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UNIQUE RESEARCH MODULE FOR STUDIES ON SHOTHA

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ABSTRACT

Background: From time immemorial, man has depended on animals for his survival, either as food or for competition & companionship. As he knew more about his surroundings, he extended this dependence to acquisition of knowledge, dating back to period of Ayurvedic stalwarts, who used animals to demonstrate various tests for poisoning etc. we are five thousand years away from the time when Ayurveda was practiced uniquely. The principles of this science then & now are the same but these are to be reviewed in the context of modern life style & ever progressive scientific research. The commencement of any Ayurvedic research primarily requires a complete understanding of all basic principles laid down by the ancient Ayurvedic experts. *Ayurveda* is based on *tridosha* & *pancha-mahabhuta siddhanta* which are the base for diagnosis and treatment aspects. Like-wise *tri-sutra* i.e. *hetu* (aetiology), *linga* (signs) *& aushadha* (treatments) were given equal importance in the clinical purview. *Ayurvedic* system of approach to diseased is entirely different from other system of medicine, for both diagnosis & treatment; *hetu* or aetiology is considered first & given foremost importance in almost all diseases, then for other factors. **Aims & Objectives**: 1) To assess the effect of parthenium in inducing shotha by cell mediated immunity. 2) To evaluate the efficacy of selected *Kushtaghna Dashemani* against Parthenium induced dermatitis in experimental models. **Materials & Methods:** Review of classical literature bearing the explanations of shotha & for experimental Source wistar strain albino rats taken from Animal house of S.D.M College of Ayurveda, Udupi. **Conclusion:** Parthenium hysterophorus is allergogenic and produced CMI- mediated pedal oedema *(shotha)* & selected *dravyas* of *kushtaghna dashemani* proved to be an effective against cell mediated immunity (CMI).

Keywords: *Shotha*, Parthenium, *Hetu*, *Kushtaghna* etc.

INTRODUCTION

In present era, more emphasis is given to healthy state of an individual as well as skin care, since it has enormous cosmetic value & performs many important physiological functions in human, but it is always exposed to many elements of environment. The outward appearance of skin is dependant not only on environment, but also on complex metabolic activities undergoing within the skin & in other parts of the body. In *Ayurveda Shotha* & *Kushta* were explained pertaining to skin in understanding the various pathologies. *Shotha* is classified into two types i.e. *nija* (endogenous) & *aganthuja* (exogenous). *Nija shotha* manifested by aggravation of *doshas*, whereas *aganthuja shotha* is from external factors, which involves person coming in contact with harmful leaves, creepers etc. For example,

drugs like *kapikacchu* (Mucuna Pruriens) are been named to exemplify this phenomenon, *kapi*; stands for monkey & *kacchu;* stands for itch. This in modern parlance considered to be contact dermatitis. In the universe many herbs, shrubs tends to produce varied skin manifestation, one among them is ***Parthenium hysterophorus***.

During the 18th & 19th century a large number of cutaneous reactions due to contact with plants were documented. Parthenium is a weed originally a resident of Mexico, introduced to India through wheat shipments from USA in midst of 1950's & since then has spread far and wide throughout the India except some mountainous and desert regions.

In the context of contact dermatitis, Parthenium weed tends to produce various patterns of hypersensitive reactions like allergic, irritant & phototoxic dermatitis.

Acharya Charaka in *chikitsa sthana* i.e. in *shvayathu chikitsa*, given hint to treat the *aganthuja shotha* by employing *visarpa*[9] and *kushta*[10] line of management

Keeping all these as background, a study has been planned to make a model for shotha using the weed Parthenium hysterophorus and as a remedy kushtaghna dashemani drugs selected.

Objective:

1) To assess the effect of parthenium in inducing shotha by cell mediated immunity.
2) To evaluate the efficacy of selected *Kushtaghna Dashemani* against Parthenium induced dermatitis in experimental models.

SHOTHA:

Shotha (swelling) is a disease caused due to the Derangement of *Doshas*, which may appear in any part of the body involving *Twak* and *Mamsa*. It is characterized by swelling, pain, Redness and raised local temperature.

'*Shotha*' is found as a main symptom in much number of ailments like *Visarpa*, *Pidaka*, *Arbuda* etc[1]. But that which is going to spread vastly, which is nodulated, equal or unequal (*Sama* or *Vishama*) and particularly located *dosha-samuha* in the *Twak* (skin) and *Mamsadi dhatus* (tissue elements) is *Shotha*.

Shotha, *Shwayathu*, *Shopha* and *Utsedha* were termed to be synonymous to word *Shotha* which means marked swelling of the skin in any place of the body.

BHEDA (TYPES):

- According to **Charaka**:

Even though all the three *doshas* involved in the manifestation of all the types of the *Shotha*, it is on the basis of the predominance of the respective *doshas* that *vataja, pittaja* and *kaphaja* varieties of disease are determined and therapies are prescribed accordingly.

All the varieties of the *Shotha* are considered to be *tridoshaja* i.e. they are caused by the vitiation of all the three *doshas* even so the causes of inflammation differs from one to another according as the particular *dosha* which is predominantly vitiated. The physician should therefore determine the line of treatment according to the predominance of one *dosha* or the other.

1) On the basis of *Dosha*

a) *Vataja b) Pittaja c) Kaphaja*

2) On the basis of *Karana*

a) *Nija* b) *Agantuja*[2]

3) On the basis of *Sthana*

a) *Ekangaja* b) *Sarvangaja*[3]

- According to **Susrutha:**

Shotha develops from the six factors *Vataja, Pittaja, kaphaja, Raktaja, Sannipataja* and *Agantuja*.

Depending upon signs, symptoms and treatment earlier six types has been explained but *sarvasara* that is the *shotha* which spread all over the body are of 5 types that is *Vataja, Pittaja, kaphaja, Sannipataja* and *Vishaja*[4].

- **According to Vagbhata & Madhavakara:**

Based on different causes and symptoms it is of nine types from each *dosha* separately, from the combination of two *doshas* and from the combination of all them, from trauma/injury and from the poison.

Mainly, it is of two types;

a) *Nija, Agantuja*

b) Sarvanga, Ekanga

It is known to be of three types

a) *Prthu* (hard)

b) *Unnata* (raised/elevated)

c) *Grathita* (glandular) [5].

***PURVA RUPA* (PREMONITORY SYMPTOMS):** Feeling of increased temperature, burning sensation in eyes etc. and dilatation of the vessels of the locality are the premonitory symptoms[6].

AGANTUJA SHOTHA:

***Nidana* (aetiology):** *Agantuja Shotha* is one which is caused by the external factors like contact of harmful leaves, creepers and shrubs[7].

Difference between *Nija* & *Agantuja shotha*[8]: The *Aganutuja shothas* are diagnosed by the characteristic aetiology, signs and symptoms even though ultimately the *Agantuja shotha* may share the characteristic signs and symptoms of *Nija shotha*. The difference lies in the priority or post priority of certain features common to both type of *shotha*. The *Nija shotha* starts with the vitiation of *doshas* and then brings about pain. The *Agantuja shotha* on the other hand starts with pain and then brings about the vitiation of dosha.

PLANT DERMATITIS: With the expansion of travel and exploration in the 15th & 16th centuries, reports of reactions due to contact with exotic plants started appearing. During the 18th & 19th centuries a large number of cutaneous reaction to contact with plants were documented & Kapikaccu (Mucuna prureins) is one among them. Kapikacchu is an herbaceous twinning & the hair lining of the seed pods and small spicules on the leaves contain 5- hydroxytryptamine (serotonin) which causes severe itching (pruritus) when touched. The calyx below the flowers is also a source of itchy spicules and the stinging hairs on the outside of the seed pods are used in itching powder. Once this itching starts, one tends to scratch vigorously & uncontrollably for this reason, one should avoid scratching the exposed area since this causes the hands to transfer the chemical to all other areas touched.

Most plants are harmless but a few of them cause allergic, irritant & phototoxic dermatitis. The incidence of plant dermatitis varies from country to country & depends on local flora. Poison-ivy & poison oak dermatitis is very common in North America; on the other hand, Parthenium dermatitis has assumed epidemic proportions all over India. The clinical picture is diverse & reflects mainly the difference between allergic, irritants & photo contact reactions. The mode and amount of exposure, the site of contact, the patient's age, sex & the climate are modifying factors. Typically features involves the exposed skin i.e. hands, forearms, face & neck. Fissuring &

hyperkeratosis of fingertips is common in plant dermatitis due to direct contact.

Weed Dermatitis: Variants of weed dermatitis occur in several regions of the world and have been described by various trivial names although all refers to essentially the same skin condition, thus 'Ragweed dermatitis', 'Australian bush dermatitis' & 'Parthenium dermatitis' all are variants of weed dermatitis.

PARTHENIUM DERMATITIS: In India, ***Parthenium hysterophorus*** is the most notorious compositae weed known to produce contact hypersensitivity. This plant is variously known as congress grass, carrot weed, fever few, bastard fever few & white top.

Originally a resident of Mexico, this plant was introduced into India along with wheat shipments from USA in the 1950's & since then has spread far & wide, covering almost the whole of India except for mountainous and desert areas.

The weed grows wildly on waste lands & along canals, railway tracks & roads. Though it grows more profusely during the rainy season, the growth is almost perennial.

The first report of contact hypersensitivity to ***Parthenium hysterphorous*** in India was recorded from Pune in 1966. Since then there have been many such reports from different parts of India.

Parthenim hysterophorous has been found to contain parthenin as well as hymenin, ambrosin & coron-opilin. The various dermatitis patterns described are airborne contact dermatitis, atopic dermatitis, photo dermatitis, seborrhoeic dermatitis and even exfoliative dermatitis. Eye lid involvement is quite common & some cases in the early phase of the disease present only with eyelid dermatitis. In the initial stage, there is worsening of lesions during the summer & monsoon with partial remission during the winters, but later on the disease persists throughout the year with bouts of exacerbations[9].

DRUG REVIEW

Kushtaghna dashemani:

Drugs included under the *kushtaghna dashemani* are *Khadira, Abhaya, Amalaka, Haridra, Arushkara, Saptaparna, Aragvadha, Karavira, Vidanga* and *Jatipravala*[10].

In the present study 4 drugs were selected from above group, those are *Aragvadha, Haridra, Khadira, Vidanga.*

MATERIALS AND METHODS:

PHASE I

AOT STUDY I

Table: 01 showing the details of AOT Study experimentation

1	**Animal species**	**Rats**
2	**Strain**	Wistar albino
3	**Source**	Animal house attached to SDM Research center, SDM Ayurveda College Udyavara.
4	**Selection**	A total of 8 healthy either sex of body weight 160-260g Rats were selected according to AOT software.
5	**Acclimatization period**	All the selected animals were kept Acclimatization for 7 days before dosing.
6	**Numbering and**	The animal was marked with saturated Picric acid solution

	identification	in water for proper Identification. The marking within the cages is as follows.

The group number, animal number and sex of the animal were identified with the help of cage cards, as presented in the following table.

Table: 2 showing the identification of animals, its desired dose (AOT), body weight & calculated dose.

Sl. no	Identification of animals	Desired dose (according to AOT)	Body weight (grams)	Calculated dose (ml)
1	Head	175mg/kg	275	0.8
2	Neck	550mg/kg	246	1.12
3	Back	175mg/kg	250	0.72
4	Base of the tail	550mg/kg	192	0.88
5	Tip of the tail	175mg/kg	240	0.7
6	Fore limb	550mg/kg	226	1.2
7	Hind limb	2000mg/kg	230	2.3
8	No mark	550mg/kg	225	1.03

Husbandry condition:

1) **Housing:** Rats were housed in each cage of poly propylene with Stainless steel top grill The dry paddy husk was used as bedding material and was changed every morning
2) **Environment:** The animals were exposed to 12 hours light and 12 hours **Dark** cycle with the relative humidity of 50 to 70 % and the ambient temperature was 22 ± 03^0C degrees.
3) **Diet:** Sai Durga feed Bangalore rat pellet, was provided throughout the study period except on previous night of dosing i.e. (over-night) fasting before dosing. The drinking water was given *ad-libitum* in polypropylene bottles with stainless steel sipper tube.

Preparation of Test formulation for administration:

1. Test drug: Parthenium whole plant aqueous extract

2. Vehicle: Gum acacia

3. Dose preparation: The test drug was made in to fine suspension in vehicle ith suitable concentration all the animals were dosed Constant dose volume (1 ml/ 100g body weight) 175mg/kg, 550mg/kg, 2000mg/kg

4. Schedule: Single dose per animal

a) Administration: The test formulation was administered through intra-Peritoneal at different dose levels to respective animal through sterile disposable syringe
b) Dose fixation: According to the AOT Software.
c) Route: Intra-peritoneal
d) Dose: 175mg/kg, 550mg/kg, 2000mg/kg test substance
e) Dose volume**:** 1ml/100g animal

Observation

Examination of Physical and Behavioral changes: The animal was observed continuously for 4 hours after the dosing. The careful cage side observation was done without disturbing the animal attention and at the end of the every hour the animal was individually exposed to open arena for recording the behavioral changes like in-

creased or decreased motor activity , convulsions, straub's reaction, muscle spasm, catatonia, spasticity, ophisthotonus , hyperesthesia , muscle relaxation, anesthesia, arching and rolling, lacrimation, salivation , diarrhea, writhing , mode of respiration, changes in skin color etc. exitus, CNS depression – hypo activity, passivity, relaxation, ataxia, narcosis, etc.

Mortality: All the animals were observed at ½, 1, 2, 3, 4, 24 h, 48 h after dosing and there after daily once for mortality during the entire period of the study (i.e.14 days).

RESULTS:

Experimental evaluation of Parthenium aqueous extract for acute toxicity

1. As per the guidelines 175 mg/kg of Parthenium aqueous extract was administered for the rat weighing about 275g i.e. 0.8 ml of solution. **Observation:** The animal looked active in each hour.
2. As there was no mortality in previous dosed rat, for the next rat 550 mg/kg of Parthenium aqueous extract was given as per the protocol and verified with AOT software. The weight of that rat was 246g i.e., 1.12 ml of solution was administered.

   Observation: Jerk movements were present at 30 minutes & rat died after 30 minutes of drug administration.
3. As there was mortality in previous dosed rat, once again rat was dosed with 175mg/kg of Parthenium aqueous extract was administered for the rat weighed about 250g. i.e., 0.72ml of solution.

   Observation: Straub's reaction present at 1 to 4 hours, irritability present at 1 to 48hours, rearing present at 1 to 48hours and jerk movements were present at 1 to 4 hours of drug administration.
4. As there was no mortality in previous dosed rat, for the next rat 550 mg/kg of Parthenium aqueous extract was given as per the protocol and verified with AOT software. The weight of that rat was 192g i.e., 0.88 ml of solution was administered.

   Observation: Rearing and jerk movements were present in 1 hour of drug administration. Rat died after 60 minutes after drug administration.
5. As there was mortality in previous dosed rat, once again rat was dosed with 175mg/kg of Parthenium aqueous extract was administered for the rat weighed about 240g. i.e., 0.7 ml of solution.

   Observation: Straub's reaction present at 3^{rd} to 4^{th} hour, Irritability, rearing and jerk movements were present in 1-4 hour of drug administration.
6. As there was no mortality in previous dosed rat, for the next rat 550 mg/kg of Parthenium aqueous extract was given as per the protocol and verified with AOT software. The weight of that rat was 226g i.e., 1.2 ml of solution was administered.

   Observation: The animal looked normal with little sign of toxicity. The increased motor activity and auditory response were observed after 1-48 hour of drug administration. Rearing present in 1-4 hours & Straub's reaction was present 1-48 hour of drug administration.
7. As there was no mortality in previous dosed rat, once again rat was dosed with 2000mg/kg - the rat weighed

about 230g. i.e., 2.23ml of solution was administered.

Observation: Rat was active**,** Straub's reaction & convulsion was observed in 30 minutes. Rat died after 30 minute of drug administration.

8. As there was mortality in previous dosed rat, once again rat was dosed with 550 mg/kg of Parthenium aqueous extract was given as per the protocol and verified with AOT software. The weight of that rat was 225g i.e., 1.03 ml of solution was administered.

Observation: Bleeding seen in lacrimal sac & hyperpigmentation in injected site was noticed, Rat was active in 1 – 48 hours, increased motor activity seen 1- 48 hours, Straub's reaction present in 2-24 hours, increased auditory response seen in 3^{rd} - 48^{th} hour, rearing seen in 1-4 hours & rat died after 4 hours of drug administration. The data was fed into the AOT software to obtain the LD 50 value with confidence limits.

The LD 50 value was found to be 550mg/kg with a confidence limit of 196.4 to 884mg/kg. The AOT software generated data sheet can be seen further.

PHASE II

A) i) Drug Used:

a) Whole Parthenium plant aqueous extract.
b) *Kushtaghna Dashemani* drugs like *Aragvadha, Khadira, Vidanga* & *Haridra* aqueous extract.

ii) Chemicals Used:

a) Potash Alum
b) Normal Saline
c) Cyclophosphamide
d) 10% Sodium Carbonate
e) 30% SRBC solution (Sheep blood would be collected from city slaughter house in a sterilized bottle.)

iii) Equipment's & glass ware to be used: Glass tubes, Glass beakers, P^H Meter, Syringes etc.

Dose for Rats:

1) **Parthenium whole plant aqueous extract:** From AOT study LD50 = 550mg/kg, then $1/5^{th}$ of LD50 is 110mg/kg
$1/10^{th}$ of LD50 is 55mg/kg.
2) ***Kushtagna Dashemani* drugs aqueous extract:** Drugs like *Aragvadha, Khadira, Vidanga* & *Haridra* made into aqueous extract form. By AOT study dose has been calculated like-As LD50 is more than 2000 mg/kg, so $1/10^{th}$ of LD50 is 200mg/kg 200mg/kg (TED) & 400mg/kg (TEDx2)

Route of Drug Administration:

The test drug Parthenium was administered according to the body weight of the animals by intra-peritoneal route & SRBC by subcutaneous route with the help of a sterile injection syringe & *Kushtaghna Dashemani* drugs was administered according to the body weight of the animals by oral route with the help of an oral feeding tube attached to injection syringe.

B) Animals :

Wistar strain albino rats of either sex weighing between 140-280g were used for experimental study with the following conditions.

Rats were used for experimental study with the following conditions.

- The animals were obtained from animal house attached to the Pharmacology Laboratory S.D.M Centre for Research in Ayurveda and Allied Sci-

ences. ETHICS NO: SDM-CAU/IAEC/13-14-08.

- They were exposed to natural day and night cycles with ideal laboratory condition in terms of ambient temperature, humidity.
- They were fed with pellets from "Sai Durga Feeds", Bengaluru and water *ad libitum.*

Inclusion Criteria

1. Animals selected are adult albino rats having weight from 140-280g.
2. Healthy Wistar strain rats of either sex.

Exclusion Criteria

1. Wistar strain rats weighing less than 140g and above
2. Pregnant and diseased rats.
3. Rats used for and under trial of other experiments.

STOCK SOLUTION PREPARATION:

a) The aqueous extract of Parthenium should be stored in a container and kept in desiccator for future usage. Dose of Parthenium which is set by AOT study is referred as a standard marker and to assess the cell mediated immunity required dose should be taken i.e. $1/10^{th}$ of LD50 dose and mixed with 10ml of distilled water.

b) Two grams of individual drug extract weighed individually and mixed well using mortar & pestle and after thorough mixing, drugs were stored in a container and kept in desiccator. Later for dosage purpose daily 200mg of *Kushtaghna Dashemani* drugs taken and 10ml of Distilled water with 50 mg of Gum acacia used for test 1 group & 400mg of *Kushtaghna Dashemani* drugs taken and 10ml of Distilled water with 50 mg of Gum acacia used for test 2 group.

Drug administration:

Test drugs were administered for 7 days to assess cell mediated immunity in the morning session between 9-10 AM orally & on experiment day injection was carried out on plantar aponeurosis of animals in the morning session between 9-10 AM.

C) Grouping:

ASSESMENT OF CELL MEDIATED IMMUNITY:

The rats were grouped into different groups randomly irrespective of sexes and each group comprised of six animals.

Group 1: Water control + Parthenium.

Group 2: Cyclophophamide control

Group 3: *Kushtaghna Dashemani* solution (TED)

Group 4: *Kushtaghna Dashemani* solution (TEDx2)

The rats were sensitized subcutaneously (1ml/100g body weight) on first day & seventh day of drug administration with the following solution:

i. Parthenium Solution – 1ml
ii. Normal Saline – 4ml
iii. Potash Alum-1ml
iv. P^H of the above reagent (i.e. potash alum adjuvant) was maintained between 5.6-6.8 using 10% sodium carbonate

On Seventh day initial paw volume of left hind paw were noted and 0.1 ml of (Parthenium Solution – 1ml, Normal Saline – 4ml, Potash Alum-1ml) were injected into plantar aponeurosis of left hind paw, volume of immunological edema thus produced was measured by volume displacement method. After 24 hours & 48 hours with plethysmograph Percentage increase in paw volume, which is the induced edema formation over initial value, was calculated. The values from control

group were compared with the values from the test drug administered groups to assess the cell mediated immunity response of the drug.

OBSERVATION AND RESULTS:

CELL MEDIATED IMMUNITY:

Table: 3 showing the effect of *Kushtaghna Dashemani* on cell-mediated immunity in 24 & 48 hours.

Group	Initial MEAN ± SEM	24 hr MEAN ± SEM	48 hr MEAN ± SEM
Parthenium control	0.72 ± 0.03	1.10 ± 0.04**	1 ± 0.06**
Cyclophosphamide	1.02 ± 0.06	1.34 ± 0.10**	1.21 ± 0.07*
Test 01	0.77 ± 0.03	1.13 ± 0.08**	1.05 ± 0.05**
Test 02	0.82 ± 0.01	1.13 ± 0.05**	0.94 ± 0.02**
Data: MEAN ± SEM ** P<0.01			

Table: 4. showing the effect of *Kushtaghna dashemani* in cell mediated immunity (% change in 24hrs):

Group	% change in 24hrs MEAN ± SEM	% change
Parthenium control	54.40 ± 4.23	----
Cyclophosphamide	31.94 ± 9.72	41.28↓
Test 01	54.34 ± 7.35	0.11↓
Test 02	38.02 ± 3.34	30.11↓
Data: MEAN ± SEM		

The data shows there was decrease in Percentage change in 24 hours in cyclophosphamide group TED & TEDx2 groups when compared to the Parthenium control group, the observed decrease was found to be statistically non-significant.

Table: 5. showing the effect of *Kushtaghna dashemani* in cell mediated immunity (% change in 48hrs):

Group	% change in 48hrs MEAN ± SEM	% change
Parthenium control	38.64 ± 4.74	----
Cyclophosphamide	26.05 ± 13.45	32.58↓
Test 01	42.28 ± 7.57	9.42↑
Test 02	15.27 ± 2.47	60.48↓
Data: MEAN ± SEM		

The data shows there was decrease in Percentage change in 48 hours in cyclophosphamide group, TEDx2 group when compared to the Parthenium control group, the observed decrease was found to be statistically non-significant.

The data shows there was increase in Percentage change in 48 hours in TED group when compared to the Parthenium control group, the observed increase was found to be statistically non-significant.

DISCUSSION

Parthenium hysterophorus is a weed, basically brought through wheat shipments from Mexican countries. Parthenium has been found to contain par-

thenin, hymenin, ambrosin. The dermatitis patterns observed are airborne, atopic, photo, seborrhoeic & exfoliative dermatitis. So by all these explanations it is true that parthenium is one of the factors which cause contact dermatitis. In Ayurveda for any time of dermatitis can be explained under the term *Shotha*. According to some scholars it is opined that there are two types of *shotha*, one is from *nija karana* (doshic vitiation) termed to be *shotha* having common feature of *utsedha* (swelling) and other is from *agantuja karana* (external factors) which is of *pakayuktha utsedha* representing the *vrana shotha* (inflammation). Several *nidana's* were mentioned for the *agantuja shotha* one among them is person coming in contact with toxic plants. So, here *hetu* can be considered to be parthenium causing *Vrana Shotha* (inflammation). Premonitory signs & symptoms include increased body temperature, burning sensation, discoloration of body parts, itching etc. Considering all these factors, *chikitsa* should be planned. Acharya Charaka explained to treat *agantuja shotha* in the line of *Kushtahara chikitsa*. Several *Kushtahara*yoga's were mentioned one among them is Charakokta *Kushtaghna dashemani.*

It is a well-known fact that to assess effect of test drug on cell mediated immunity egg albumin paw edema in pre-sensitized animals is used as a model. In this case egg albumin or similar antigenic agent is injected with adjuvant containing potassium alum. To ascertain whether such a CMI is elicited by parthenium suspension was injected in to the plantar aponeurosis of animals pre-sensitized with parthenium-potassium alum suspension. The injection of parthenium suspension elicited significant edema indicating that it has the potential to elicit cell mediated immunity (CMI). This was though non-significant was suppressed by cyclophosphamide. TED dose of test formulation had only a marginal effect whereas TED x 2 dose produced more than 60% inhibition of 48 hour immunological oedema. Thus the study meets both the requirements mentioned in the objective. The first one clearly shows that parthenium is allergogenic and produced CMI- mediated pedal oedema like egg albumin. This may be the reason for the strong contact dermatitis many a times associated with exposure to parthenium. Secondly *kusthaghna dashameni gana* drugs were moderately effective like cyclophosphamide in suppressing this CMI eliciting effect. Further refinement of the formulation may provide better effect. This clearly proves that this *Kushtaghna dashemani gana* has good potential in the treatment of allergic dermatitis.

Analysis of the data shows in the control group weak suppression of immunological oedema at 24^{th} and 48^{th} hour after injection of the paw edema eliciting agent was observed. In test drug *(Kushtaghna dashemani)* administered group significant decrease was observed i.e. suppression of paw oedema was observed in 24^{th} hour and stimulation in test 1 group and suppression in test 2 group of paw oedema was observed in 48^{th} post injection. This indicates the effect and test drug formulation (*kushtaghna dashemani* drugs) possess very good immunological suppression effect and slight stimulation which is of higher magnitude. The immunological oedema represents expression of cell mediated immunity hence based on the results obtained it can be inferred that *Kushtaghna*

dashemani dravyas has cell mediated immunity suppression effect. It is pertinent to recollect here that most of the contact dermatitis type of allergy is due to CMI its suppression by the test drug group may provide evidence for their efficacy against it. Parthenium extract with potassium alum produced significant CMI mediated paw oedema. CMI is elicited by two mechanisms. The first mechanism is through activation of helper T cells. These cells release cytokines especially like interferon-g which greatly helps to kill the invading microbes. This cytokine also stimulates natural killer cells. The second mechanism involved in CMI elicitation is activation and increased formation of cytotoxic –T cells. These cells attach themselves to the targets damage them. The damage is caused by use of pore-forming molecules in the invading organism or triggering apoptosis in the involved cells. The exact mechanism involved in parthenium elicited CMI is not known. It would be interesting to elucidate this mechanism. Cell mediated immunity is the responsible for delayed type hypersensitivity and certain T cells suppress antibody production. The test sample was evaluated to assess their effect on cell mediated immunity against an experimental model, which is supposed to represent cell mediated immunity. It involved producing immunological edema. T_H-1 T-lymphocyte pathway controls cell mediated immunity. The first step in the reaction is the antigen processing and presentation by macrophages and other related antigen presenting cells followed by differentiation of T-cells into different types including T_H-1 type. T_H-1 cells produce IL-2, tumor necrosis factor-b (TNF-β) & γ- interferon (IFN-γ). These cytokines activate macrophages enhancing their phagocytizing capacity & stimulate another subset of T-lymphocyte known as CD8+, which mature into cytotoxic cells, which will neutralize macrophages leads to generation of large amounts of chemical mediators, reactive oxygen metabolites and neutral proteases, which are responsible for the inflammation observed during this reaction. Taking into consideration the above background material – the following mechanism can be suggested for cell mediated immunity suppression observed with the test formulation may be due to:

1. Interference with induction stage.
2. Interfering with the activation of T_H-1 cells, CD8+ cells, macrophages.
3. Inhibition of synthesis and release of cytokines.
4. Inhibition of synthesis and release of phlogistic factors from the activated cells.
5. Interference with the activity of the phlogistic mediators.

CONCLUSION

Shotha is an independent disease caused by derangement of *doshas*, which appear in any part of the body involving the *tvak* & *mamsa*. It is of two types one among them is *agantuja shotha*, which manifested by contact of various types of poisonous herbs. In modern parlance allergic contact dermatitis which causes varied type of hypersensitivity reactions can be considered and *Parthenium Hysterophorus* is a weed which is proved to be a causative factor for various dermatitis patterns. The selected drugs of *Kushtaghna dashemani* like *Aragvadha, Haridra, Khadira* & *Vidanga* possessing pharmacological actions like *Kushtaghna, Krimighna, Shothaghna* etc. which is sufficient to act on varied skin

manifestation.Analysis of the results clearly indicates that parthenium extract with adjuvant elicits immunological oedema in pre-sensitized animals indicating CMI eliciting effect. This effect was moderately suppressed by both cyclophosphamide and TED x 2 dose of test formulation. Thus it can be concluded that selected drugs of kushtaghna dashemani has cell mediated immunity eliciting effect & Parthenium Hysterophorus proved to be an allergogenic and produced CMI- mediated pedal oedema (shotha).

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