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EVALUATION OF IN VIVO EFFICACY OF DHANYAK LEAVES LEPA AND SILVER NITRATE GEL AGAINST BHALLATAKA INDUCED LOCAL TOXICITY IN WISTAR RATS

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ABSTRACT

Thus, Accidental contact dermatitis resulting from the local toxicity of *Bhallataka* has been a persistent issue in our society. In allopathic medicine, the treatment for the local side effects of *Bhallataka* typically focuses on alleviating the presenting symptoms rather than offering targeted medication. This usually involves cleaning the affected areas with fresh water, followed by the application of mild emollients or medicinal creams containing active ingredients like Silver Nitrate or Silver Sulfadiazine. As compared to this, *"Dhanyak leaves lepa*" can prove to be a better treatment for the local side effects of *Bhallataka. Dhanyak lepa* can provide as a better and more cost-effective therapy option for local toxicity in *Bhallataka*, which can be utilised at the household level because *Dhanyak* is easily available plant, which can also be cultivated in small pots. *Dhanyak lepa* is also easy to prepare. No complicated machines or training is required. If *Dhanyak Lepa* is verified, *Ayurveda* as a life science would be glad for resisting the toxicity of *Bhallataka.*

KEYWORDS:- *Dhanyak leaves lepa, Bhallataka, Ayurveda.*

INTRODUCTION

गदो रोगः, अगदो रोगप्रतिकारः, तदर्थं तंत्रं अगदतंत्रम्

सुश्रुतसंहिता सूत्रस्थान १/१४ (डल्हण टीका)

The term *"Agada,"* derived from its etymology, refers to a substance that counteracts *"Gada,"* which specifically denotes *"Visha"* (poison). Additionally, *"Gada"* has other synonyms such as *Vyadhi, Aamaya, and Roga*, which broadly signify "disease." Therefore, *Agada* is not only an antidote that directly combats poison but also functions as a medicine that treats diseases caused by that poison.[1]

Agadatantra is a distinct branch of *Ayurveda* that specifically addresses *Agada* (Antidotes) for the toxic effects of Visha (Poison) originating from both *Jangama* (Animate) and *Sthavara* (Inanimate) sources. This specialty is well-documented in major *Ayurvedic* texts, where numerous *Agada Kalpa* are described for the treatment of poisoning.

Semecarpus anacardium Linn., commonly known as the "marking nut" and referred to as "*Bhallataka"* or *"Bhilawa"* in local terms, has been utilized in various traditional medicine systems for centuries to treat a range of ailments both internal and external treatment of ailments such as *Kushtha* (Skin disorders), *Gulma* (Abdominal mass), *Arsha* (Haemorrhoids), *Kaphaja roga*, etc.[2] Bhallataka is also used topically to treat pain in patients suffering from leukoderma, psoriasis, and leprosy in many parts of India. The nuts are rich in biologically active compounds, including biflavonoids, phenolic compounds, bhilawanols, minerals, vitamins, and amino acids,[3] all of which exhibit various medicinal properties. The fruit and nut extract shows various activities like anti-atherogenic, anti-inflammatory, antioxidant, antimicrobial, anti-reproductive, CNS stimulant, hypoglycemic, anticarcinogenic and hair growth promoter.[4-11]

Bhallataka is generally classified in *Ayurveda* under the category of toxic plants.[12] *Rasatarangani*[13] and *Dhanvantari Nighantu*[14] have included *Bhallataka* in the *upavisha varga*. Schedule E1 of the Drugs and Cosmetics Rules of 1945 classifies *Bhallataka* as toxic.[15] According to *Acharya Charaka* when the fruit or bloom of *Bhallataka* comes into touch with the skin, it generates *agantuja shotha*. The tarry oil found in the pericarp of the fruit contains Anacardic Acid, which includes urushiols that can cause blisters upon contact. This poses a risk of accidental poisoning and can lead to contact dermatitis, particularly in children, as well as in adults during the purification process *(shodhana*) of Semecarpus anacardium Linn. The evil eye is a malevolent glance believed in many cultures to bring

injury or misfortune to the person it targets, often due to envy or dislike. In India, the concept of the "buri nazar" (evil eye) holds significant importance. It is widely believed that being cursed with it can lead to various illnesses and misfortunes.

In the Malwa region of Madhya Pradesh, a common practice for warding off the evil eye involves using the seeds of Semecarpus anacardium Linn. Typically performed by women, the procedure involves waving the seeds from top to bottom over children, followed by burning the seeds. The resulting smoke can cause allergic contact dermatitis in susceptible individuals. This practice is primarily observed with children, and the women carrying it out often do so as part of family traditions.

It is vital to identify whether the toxicity of *Bhallataka* is accidental or deliberate. By putting it to the cervical os, *Bhallataka* juice or oil is utilised as an abortifacient. It is also employed in the creation of indigenous hair dye and in the treatment of alopecia areata.

When the oil in the pericarp of *Bhallataka* fruits comes into contact with the skin, it produces irritation, erythema, oedema, burning sensation, blisters, and acid serum. After sloughing, it has prominent pruritus and ulceration. Excessive scratching might result in subsequent bacterial infection of vesicles. As a result, while extracting *Bhallataka* oil from its fruits and during the time of *Bhallataka shodhana* (purification of Semecarpus anacardium, Linn) there is a risk of it accidentally pouring over the body, causing local effects such as discoloration, blister development, and so on.

Many formulations are given in classical texts to combat the local toxicity of *Bhallataka*. According to *Acharya* Prabhakar Balaji Ogale (Chikitsa Prabhakar), the local manifestations of *Bhallataka* poisoning can be pacified by *Lepa* (External application) o*f Kothimbir lepa (i e, Dhanyak lepa).* The pharmacological properties of *Dhanyak lepa* have already been mentioned in the literature. As a *Lepa Kalpana*, or local application, it is evident that this treatment is intended for local manifestations of *Bhallataka*. *Charaka* also includes *Lepa Chikitsa* in the *Chaturvinshati Upakrama*, which outlines 24 modalities for treating poisoning. Consequently, *Lepa Chikitsa* (external application) plays a crucial role in the local treatment of any dermatological lesions resulting from exposure to *Visha*.

Modern medical science emphasizes that a key principle in treating poisoning is the removal of unabsorbed toxins. It is crucial to eliminate the poison from its local site of contact. In

cases of contact poisoning, the affected area should first be washed thoroughly with water or soap and water. Therefore, modern medicine also underscores the importance of local treatment for contact poisoning. Ayurveda seems to be ahead of modern science in that it recommends neutralizing both remaining and absorbed poison at the local site of exposure through the application of *Lepa* (external application). If the poison is not completely removed, residual toxins can cause further toxic effects or may transform into *Dooshivisha* (latent poison). Thus, *Lepa Chikitsa* (local application) is essential for addressing all types of local manifestations of poisoning.

Considering the importance of *Lepa Chikitsa* (Local application) in all types of poisoning, "*Dhanyak leaves lepa*" has been selected for the present research work as a local application for local side-effects caused due to *Bhallataka Taila.*

Primary objective

To study the efficacy of Dhanyak Lepa and Silver Nitrate gel against Bhallataka induced local toxicity in Wistar rats till wound healing.

Materials

- Bhallataka oil, Dhanyak leaves lepa, Silver Nitrate gel 0.2%.
- Wistar Rats, Cage, RO water, Standard Pelleted food.
- Gloves, Hair trimmer, pen.
- Ketamine/ Xylazine, Swab holder, Surgical cotton, Spirit, Micro pipette**.**

Collection of drug

1. Bhallataka seeds collected from Ayurvedic raw drug supplier.
2. Dhanyak collection from self-cultivated garden.
3. Silver Nitrate gel collected from medical store.

Procurement of wistar rats

It was procured from Authorized research Institute.

Methods

Authentication of drugs

Authentication of drugs was done in research laboratory of well-known institute.

Method of extraction of bhallataka taila

Bhallataka fruits were punctured with the help of large needle and holes were made.With the help of Torque forceps, the seeds were squeezed and oil was extracted.

Method of preparation of dhanyak lepa

The plants were dipped for 2-3 minutes under water, which helped in effective cleaning. Dhanyak was chopped in pieces and later fine paste was made in a mixer grinder.

Figure no. 1: Collection of drugs.

Dose calculation

Dose calculation of bhallataka taila

As per discussion with experts with reference to previous study on Bhallataka Taila local toxicity conducted, Bhallataka Taila is applied considering the weight and age factor of the Wistar rats.

Dose calculation of dhanyak lepa

According to Sharangdhar Samhita, thickness of lepa for vishagna local application is 1/3rd of anguli i.e., 1-2 mm. Considering the age and weight factor of the Wistar rats, Lepa was in such a dose that cover the whole blister and inflammation around it.

Study population

Table - Study population

Sr No		
1	Animal species	Wistar rat
2	Strain	Wistar
3	Gender of animal	Both male and female
4	Age of animal	6-8 weeks
5	Average weight of animal	190 ±20 gm
6	No. of groups	3
7	Animals in each group	6
8	Total number of animals	18

Grouping of animal

Table - Grouping of animal.

Group	No. of Rats	Drugs	Form
Control group Group 1	6	Bhallataka oil	Local application of bhallataka oil(no intervention group)
Standard group Group 2	6	Silver nitrate gel 0.2%	Induction of bhallataka oil and local application of standard drug (silver nitrate gel 0.2 %)
Test group Group 3	6	Dhanyak leaves lepa	Induction of bhallataka oil and local application of Dhanyak leaves lepa

Methods of selection of study subject

Inclusion criteria

i. Healthy rats

ii. Young adult of age 6-8 weeks

iii. Weight of 200-250 grams.

Exclusion criteria

i. Rats under trial for other experiments

ii. Pregnant and breastfeeding rats.

Route of administration

External application (Dorsal surface).

Operational definition

The discoloration is caused by the local use of *Bhallataka* Taila, which causes irritation, blister development and is accelerated by allergic contact dermatitis. SilverNitrate 0.2% gel is often used to treat symptoms.

Data collection

Conceptual Study- Reference from classical text & modern literature related to local toxicity of Bhallataka including presented paper, journal, previous work done was collected and analysed.

Experimental study

Place of animal experiment

It was performed at Authorized Institute.

Duration of experiment

Duration was 7 days.

Institutional Animal Ethics Committee approval was received before conducting the study.

Method of experiment

To know the efficacy of ground nut oil in blister induced by Bhallataka, it includes following steps.

I. Pre Procedure Stage

II. Procedure Stage

III. Post Procedure Stage.

I. Pre procedure stage

Selection of animals: Total 18 Wistar Rat was selected according to inclusion criteria.

Grouping of animals: 6 animals each was categorized into 3 groups such as Control, Standard and Trial.

Marking of animals: Animals identification marking was done using tail marking method with the help of permanent marker.

Acclimatization: Rats were acclimatized for period of 7 days before experiment.

II. Procedure stage

- Animals were anaesthetized under Ketamine (75mg/kg) & Xylazine (10mg/kg) anaesthesia.
- After animals were sufficiently anaesthized, they were kept on Dissection platein prone position.
- Hairs on the dorsal part were removed with the help of hair trimmer.
- After 24 hours, again anesthesia was given and Bhallataka oil was applied on the shaved area of each animal.
- Change was noted after 24 hrs where oil was applied.

III. Post procedure stage

- External application of medicine were started to the respective groups from 1st day of wounding.
- Every post wounding day, the trial drug i.e. Dhanyak leaves lepa was applied to trial group. The standard drug i.e. Silver Nitrate gel 0.2% was applied to standard group
- The control group rats received normal diet and water, they were not receiveing any kind of drug application in order to rule out natural healing.
- To monitor the changes in wound shapes wound margins were traced from the day of wounding and continued till the complete healing of the wound.
- The observation of percentage of wound closure was made on 1^{st} day ,4^{th} day,7^{th} day The animals was inspected daily and health was assessed based on physical parameter and normal wound healing and epithelisation.
- At the end, Histopathological tests was done to compare the efficacy of all groups
- Tissue collection procedure

At the final stage of experiment the animals were sacrificed and skin tissues was collected. Histopathological changes was observed and then recorded.

Method of data collection relevent to objective

- Measurements from the affected area was noted down on 1^{ST} day 4^{TH} day and 7^{th} day.
- Duration required for complete wound healing was observed.

Statistical analysis

1. For body weight

Body weight in all the three groups during each follow up in both male and female increased significantly.

2. Erythema score

Erythema Score in all the three groups decreased significantly but as per p value there is no significant difference in Standard Control Group and Test Group. So, it can be concluded that, *'Dhanyak Leaves Lepa'* is not as effective as 'Silver Nitrate' for 'Erythema Score'.

3. Epithelialization day

Epithelialization Day in Control Group was seen on 7th day, for Standard Control Group- approximately on 4th day and for Test Group it was seen on 6th day. So, it can be concluded that, as 'Epithelialization Day' is less 'Silver Nitrate' group. So, *'Dhanyak Leaves Lepa'* is less effective than 'Silver Nitrate' for 'Epithelialization Day'.

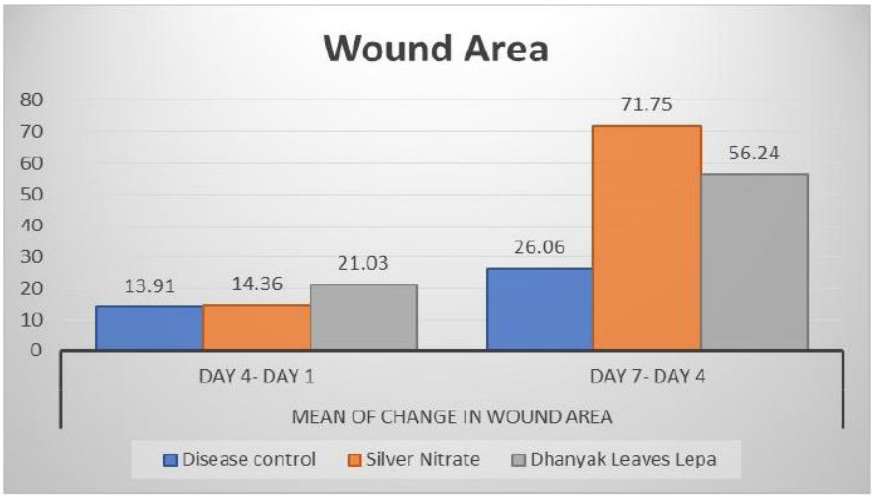
4. Wound area measurement-

The wound area measurement decreased significantly in consecutive three followups in all the groups. As per p values, there is no significant difference in 'Silver Nitrate & *Dhanyak Leaves Lepa',* and also no significant difference in 'Disease Control' and' Dhanyak Leaves Lepa'

So, it can be concluded that, *'Dhanyak Leaves Lepa*' is not as effective as 'Silver Nitrate' for Wound area.

5. Relative organ weight

There was no significant difference in all groups regarding 'Relative Organ Weight'. It means 'Silver Nitrate' and '*Dhanyak Leaves Lepa'* doesn't show any toxic effect on any organ.

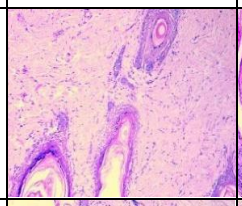
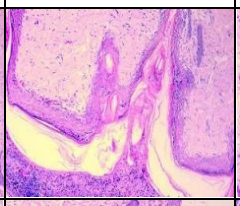
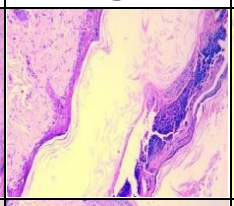
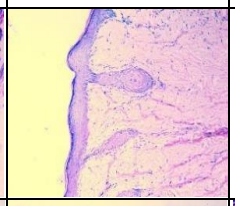
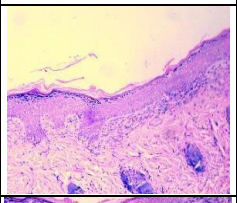
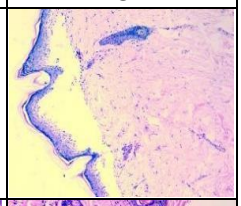
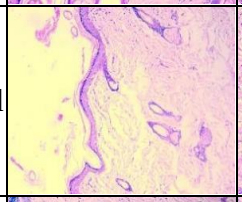
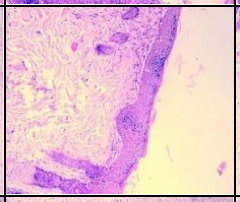
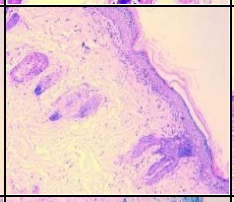
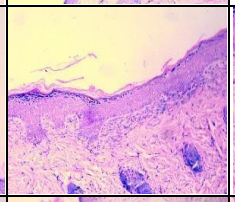
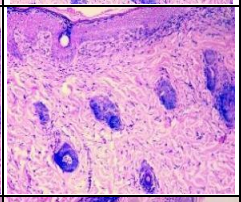
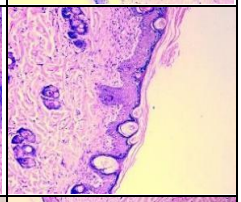
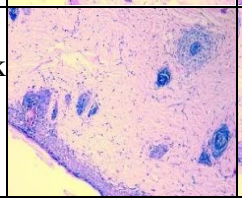
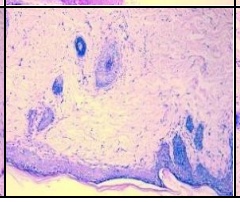
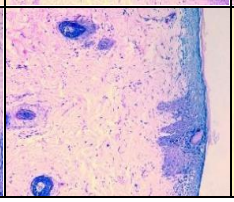
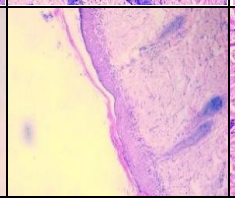
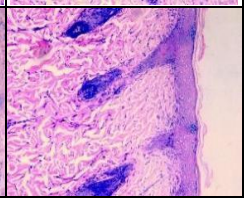
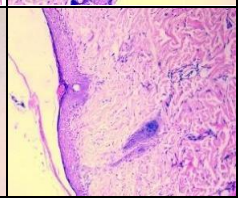


Interpretation: As p value < 0.05, there is significant difference in 'Disease control & Silver Nitrate'.

As per p values, there is no significant difference in 'Silver Nitrate & Dhanyak Leaves Lepa', and also no significant difference in 'Disease Control' and' Dhanyak Leaves Lepa'

So, it can be concluded that, 'Dhanyak Leaves Lepa' is not as effective as 'Silver Nitrate' for Wound area.

Histopathology of skin

Group	1	2	3	4	5	6
Disease Control						
Standard						
Dhanyak Leaves Lepa						

RESULT

From the observations, *Dhanyak leaves lepa* showed efficacy in the local toxicity of *Bhallataka but not as effective as Silver Nitrate* and also didn't show any adverse effect.

Hence, *Dhanyak leaves lepa* is not as effective as Silver Nitrate in local toxicity of *Bhallataka* in Wistar Rats.

DISCUSSION

Discussion on drug review

Bhallataka has been recognized since ancient times, appearing in texts from various historical periods such as the *Vaidika Kaala* (2500-600 BC), *Pauranika Kaala* (1500-300 BC), and *Samhita Kaala* (1000 BC-7th Century AD). It is mentioned in the *Upavisha Varga* of the *Dhanvantari Nighantu* (10th-13th Century) and the *Rasa Tarangini* (20th Century). More recently, it has been classified as a poisonous medicinal plant under the Drug and Cosmetics Act of 1940 in India. This highlights its long-standing acknowledgment as a *Visha Dravya* (toxic substance), with our ancestors recognizing its significance throughout history.

Interestingly, a poison can serve as an effective medicine when used correctly, while a medicine can become toxic if misused. This principle, understood by the ancient sages of *Ayurveda,* is emphasized by *Acharya Charaka* in the introductory chapter of his texts. Consequently, *Bhallataka* has been utilized for medicinal purposes for centuries. In *Ayurveda,* it has been prescribed for various ailments such as *Kushtha, Gulma, Udara, Arsha, Aamvaata,* and *Kaphaja Rogas.* It has been employed both internally, in formulations like *Rasayana Kalpa* (Rejuvenating medicine) and *Sanjivani Vati,* and externally for conditions like piles and skin disorders.

Given *Bhallataka's* extensive historical background, it is valuable to examine its timeline of references. These insights can illuminate the challenges humans faced due to their interactions with *Bhallataka,* as well as the evolution of knowledge and beliefs surrounding it from ancient times to the present day.

Discussion on *dhanyak leaves lepa*

Dhanyak is easily available plant, which can also be cultivated in small pots. *Dhanyak lepa* is also easy to prepare. No complicated machines or training is required. *Dhanyaka lepa* can provide as a better and more cost-effective therapy option for local toxicity in *Bhallataka,* which can be utilised at the household level.

Discussion on animal experiment

Animal study was carried out in Authorized Animal Research Laboratory prior permission of animal ethical committee.

Total 18 Rats were used for study.

In this study there are 3 groups. In each group 5 parameters are measured on 6 rats. They are as follows-

1. Body weight
2. Wound area measurement
3. Epitheliazation
4. Erythema
5. Organ weight and relative organ weight

Above observations are taken to access the changes and for statistical analysis.

Also, Histopathology of skin tissue was done.

CONCLUSION

- The conclusion drawn from the experimental study, Observations and Statistical Analysis that *Dhanyak leaves lepa* is not as effective as Silver Nitrate gel in local toxicity of *Bhallataka* in Wistar Rats.
- Thus, the Null hypothesis that is – *Dhanyak leaves lepa* is not as effective as Silver Nitrate gel against *Bhallataka* induced local toxicity in Wistar rats is accepted.

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