

## THERAPEUTIC EFFICACY OF MODIFIED DANTYADI LEPA AGAINST DMBA INDUCED FIBROADENOMA IN SPRAGUE DAWLEY RATS W.S.R TO STANA GRANTHI

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### ABSTRACT

Fibroadenoma is one of the most common breast lumps in young women under the age of 30. Breast fibroadenoma accounts for approximately 25% of all lesions in asymptomatic women. The lump if left untreated has less chance of malignancy associated with breast fibroadenoma. After a systematic review of conservative management available, surgical excision of the lump is the option which most of the patients do not feel comfortable. So, to prevent these, a non-hormonal drug formulation, quoted in *Chakradatta Granti Chikitsa* the use of *Dantyadi Lepa* which is a *kaphaja grantihara* formulation was undertaken. The present study is an *In vivo* study and aimed to assess the efficacy of modified *Dantyadi lepa* in *stana granthi*.

**Keywords:** *Stana Granthi; Fibroadenoma; Dantyadi Lepa; DMBA; Experimental Study*

### INTRODUCTION

The importance of health of woman is highlighted as - only she can procreate and thus lay foundation for a healthy society. Throughout the ages, the female body has been revered as a work of art and beauty and as a source of life, from which all humans are born. Breast is a part of accessory reproductive organ which is most predominant feature of women and stands out as a symbol of womanliness and livelihood. Disturbed body image due to any destruction in breast structure usually induces impairment in psychological wellbeing, social life and disturbed relationship resulting in a decreased quality of life for women.

Fibroadenoma is one of the most common benign tumors of the breast, clinically and pathologically in

adolescent and young women which also may be discovered at different stages of life. Often, surgery is known to be the ideal treatment of fibroadenoma, even though the prevalence rate of the fibroadenoma turning of malignant is very low which is confirmed by radiological imaging.<sup>1</sup>

Fibroadenoma are caused by growth of fibrous (stromal) and glandular (epithelial) tissue<sup>2</sup>. The typical case is the presence of painless, firm, solitary, mobile slowly growing lump. This is co-related to *stana granthi*. The disease arises due to vitiation of *mamsa dhatu* along with vitiation of *vata* and *kapha dosha*. Hence, *stana granthi* is having similar feature like that of *kaphaja* and *mamsaja granthi*. The conservative

management in the form of hormones is sometimes difficult to be prescribed to young age group. Keeping in mind the side effect of hormonal treatment, surgery becomes the ideal treatment but it also has its own physical and psychological impact on woman's life. A non-surgical method as mentioned in Chakradatta Granthi Chikitsa Adhyaya<sup>3</sup>, is the use of Dantyadi Lepa which is a kaphaja granthihara formulation. A preclinical study to know the efficacy of modified Dantyadi Lepa on stana granthi has been undertaken.

**OBJECTIVES:** To evaluate effect of *Dantyadi lepa* on hormonal change, haematological, histopathology and antioxidant changes in mammary gland of *Sprague Dawley Rats*.

#### **MATERIALS AND METHODS:**

##### **Source of data:**

Test drug - Dantyadi lepa (Danthi, Citraka, Snuhi ksira, Arka ksira, Guda, Bhallataka and Kasisa)

Chemical - 7, 12- DIMETHYLBENZ (A) ANTHRACENE [DMBA]

Study is being conducted after obtaining IAEC certificate and as per CPSCEA guidelines governing animal experiments.

42 Female Sprague Dawely rats (200±50g body weight) were obtained from animal house attached to Pharmacology and Toxicology laboratory at SDM Centre for Research in Ayurveda and Allied Sciences Udupi, India. The animals were maintained at standard laboratory conditions.

The present study is designed and divided into two protocols.

**Protocol I:** To standardize dose of DMBA for induction of fibroadenoma.

The selected rats were grouped into 3 different categories of 6 each. Group I were treated at a dose of 0.5mg/kg DMBA, Group II were treated at a dose of 1 mg/kg DMBA, Group III were treated at a dose of 1.5mg/kg DMBA. All rats were given a subcutaneous injection (once only) near the mammary gland on day 1 with their respective group dose and observed for its physical and behavioral changes with the DMBA induced fibroadenoma. After a period of 30 days,

1.5 mg/kg DMBA was the dose finalized to produce fibroadenoma in the main study which was chosen on basis of color change, duration of formation of tumor, size of the tumor formed, behavior of rats with DMBA, weight loss/ gain

**Protocol II:** To evaluate the therapeutic efficacy of modified Dantyadi lepa in fibroadenoma induced rats.

The selected rats were grouped into 4 different categories of 6 each. Group I served as normal control group. Group II was administered with DMBA and served as positive control group. Group III was administered with 1.5mg/kg DMBA and Dantyadi lepa. Group IV was administered with DMBA and Methotrexate to serve as reference standard group.

**Drug administration method** – Topical application (Lepa)

**Total duration of the study:** The group specific drug was administered for 60 days and the parameters were performed to evaluate the change in fibroadenoma.

##### **INCLUSION CRITERIA:**

- Healthy 42 female Sprague Dawely rats.
- Body weight 200±50g

##### **EXCLUSION CRITERIA:**

- Unhealthy female Sprague Dawely rats.
- Pregnant rats.
- Sprague Dawely rats which are under trial of other experiment.

##### **PARAMETER ASSESSED:**

- Hormonal assay – serum estradiol, serum prolactin & serum progesterone
- Haematological parameters - Haematocrit, Haemoglobin Concentration, Erythrocyte Count, PCV, MCV, MCHC, RDWC, RDWSD & platelet.
- Antioxidant parameters - Lipid Peroxidation, Protein Estimation, Catalase Activity, Glutathione Peroxidase.
- Histopathology of the breast tissue.
- Effect of Dantyadi Lepa on Body weight of rats.

##### **STATISTICAL ANALYSIS:**

The data obtained was expressed as Mean ±SEM and analyzed by employing one way ANOVA. Followed by Dunne's multiple t-test. P value <0.05 will be considered as statistically significant.

## OBSERVATION AND RESULT:

**Table 1:** Summarized data of the active profile of test drug preparation on body weight changes in Sprague Dawley Rats.

Parameter	Compared with normal control	Compared with positive control	
	Positive	Standard group	Test drug group
Body weight (%)	SD	NSD	NSI

There is a remarkable decrease of body weight in positive control group rats when compared to normal control group this is mainly due to the mammary tumour due to chemical DMBA. Studies show that the incidence of DMBA reduces significantly the calories restriction by 20 to 40% in female Sprague Dawley rat.

On other hand there is a non-significant increase in body weight in test drug group and non-significant decrease when compared to the positive control group which may be probably due to the nutritive value present in guda (jaggery), and also over comes the DMBA effect and thereby increasing the survival rate of the rats.

**Table 2:** Summarized data of the active profile of test drug preparation on Haematological changes in Sprague Dawley Rats

Hematological Parameter	Compared with normal control	Compared with positive control	
	Positive	Standard group	Test drug group
Hb%	NSI	NSI	SI
TC	NSI	NSI	NSI
RBC	NSI	NSI	SI
PCV	NSD	NSI	SI
MCV	SD	NSD	NSD
MCH	NSI	NSD	NSD
MCHC	SI	NSI	SI
RDWCV	NSI	SI	NSD
RDWSD	NSD	SI	NSD
PLATELET	NSI	SI	NSI

The significant increase in haemoglobin percentage seen in test drug group when compared to positive control is probably due to presence of kasisa and guda in *Dantyadi Lepa*. *Kasisa* is known for its panduhara karma due to the content of ferrous compound.

The non-significant increase of total count in test and standard group is due the fact that DMBA selectively targets white blood cells rather than red cells or thrombocytes precursor.

The non-significant increase of platelet count in test drug group indicates the usefulness of the drug in maintaining the platelet, helps in reducing the angiogenesis. The significant increase of platelet count in standard drug suggests that high platelet count is associated with breast cancer, since it secretes various growth factors and cytokines that promote angiogenesis.

**Table 3:** Summarized data of the active profile of test drug on Hormonal changes in Sprague Dawley Rats

Hormones	Compared with normal control	Compared with positive control	
	Positive	Standard group	Test drug group
Estradiol	NSD	NSI	NSD
Progesterone	NSI	NSD	NSI
Prolactin	NS	NE	NE

There is non-significant increase of progesterone level and non-significant decrease of estradiol level in test drug group when compared to positive control group. In the present study, the non-significant decrease in

the level of estradiol is probably due to initial phase of fibroadenoma.

**Table 4:** Summarized data of the active profile of test drug preparation on antioxidant activity changes in Sprague Dawley Rats.

Antioxidant parameters	Compared with normal control	Compared with positive control	
	Positive	Standard group	Test drug group
Lipid peroxidation	NSD	NSD	NSI
Protein estimation	NSI	NSI	NSI
Catalase activity	NSD	NSD	NSD
Glutathione peroxidase	NSD	NSD	NSD

Naturally occurring polyphenolic components are evident to possess high antioxidant, anticancer, anti-inflammatory, anti angiogenic and apoptotic potentials. Flavonoids are a group of natural substance which serves several biological activities like antioxidant, anti tumour and anti-inflammatory.

*Dantyadi Lepa* made of 7 single drugs, among them *Danthe*, *Citraka*, *Snuhi*, *Arka* are having good amount of flavonoids and *Bhallataka* and *Guda* are rich in phenolic compounds, hence these phytoconstituents present in *Dantyadi Lepa* may probably help in regression of the tumour and also showed their effective anti-oxidant property to release it form oxidative stress.

**Note:-** The changes summarized above are with reference to values obtained in positive control group.

SD – SIGNIFICANT DECREASE

SI – SIGNIFICANT INCREASE

NSD – NON- SIGNIFICANT DECREASE

NSI – NON SIGNIFICANT INCREASE

HISTOLOGICAL EXAMINATION

Summarized data of the active profile of test drug preparation on Histopathology changes in Sprague Dawley Rats-

On histopathological examination following changes were seen in each group –

a) In positive control group, there was a normal epithelium with inflammatory cells and oedema in dermis suggesting that there were inflammatory changes.

b) In standard group, there were normal epithelium and showing acute inflammatory cells suggests that there is no gross specific change in tissue.

c) In test drug group, there were normal epithelium and dermis, also sheets of mammary gland in fat tissues suggesting that there no change in the tissue or reversal of breast tissue was seen.

## DISCUSSION

***Dantyadi Lepa*** - The importance of understanding *rasa*, *guna*, *veerya*, *vipaka* and *prabhava* of drugs lies in the beauty of the particular action of its assertion on the disease (with complete eradication of *granthi*). In *Chakradatta Granti Chikitsa*, *Dantyadi Lepa* is quoted in *kaphaja granthihara chikitsa*. *Kapha vata dosa* along with *mamsa dhatu* is responsible for formation of *stana granthi*. As *stana granthi*, involves *dosa* and *dusya*; *kapha-vata* with *mamsa dhatu* it is appropriate to consider this yoga for the *stana granthi*. *Dantyadi Lepa* has the property of *katu – tikta rasa*, *tiksna guna*, *usna virya*, *katu vipaka* and *kapha vata samaka*<sup>4</sup>. The *Katu rasa* having *ruksha*, *usna*, *laghu*, *tiksna* and *visada guna* helps in deep penetration of the drug to the target cells. According to *Caraka katu rasa* is *marga vivrnoti* i.e. it clears and dilates the passages and alleviates the *kapha*.

The *tikta rasa* has *ruksha*, *sita* and *laghu guna*. It is *visaghna* and *krimighna* probably helping in curing *sotha*. *Tikta rasa* having *lekhana* property so it causes depletion or dryness of *kleda*, *meda*, *puya* improving

sloughs and bringing in good blood circulation. According to Acharya Charaka, as *granthi chikitsa* follows *sotha chikitsa*, *tikta rasa* present in *Dantyadi Lepa* acts as anti-inflammatory activity over the tumour.

*Tikshna guna* formed predominantly by *Agni mahabhuta* is *kapha vata hara*. It destroys *dushita dhatu* because of its *lekhana* property. This *guna* help to remove or burst out the *granthi* from the capsule.

All the ingredients in the *Dantyadi Lepa* have *ushna virya* thus promotes the action of *vispotana* of the *granthi* due to excessive heat production and also helps in healing of the wound.

The Phytoconstituents present in most of the ingredient of *Dantyadi Lepa* have flavonoids and phenolic compounds which acts as anti tumorigenesis, anti cancerous, anti oxidant and free radical scavenging activity.

## CONCLUSION

We can conclude that on application of *Dantyadi Lepa* over the induced fibroadenoma in rats, even though they were non-significant statistically but experimentally showed good result. The data harvested from the animal experimentation proves that there is definite activity of *Dantyadi Lepa* in the effective treatment of fibroadenoma or *stana granthi*.

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**Source of Support: Nil**

**Conflict Of Interest: None Declared**

How to cite this URL: Suman Paul et al: Therapeutic Efficacy Of Modified Dantyadi Lepa Against Dmba Induced Fibroadenoma In Sprague Dawley Rats W.S.R To Stana Granthi. International Ayurvedic Medical Journal {online} 2019 {cited October, 2019} Available from: [http://www.iamj.in/posts/images/upload/1712\\_1716.pdf](http://www.iamj.in/posts/images/upload/1712_1716.pdf)