Visarpa* (erysipelas) *Daha* (burning sensation)
4	*Lodhra*[9] (*Symplocos racemosa* Roxb.)	*Grahi* *Chakshushya* (improves the eye sight)	*Raktapitta* (bleeding diseases) *Pravahika* (ulcerative colitis) *Atisara* (diarrhea) *Netraroga* (eye diseases) *Jwara* (fever) *Kusta* (leprosy)
5	*Ela*[10] *Elettaria cardamomum* (L.) Maton.	*Hridya* (cardioprotective) *Deepana* (gastrostimulant)	*Hridroga* (cardiac disease) *Swasa* (difficulty in breathing) *Kasa* (cough) *Mutrakrichra* (dysuria) *Chardi* (emesis) *Arshas* (piles)
6	*Suvarchika*[11] (*Tribulus terrestris* Linn.)	*Vrishya* (aphrodisiac) *Rasayana* (Rejuvenation of body)	*Mutrakrichra* (dysuria) *Ashmari* (renal calculus) *Prameha* (diabetes) *Hridroga* (cardiac disease) *Swasa* (difficulty in breathing) *Kasa* (cough) *Arshas* (piles)
7	*Kutannata*[12] (*Oroxylum indicum* (L.) Kurz)	*Deepana* (gastro-stumulant) *Pachana* (digestive) *Grahi*	*AmaVata* (rheumatoid arthritis) *Aruchi* (anorexia) *Atisara* (diarrhea) *Kasa* (cough) *Vataroga* (all types of neurological

			disorders)
8	*Tagara*[13] (*Valeriana wallichii* DC.)	*Vishagna* (anti-poisonous)	*Apasmara* (epilepsy) *Anidra* (insomnia) *Shiroroga* (disorder of head) *Netraroga* (eye diseases)
9	*Kushta*[14] (*Saussurea lappa* Clarke.)	*Lekhaniya* (scraping) *Vrishya* (aphrodisiac) *Vishagna* (anti-poisonous)	*Kushta* (leprosy) *Hikka* (hiccups) *Kasa* (cough) *Swasa* (difficulty in breathing) *Hridroga* (cardiac diseases) *Kandu* (itching) *Visarpa* (herpes)
10	*Yashtimadhu*[15] (*Glycyrrhiza glabra* Linn.)	*Rasayana* (Rejuvenation of body) *Vrishya* (aphrodisiac) *Chakshushya* (improves the eye sight)	*Vrana* (wound) *Shotha* (swelling) *Chardi* (emesis) *Trishna* (thirst) *Daha* (burning sensation) *Raktapitta* (bleeding diseases) *Hridroga* (cardiac diseases)
11	*Chandana*[16] (*Santalum album* Linn.)	*Vrishya* (aphrodisiac) *Chakshushya* (improves the eye sight) *Vishagna* (anti-poisonous)	*Raktapitta* (bleeding diseases) *Bhrama* (giddiness) *Daha* (burning sensation) *Jwara* (fever)
12	*Gairika*[17] (Red ochre)	*Dahagna* (reduces burning sensation) *Rakta stambaka* (stops bleeding) *Vishagna* (anti-poisonous)	*Raktapitta* (bleeding diseases) *Sheetapitta* (urticaria)

Dooshivishari Agada* Ingredients as per other *Acharyas

Sl. No.	***Sushruta Samhita*** [18]	***Bhavaprakasha*** [19]
1	*Pippali (Piper longum* Linn.)	*Pippali (Piper longum* Linn.)
2	*Dhyamaka (Cymbopogon martini* Roxb.)	*Dhyamaka (Cymbopogon martini* Roxb.)
3	*Jatamamsi (Nardostachys jatamansi* (D.Don) DC.)	*Jatamamsi (Nardostachys jatamansi* (D.Don) DC.)
4	*Shaavara (Lodhra) (Symplocos racemosa* Roxb.)	*Lodhra (Symplocos racemosa* Roxb.)
5	*Paripelava (Vanyaka)(Cyperus esculentus)*	*Bruhat Ela (Amomum subulatum)*
6	*Suvarchika (Tribulus terrestris* Linn.)	*Suvarchika (Tribulus terrestris* Linn.)
7	*Ela (Elettaria cardamomum* (L.) Maton.)	*Maricha (Piper nigrum)*
8	*Toya (Vaalaka) (Pavonia odorata* Willd.)	*Baalaka (Pavonia odorata* Willd.)
9	*Kanaka gairika* (Red ochre)	*Sukshama Ela (Elettaria cardamomum* (L.) Maton)
10	-	*Kanaka gairika* (Red ochre)

Method of Preparation

As per *Acharya Bhavaprakasha*, it is administered in the form of *Kashaya*[19]. As a specific preparation method is not mentioned, a general preparation method can be adopted.

All the above said 11 herbal ingredients are made into coarse powder by pounding in *Khalva yantra* separately. *Gairika* is made into powder form by pounding in *Khalva yantra* (pestle and mortar), it is done *Shodhana* (purification) by frying with cow's ghee in an iron vessel, till it turns to a slightly brown colour.[17] The powders are mixed to get a homogeneous mixture. 1 part of this powder is added with 8 parts of water in a vessel and heated over

Mandagni (mild fire) till the water is reduced to 1/4th. [20]

Anupana **–** *Madhu* (Honey)[19, 21]

Indications [5, 21] - *Dooshivisha* (Cumulative toxicity)

Pharmacological actions

1. Apoptosis activity [22]

Cells were incubated with different concentrations of methanolic extract of *Dooshivishari agada*, and cell morphologic changes and apoptosis were determined by the normal inverted microscope, Annexin V, and propidium iodide (PI), followed by Flow cytometric analysis, respectively. Sample *Dooshivishari agada* at 80µg/ml and 160µg/ml treatment have induced early and late apoptosis in JURKAT with 13.65%, 25.59%, and 2.36%, 10.24% apoptotic cells respectively, 1.88% and 4.08% necrotic cells were found when compared to control cells with 3.64%. This preclinical study demonstrated a JURKAT cell line to be highly sensitive to DVA methanolic extract-induced apoptotic cell death.

2. Cell cycle arrest [23]

Cells were incubated with different concentrations of methanolic extract of DVA, and the percentage of cells in various stages of the cell cycle in compounds treated and untreated populations was determined using FACS. The treatment of cells at the concentrations of 80µg/ml and 160µg/mL of sample DVA has shown G2M arrest from 5.58% (control) to 1.47% and 12.31%, respectively. S-phase arrest was found to be 13.54% and 15.51% at the same concentrations. This laboratory study demonstrated the cytotoxic effect of the sample methanolic extract of DVA through cell cycle arrest.

3. Antimicrobial, antifungal, and antioxidant activity [24]

Dooshivishari Agada showed an average zone of inhibition ranging from 17 to 33mm suggesting its activeness against the tested microorganisms and confirmed its antimicrobial activity. Antioxidant activity was calculated in terms of ascorbic acid which was observed as 10.91. DVA undoubtedly exhibits its antimicrobial, antifungal, and antioxidant potentials.

4. Butyrylcholinesterase activity in Alzheimer's disease [25]

Test samples *Dooshivishari Agada* (methanol) and (aqueous) extracts were tested for Butyrylcholinesterase inhibitory activity using colorimetric method in 96 well plates. The methanol extract has showed better activity with an IC50 value of 96.09µg/ml followed by the sample aqueous extract with IC50 value of 124.4µg/ml. Tacrine used as the standard Bche inhibitor showed an IC50 of 3.19µg/ml.

5. Anti-allergic action [26]

In modern mast cells are the major effector cells in the pathology of allergy. Concept of allergy is much more similar to that of *Dooshivisha*. Ingredients of DVA are proved to have anti-inflammatory, immunomodulator activity. Hence DVA may prove beneficial in allergic conditions.

6. GSK3 inhibition activity [27]

The effect of DVA on GSK-3 gene expression was studied in SHSY5Y by semi-quantitative PCR was analysed. The internal control beta actin was used to normalize the gene expression. The study revealed that GSK3 expression was upregulated as the treatment concentrations increased. Expression levels of GSK3 at 80µg/ml showed 1.16 and 160µg/ml showed 1.29 fold expression when compared to control.

DISCUSSION

Dooshivisha (cumulative toxicity) is an attenuated or denatured poison that functions as a latent toxin in the body. It is having mild potency, is not fatal for an individual, and has delayed action as it is covered by *Kapha dosha* (phlegm). It resides in the body for many years and produces different untoward effects. In classical treatises of Ayurveda while describing six tastes (*Rasa)* it is indicated that none of them should be used in excess. Similarly, excessive long-term usage may lead to many diseases.

Acharya Sushruta, *Vagbhata,* and *Bhavaprakasha* have been given the same name as *Dooshivishari agada* in the management of *Dooshivisha* (cumulative toxicity). As per *Sushruta*, *Vagbhata,* and *Bhavaprakasha,* it contains 9, 12, and 10 drugs respectively. *Acharya Sushruta* has not mentioned *Kutannata*, *Nata*, *Kushta*, *Yashtimadhu*, *Chandana*; and added *Paripelava* and *Toya*. *Acharya Bhavaprakasha* has not mentioned *Kutannata*, *Nata*, *Kushta*, *Yashtimadhu*, *Chandana*; and added *Maricha*, *Baalaka,* and *Bruhat ela*. The dosage form is not mentioned by *Sushruta* and *Vagbhata*, but *Bhavaprakasha* has said to use this formulation in *Kashaya* (decoction) form.

Based on *Rasa* (Figure 1)– about 32% of the ingredients have *Madhura rasa* (sweet taste), 28% of the ingredients have *Tikta rasa* (bitter taste), and 20% of the ingredients have *Katu* (pungent) and *Kashaya rasa* (astringent taste). *Katu*, *Tikta*, *Kashaya rasa* (pungent, bitter, astringent taste) pacifies *Kapha dosha* (phlegm). *Kashaya*, *Tikta*, and *Madhura rasa* (pungent, bitter, sweet taste) pacifies *Pitta dosha* and *Madhura rasa* (sweet taste) pacifies *Vata dosha*. [28]

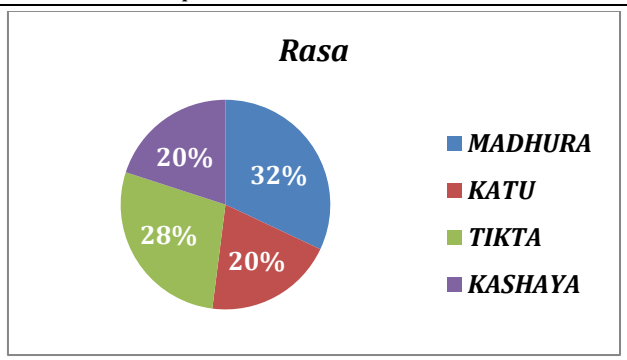

Figure 1

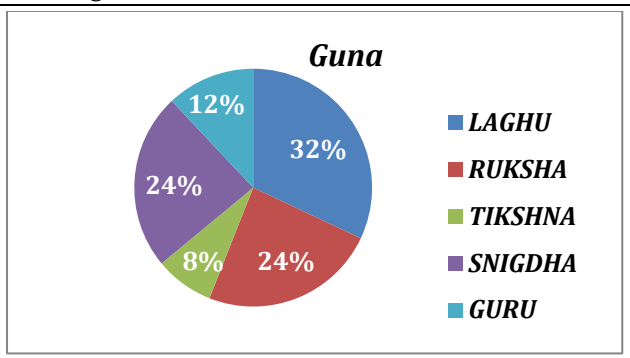

Figure 2

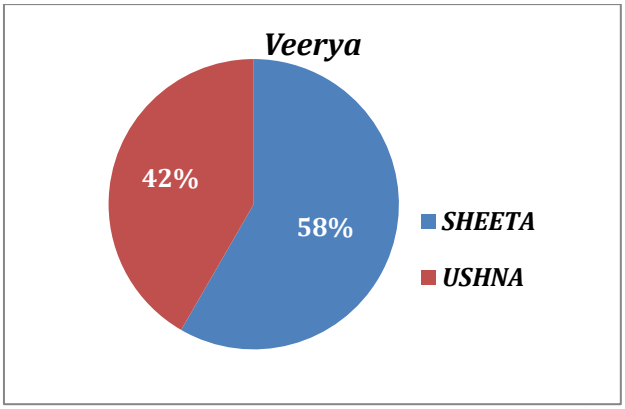

Figure 3

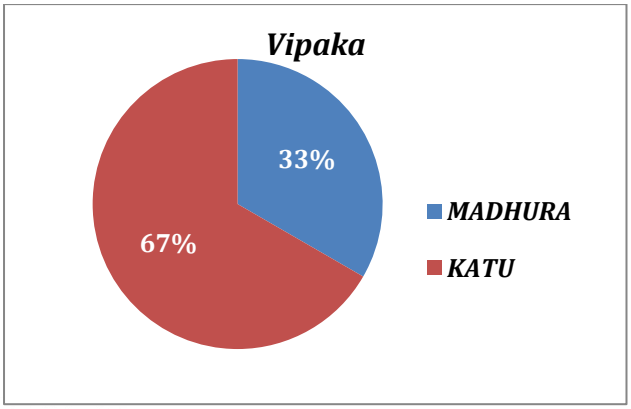

Figure 4

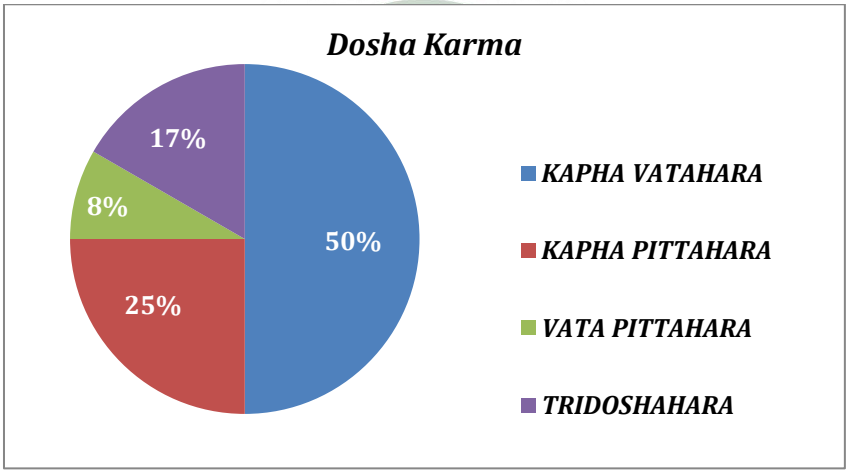

Figure 5

Based on *Guna* (property) (Figure 2) – 32% of the ingredients have *Laghu guna* (light property), 24% of the ingredients have *Ruksha* (rough) and *Snigdha guna* (unctuous property), 12% of the ingredients have *Guru guna* (heavy property), and 8% of the ingredients have *Tikshna guna* (sharp property). *Ruksha* (rough), *Laghu* (light), and *Tikshna guna* (sharp property) help for fast spreading and penetration of the medicines thus providing faster action. *Snigdha* (unctuous) and *Guru guna* (heavy property) provides strength as *Rogi bala* (patient strength) will be reduced in *Visha* (poison).

Based on *Veerya* (potency) (Figure 3) – 58% of the ingredients have *Sheeta veerya*, and 42% of the ingredients have *Ushna veerya* (hot potency). *Sheeta veerya* (cold potency) drugs have *Pittahara* as well as *Rakta prasadaka* (blood soothers) and *Stambhaka karma* (restraining action). *Ushna veerya* (hot potency) helps to balance *Kapha* and *Vata dosha* removes the *Avarana* (enveloping) present in *Dooshivisha* (cumulative toxicity) and helps for digestion of drugs.

Based on *Vipaka* (metabolic property) (Figure 4)–67% of the ingredients have *Katu* (pungent) *Vipaka*, and 33% of the ingredients have *Madhura* (sweet) *Vipaka*. *Katu* (pungent) *Vipaka* subside the increased *Kapha dosha* which is predominantly affected in *Dooshivisha* (cumulative toxicity), whereas *Madhura* (sweet) *Vipaka* balances the *Pitta* and *Vata dosha*, hence equilibrium is maintained.

Based on *Dosha karma* (Figure 5) – 50% of the ingredients have *Kapha Vatahara* property, 25% of the ingredients have *Kapha pittahara* property, and 17% of the ingredients have *Tridoshahara* property.

Most of the ingredients have *Vishaghna* (anti-poisonous), *Kushtaghna* (skin disease alleviating), *Deepana* (gastro stimulant), *Rasayana* (rejuvenating), *Vrishya karma* (aphrodisiac property). As the formulation contains *Pippali*, *Ela*, *Kutannata*, *Suvarchika*, *Kushta* has *Deepana* (gastro stimulant) and *Pachana karma* (digesting property), which corrects and maintains *Agni* (digestive fire) at the cellular level. *Dhyamaka*, *Jatamansi Lodra*, *Chandana*, *Ela*, *Tagara*, *Kushta*, and *Gairika* has *Kushtaghna* (skin disease alleviating), *Vishaghna* (anti-poisonous), *Balya* (strengthening), *Shothahara* (reduces swelling), *Rakta shodhana* (blood purification) properties and exhibit their antitoxic action and cure *Dooshivisha janya vikaras* (disease due to cumulative toxicity).

CONCLUSION

Dooshivisha (cumulative toxicity) is a condition that doesn't cause immediate death but stays in the body for a long duration without producing any symptoms. In the present modernized world disease due to cumulative toxicity are increasing due to constant exposure to radiation, chemicals, preservatives, etc. Escaping from these causative factors is not possible in this era. Proper diagnosis of disease helps for better management. In this mainly *Kapha avarana* (*Kapha* enveloping) is seen, hence *Kaphahara* treatment should be adopted as well as remove the *Avarana* (enveloping). *Dooshivishari Agada* is the medicine of choice for the management of *Dooshivisha* (cumulative toxicity) by different *Acharyas*. It is a herbo mineral formulation where the majority of the ingredients mainly have *Kaphahara* and *Vishaghna* (anti-poisonous) properties. Hence it can be used in all *Dooshivisha* (cumulative toxicity) and *Visha* (poison) conditions. Presently this medicine is commonly used by Ayurveda toxicologists in *Dooshivisha* (cumulative toxicity), *Ardita* (facial paralysis), *Vamana* (vomiting), *Dushta asra* (blood disorders), *Trishna* (thirst), *Arochaka* (tastelessness), *Moorcha* (fainting), *Udara rogas* (abdominal disorders), *Sthavara Visha* (plant poison), *Jangama visha* (animate poison), All other *Jwaradi vyadhi* (fever etc. diseases) and its complications.

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