



Pharmaceutical Standardization and Drug Dosage Modification of *Laghu Sudarshan Churna* with Comparative Assessment of its Antipyretic and Analgesic Activities in Albino Rats

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: *Laghu Sudarshan Churna* is a *Churna* mentioned by *Yogratnakar* indicated in the treatment of all types of *Jwara* and its action is *Tridoshanashak*. Fever is body's natural defense mechanism against infectious agents which can damage the tissue. Some studies have suggested that raising temperature may be harmful. Therefore, in clinical practices in which fever associated risk benefits, antipyretic treatment is necessary.

Aim and Objective: Drug dosage modification and pharmaceutical standardization of *Laghu Sudarshana Churna* to *Laghu Sudarshana Vati* with comparative Assessment of its Antipyretic & Analgesic activities in albino rats.

Materials and Methods: To evaluate antipyretic & analgesic activities of test drugs the most commonly employed method to induce fever in animals is brewer's yeast induced pyrexia, Tail flick test & Hot plate test for analgesic in animal models.

Observation and Results: Observation will be done on the basis of Physicochemical & Organoleptic characteristics of *Laghu Sudarshan churna* & *Laghu Sudarshan vati*. Results will be drawn on the basis of observations & applying suitable test. It will be noted & presented in the form of table, charts & graphs etc.

Conclusion: If this Antipyretic & Analgesic study is successful then this data will be used in another clinical study for intervention of Antipyretic & Analgesic studies, as it is Herbal medicine so it will show no any toxic effect in animal models. Hence, it will be easily used in humans also.

Keywords: *Laghu Sudarshan churna*; *Laghu Sudarshan vati*; antipyretic; analgesic.

ABBREVIATIONS

CCIM	: Central Council of Indian Medicine,
CCRAS	: Central Council for Research in Ayurveda and Siddha.
NCISM	: National Commission for Indian System of Medicine.
A.P.I.	: Ayurveda Pharmacopoeia of India.
HPTLC:	High Performance Thin Layer Chromatography
MGACH & RC:	Mahatma Gandhi Ayurveda college hospital & research centre.
DMIMS (DU)	: Datta Meghe Institute of Medical Sciences (deemed to be University).

1. INTRODUCTION

Ayurveda is the most ancient and renowned system of medicine in India. It is more than 5000 years old system but yet has the potential to cure many diseases in an efficient manner. *Ayurveda* is made from two words *Ayu* means life and *Ved* means knowledge or Science. Thus Ayurveda in totality means Science of life. It is qualitative, holistic science of health and longevity of life.

Bhaishajya is the weapon offered by Ayurveda from our mother nature to conquer the overspreading deadly diseases. *Bhaishajya Kalpana* is a science that deals with *Samskara* to be done over a *Bhaishajya*. The word *Bheshaja* or *Bhaishajya* literally means *Aushadh* (medicine). That which wins the fear of disease or restore the health of person by stabilizing the dosha is *bheshaja* or *bhaishajya* and is one among *Chikitsa Chatushpada* (four components of therapeutics) without which the suppression of disease is not possible. The word *Kalpana* means *Yojana* (Planning) i.e. the Ideology of making use of different *Dravyas*. Hence *Kalpana* is the Process or modification through which a substance is transformed into medicinal form [1]. The drugs are need some kind of processing and this can be achieved with the help of basic.

1.1 Panchavidh Kashaya Kalpana i.e. Swaras, kalka, Kwatha, Hima,& Phanta

The word *Kashaya* denotes distortion of the original form of *dravyas* and making it suitable for use. Many more formulations were developed later based on this to achieve ready palatability, extended shelf life, low dose, quick action, easy dispensing, and handling [2]. As per the need of time our scholars have modified the formulations without changing its efficacy with above merits but it is important to establish its effectiveness according to new era. Sometimes to complete with need of all time availability, easy dispensing and efficacy, lots of *Kalpana* have been developed. Among them, The *Churna Kalpana* is one of the most important *Kalpana* [3].

Churna Kalpana is a prominent preparation in pharmaceutical world of Ayurveda, it is considered as *Upkalpana* of *Kalka Kalpana*. The fine powder obtained after thoroughly pounding and filtering the completely dry drugs is called *Churna*. Pounding is done either manually in *Khalva* or *Ulukhala Yantra* or mechanically in pounding/ Pulverizing machines. Filtering is also done either manually using a clean cloth/ a selected Sieve; or mechanically through sieve shaker. Depending on the particle size, the powders is either course, fine or very fine [4].

Laghu Sudarshan Churna is a *Churna* mentioned by *Yogratnakar*. This Formulations contains *Guduchi, Pippalimula, Pippali, Kutaki, Haritaki, Shunthi, Devkusum, Nimba Twak, Shweta Chandana and Chirayata* in equal proportion and indicated in the treatment of all types of *Jwar* (fever) and its action is *Tridoshanashak* [5].

The word *Samskara* is introduced as *Samskaro hi Gunaantradhanam* means qualitative improvement is carried out in natural properties of drug by incorporating specific qualities. *Bhavana* is a significant process which has the above said property. It literally means saturation

of any powder with fluid, effecting, promoting, infusion, soaking and flavoring.

Bhavana is a process in which the material is completely submerged with the liquid media (*Swarasa*, *kwatha*, etc) & triturated till complete absorption of liquid into the powder [6].

Pharmaceutical Standardization of ASU (*Ayurveda*, *Sidha* and *Unani*) drug has been recommended by CCIM (Now NCISM). It has been included as one of the thrust areas in research and development of *Ayurveda*. Pharmaceutical Standardization is helpful in developing standard quality drugs and for quality control and quality assessment of prepared formulations and determination of its quality and purity.

Standardization of *Ayurvedic* formulations is gaining more significance as it is needed to establish scientific parameters for assessment of drug effectiveness, authenticity as well as safety. A great attempt to establish standard parameters for *Ayurvedic* drugs has been successfully made by CCIM and CCRAS which is available in the form of *Ayurvedic* Pharmacopoeia of India and *Ayurvedic* Formulary of India. However, there are many clinically used formulations which are not included in those databases. *Laghu Sudarshana Churna* is one of such formulation. *Laghu Sudarshan Churna* will be prepared according to the reference of *Yogarajnikar* and will be modified into tablet (*Vati*) form with its standardization and its Antipyretic & Analgesic activity will be tested in Albino rats [7].

Fever, also known as *Pyrexia*, is an abnormally high body temperature caused by the interaction of the central nervous and immune systems. It is characterized by a rise in the thermoregulatory set point. Fever is the body's natural defense against infectious pathogens that can cause tissue damage. According to several studies, increasing the temperature may be hazardous. As a result, antipyretic medication is required in clinical procedures where fever is connected with risk benefits [8].

1.2 Need of Study

In *Ayurveda* there are number of preparations are available to treat any type of *Jwara* and *Laghu Sudarshana Churna* is one of them which is often used in clinical practice. Drug dosage modification of *Ayurvedic* formulations without changing its classical composition and establishing its effectiveness according to new era is the need of the hour. Therefore, a more

suitable and palatable dosage form of *Laghu Sudarshana Churna* is needed to be developed to potentiate the drug dose. Hence in present study, it is decided to modify *Laghu Sudarshan Churna* to *Laghu Sudarshana Vati* form and to study its antipyretic & Analgesic activity in albino rats.

2. AIM AND OBJECTIVES

2.1 Aim

Drug dosage modification and pharmaceutical standardization of *Laghu Sudarshana Churnato Laghu Sudarshana Vati* with comparative Assessment of its Antipyretic & Analgesic activities in albino rats.

2.2 Objectives

- To prepare *Laghu Sudarshana Churna* according to classical reference.
- To prepare *Laghu Sudarshana vati* by *Churna kriya* (process of lavigation)
- To analyze *Laghu Sudarshana Churna* and *Laghu Sudarshana Vati* by Physico-chemical parameters.
- To assess & compare Antipyretic & Analgesic Activities of *Laghu Sudarshana Churna* and *Laghu Sudarshana Vati* in albino rats.

3. MATERIALS AND METHODS

3.1 Materials

Present work will be conducted under following headings

3.1.1 Pharmaceutical study

Three different batches of *Laghu Sudarshan churna* & *Laghu Sudarshan Vati* will be prepared to establish pharmaceutical standardization. Pharmaceutical study will be done in following steps.

3.1.2 Procurement of raw materials

All required raw materials will be procured from *Dattatraya Ayurved Rasashala* of the Institute.

3.1.3 Authentication of raw materials

Raw drugs will be verified and authenticated by Department of Dravyaguna of MGAC & RC. Raw drug will be standardized as per A.P.I. Table 1 show contents of *Laghusudarshan churna* and their quantity. Below is the flow diagram of method of preparation of *Laghusudarshan churna* & *Laghusudarshan vati*.

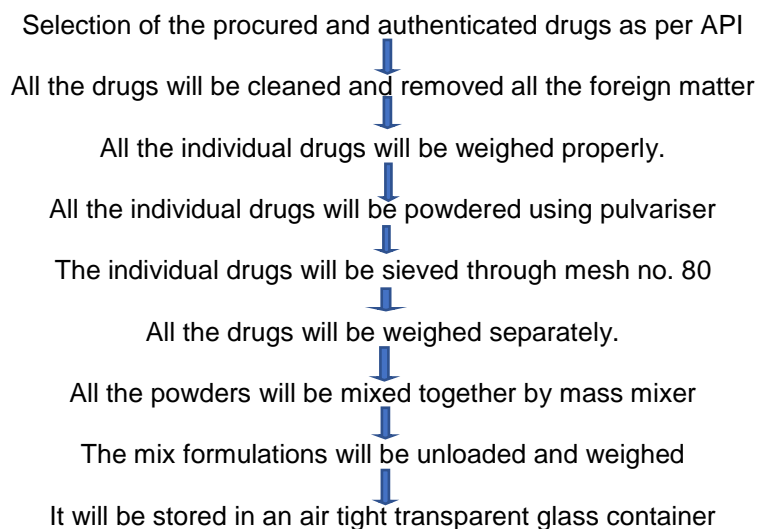
Table 1. Ingredients of LaghuSudarshan Churna [5]

Sr. no.	Ingredients	Part used	Proportion
1.	<i>Guduchi (Tinospora cordiopholia Linn.)</i>	<i>Kanda</i>	1 part
2.	<i>Pippalimula (Piper longum Linn.)</i>	<i>Mula</i>	1 part
3.	<i>Pippali (Piper longum Linn.)</i>	Fruit	1 part
4.	<i>Kutaki (Picrorhiza kurroa Royle Ex Benth)</i>	Mula	1 part
5.	<i>Haritaki (Terminalia chebula Retz.)</i>	Fruit pulp	1 part
6.	<i>Shunthi (Zingiber officinale Roscoe)</i>	Rhizome	1 part
7.	<i>Devkusum (Syzygium aromaticum Linn)</i>	<i>Pushpa kalika</i>	1 part
8.	<i>NimbaTwak (Azadirachta indica A.Juss)</i>	<i>Twak</i>	1 part
9.	<i>Shweta Chandana (Santalum album Linn)</i>	<i>Kandasara</i>	1 part
10.	<i>Chirayata (Swertia chirata Linn)</i>	<i>Panchang</i>	½ part

3.2 Methods

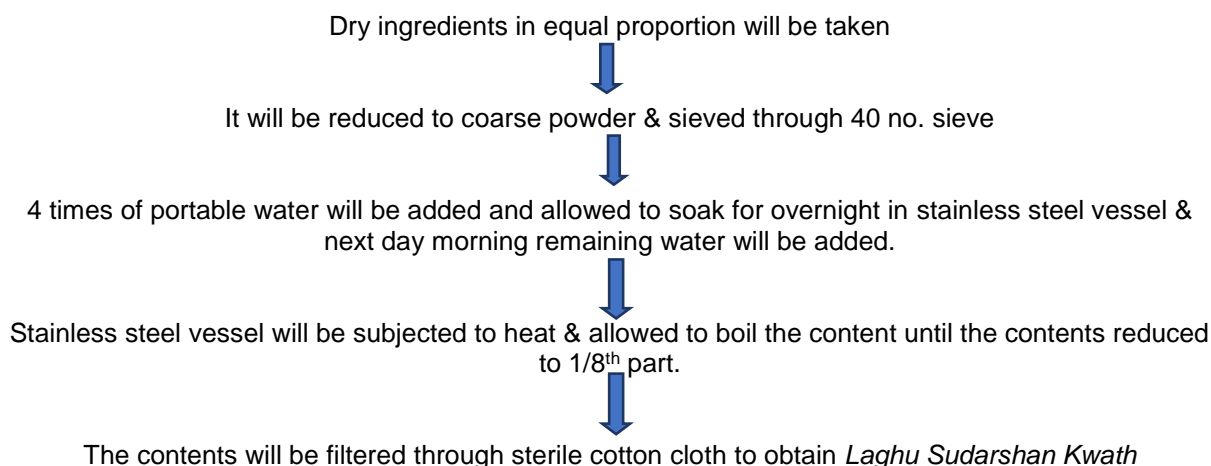
a) Classical Method of preparation of *Laghu Sudarshan Churna*

Flow Chart: 1



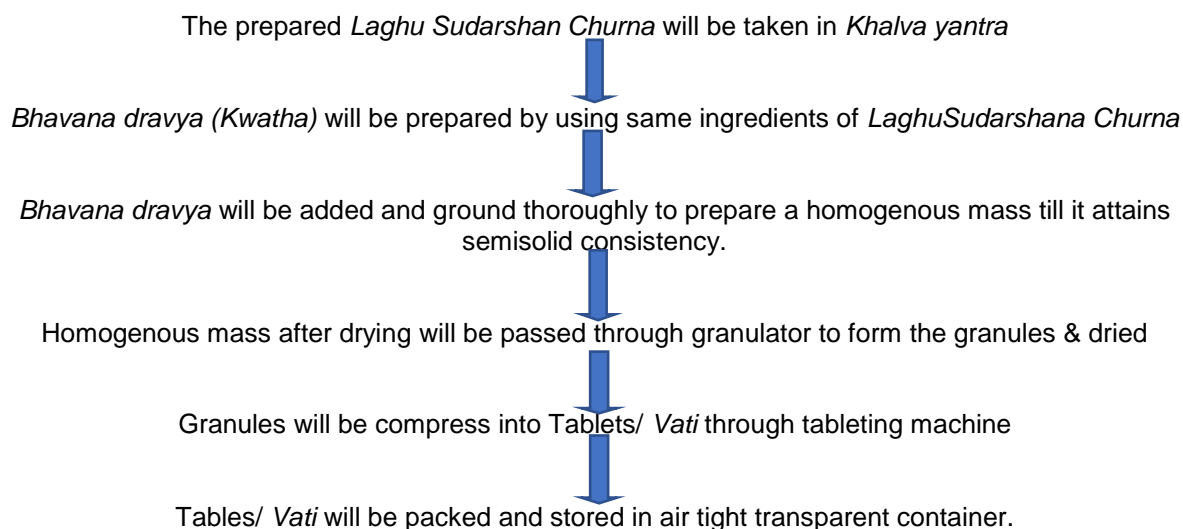
b) Preparation of *Laghu Sudarshan Churna Kwath (decoction)*

Flow chart: 2



c) Pharmaceutical preparation of *Laghu Sudarshan Vati* [9]

Flow Chart: 3



3.3 Analytical Study

Analytical parameters of *Laghu Sudarshan vati* & *Laghu Sudarshan Churna* will be studied with the help of Organoleptic characters such as *Sparsh* (Touch), *Rupa* (Appearance), *Rasa* (Taste), *Gandha* (Odour) & physicochemical parameters such as pH, particle size, loss on drying at 105°C, Acid insoluble ash, Water soluble extractives, Reducing sugar, Total ash, alcohol soluble extractive, test for heavy metals, Microbial contamination, Hardness, Uniformity of weight, Friability, HPTLC and Disintegration time [10-11].

6 albino rats (3 male and 3 female rats, Total 42 Wister albino rats). The grouping of animals are shown in Table no.2 & Table no.3

- To evaluate antipyretic & analgesic activities of test drugs (*Laghu Sudarshan Churna and Laghu Sudarshan Vati*), the most commonly employed method to induce fever in animals is brewers yeast induced pyrexia animal model.
- Being *Laghusudarshan churna* is poly herbal formulation, toxicological study is not included.

3.4 Experimental Study

- To evaluate antipyretic & analgesic activities of *Laghu Sudarshan Churna* and *Laghu Sudarshan Vati* experimental study will be done in 8 groups containing

▪ **Animals will be divided into four groups**

- Group 1: Negative control (NC)
- Group 2: Standard control (SC)
- Group 3: *LaghuSudarshana Churna (LC)*
- Group 4: *LaghuSudarshana Vati (LV)*

Table 2. Grouping of animals (Antipyretic study)

Group	Group code	Drug	No of animal	Dose
Group I	NC	Distilled water	6	2ml
Group II	SC	Paracetamol	6	1.6ml+ Water
Group III	LC	LC	6	0.216mg + Water
Group IV	LV	LV	6	9mg + Water

Table 3. Grouping of animals (Analgesic study)

Group	Group code	Drug	No of animal	Dose
Group I	NC	Distilled water	-	2ml
Group II	SC	Diclofenac sodium	6	0.9mg + Water
Group III	LC	LC	6	0.216mg + Water
Group IV	LV	LV	6	9mg +Water

3.5 Yeast Induced Pyrexia [12]

- Pyrexia will be induced in animals by injecting 20 percent w/v Brewers yeast (10mL/kg) in distilled water under the skin. Before the injection of yeast, the basal rectal temperature will be recorded by inserting a digital clinical thermometer into the rectum to a depth of 2 cm. In 18 hours after yeast injection, the rise in rectal temperature will be measured. Necessary precautions to be taken to avoid pyrogen induced fever.
- Paracetamol Suspension 1.6 ml will be given and used as a standard Antipyretic drug.
- The temperature will be measured at 1st, 2nd, and 3rd hour after administration of drug.
- Following the treatments, the animals rectal temperature will be recorded at regular intervals.
- The percentage reduction in pyrexia will be calculated using the following formula:

$$\% \text{ reduction} = \frac{B - C_n}{B - A} \times 100\%$$

where A is the normal temperature, B is the rectal temperature after 18hr of yeast injection, and C_n is the rectal temperature after 1, 2, 3h.

3.6 Tail Flick Test [13]

- The tail flick test, similar to the Hot Plate test, is a test of animal response to heat that is used to determine basic pain response and the effectiveness of analgesics by observing the animals reaction to heat.
- Most commonly, an intense light beam is focused on the animals tail and a timer is started. The timer ends when the animal flicks its tail, and the recorded time is used to calculate the pain threshold.

3.7 Hot Plate Test [14]

This is accomplished by slightly altering the procedure.

- The rats will be kept on a confined hot plate with a temperature of 55°C + 1°C. The latency is the time it takes for the rats to

respond to the thermal stimulation (typically by jumping) (in seconds).

- The rats will be separated into 4 groups (I-IV). Each group consists of 6 rats. Rats in group III & IV will be given LC & LV orally after 12 hours fast.
- The rats in group I will be given equivalent doses of distilled water (2ml/kg) and Diclofenac sodium (0.9mg) respectively.
- The latency of each rat will be recorded once it is placed on the hot plate. For each group, the mean delay + standard error of the mean (S.E.M.) will be calculated.
- The paw tissues suffer little or no harm as a result of the brief shock induced by the Hot plate surface.

3.8 Study Design

Experimental

3.9 Study Type

Pharmaceutical, Analytical and Experimental study

3.10 Place of Study

- Department of *Rasashashtra* and *Bhaishajya Kalpana* MGACH& RC, Salod (H), Wardha.
- Analytical study will be carried out at *Dattatraya Ayurved Rasashala*, MGACH& RC, Salod (H), and Wardha.
- According to need of study will be carried out at Certified or Standard Institute/Organization/Lab of National Repute and as recognized or recommended by DMIMS (DU).

3.10.1 Inclusion Criteria

Albino rats weight 150-200gm of either sex

3.10.2 Exclusion Criteria

1. Albino rats suffering from any illness or injury, albino rats of less than 150gm & more than 200 gm weight.
2. Pregnant & diseased female albino rats.

3.11 Posology: Dose Calculation [15-16]

Animal dose will be extrapolated from the human dose using the rat conversion factor. The drug doses will be calculated by extrapolating the therapeutic dose to rat dose using the surface area ratio (conversion factor 0.018 for rats) and using the Paget & Barns table as a guide.

4. DISCUSSION

Pharmaceutical study deals with the preparation of suitable dosage form of a drug material, for quality assurance of a finished product. It is necessary to evaluate and discuss the in-process conditions and the data compiled after several repetitions of the same procedure to generate a standard protocol for any formulation. Many infectious and inflammatory illnesses use fever as a proxy sign for disease activity. Inflammatory mediators (cytokines, such as interleukin-1, interleukin-6, tumour necrosis factor, and others) are primarily released by activated peripheral mononuclear phagocytes and other immune cells, according to the traditional view. Paracetamol is a pain reliever that also works as a febrifuge. In the presence of peroxides seen in inflammatory lesions, it is a weak inhibitor of cyclooxygenase [17].

In this study, two widely used screening models for evaluating analgesic activity will be used, i.e., tail flick method in rats and Hot plate test in albino rats and for evaluating antipyretic activity, brewers yeast-induced pyrexia method will be used.

Pyrexia can be caused by infection, tissue injury, graft rejection, inflammation, or disease conditions. Antipyretics are drugs that stimulate the hypothalamus to override an interleukin-induced fever and restore normal levels of temperature. Brewers yeast fever is a pathogenic fever that involves the generation of PGs.

In this study, Brewer's yeast increased the body temperature of rats, and also significantly shortened the onset. The tail flick method of analgesia is highly efficient in determining the effectiveness and strength of centrally acting analgesic drugs [18].

5. CONCLUSION

If this Antipyretic & Analgesic study is successful then this data will be used in another clinical

study for intervention of Antipyretic & Analgesic studies, as it is Herbal medicine so it will show no any toxic effect in animal models. Hence, it will be easily used in humans also.

6. SCOPE AND IMPLICATIONS OF PROPOSED STUDY

6.1 Scope

If *Laghu Sudarshan Churna* shows expected & significant result as Antipyretic & Analgesic will be helpful in conducting clinical trials in human being. *Laghu Sudarshan Churna* can be modified into *Laghu Sudarshan Vati*.

6.2 Implications

Laghu Sudarshan Churna will be used in all type of fever as a Antipyretic & in *Amavata, Shotha* as Analgesic.

6.3 Translatory Component

If this Antipyretic & Analgesic study is successful then this data will be used in another clinical study for intervention of Antipyretic & Analgesic studies.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Animal Ethic committee approval has been taken to carry out this study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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