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 brewers yeast induced pyrexia, Tail flick test & Hot plate test for analgesic in animal models.

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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 form our mother nature to conquer the disease. Bhaishajya means knowledge or Science. It is a significant process which has the potential to cure many diseases in an efficient manner. Ayurveda Chikitsa Chatushpada (Plan of Medicine) i.e. Chikitsa Chatushpada (plans or restore the health of person by stabilizing the disease) is the Process or management through which a disease is not possible. The word therapeutics (medicine) among dosha is the Process or restore the health of person by stabilizing the disease

Bhaishaja or Bhaishajya (medicines). That which wins the fear of disease by stabilizing the dosha is bhesha 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.

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 Yantraor 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 Yogratanakar. This Formulations containts Guduchi, Pippalimula, Pippali, Kark, 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 Gunanatradyanam 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, Sidhha 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 _Yogaratnakar_ 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 Churna_ and _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 lаждification)
- 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 _Laghushudarshan churna_ and their quantity. Below is the flow diagram of method of preparation of _Laghushudarshan churna_ & _Laghushudarshan vati_.

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Table 1. Ingredients of LaghuSuadrshan Churna [5]

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

3.2 Methods

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

Flow Chart: 1

1. Selection of the procured and authenticated drugs as per API
2. All the drugs will be cleaned and removed all the foreign matter
3. All the individual drugs will be weighed properly.
4. All the individual drugs will be powdered using pulvariser
5. The individual drugs will be sieved through mesh no. 80
6. All the drugs will be weighed separately.
7. All the powders will be mixed together by mass mixer
8. The mix formulations will be unloaded and weighed
9. It will be stored in an air tight transparent glass container

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

Flow Chart: 2

1. Dry ingredients in equal proportion will be taken
2. It will be reduced to coarse powder & sieved through 40 no. sieve
3. 4 times of portable water will be added and allowed to soak for overnight in stainless steel vessel & next day morning remaining water will be added.
4. Stainless steel vessel will be subjected to heat & allowed to boil the content until the contents reduced to 1/8th part.
5. The contents will be filtered through sterile cotton cloth to obtain *Laghu Sudarshan Kwath*
c) Pharmaceutical preparation of *Laghu Sudarshan Vati* [9]

Flow Chart: 3

The prepared *Laghu Sudarshan Churna* will be taken in *Khalva yantra*

*Bhavana dravya* (*Kwatha*) will be prepared by using same ingredients of *LaghuSudarshana Churna*

*Bhavana dravya* will be added and ground thoroughly to prepare a homogenous mass till it attains semisolid consistency.

Homogenous mass after drying will be passed through granulator to form the granules & dried

Granules will be compress into Tablets/ *Vati* through tableting machine

Tables/ *Vati* will be packed and stored in air tight transparent container.

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].

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 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.

- 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>
<thead>
<tr>
<th>Group</th>
<th>Group code</th>
<th>Drug</th>
<th>No of animal</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>NC</td>
<td>Distilled water</td>
<td>6</td>
<td>2ml</td>
</tr>
<tr>
<td>Group II</td>
<td>SC</td>
<td>Paracetamol</td>
<td>6</td>
<td>1.6ml + Water</td>
</tr>
<tr>
<td>Group III</td>
<td>LC</td>
<td>LC</td>
<td>6</td>
<td>0.216mg + Water</td>
</tr>
<tr>
<td>Group IV</td>
<td>LV</td>
<td>LV</td>
<td>6</td>
<td>9mg + Water</td>
</tr>
</tbody>
</table>

Table 2. Grouping of animals (Antipyretic study)

<table>
<thead>
<tr>
<th>Group</th>
<th>Group code</th>
<th>Drug</th>
<th>No of animal</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I</td>
<td>NC</td>
<td>Distilled water</td>
<td>-</td>
<td>2ml</td>
</tr>
<tr>
<td>Group II</td>
<td>SC</td>
<td>Diclofenac sodium</td>
<td>6</td>
<td>0.9mg + Water</td>
</tr>
<tr>
<td>Group III</td>
<td>LC</td>
<td>LC</td>
<td>6</td>
<td>0.216mg + Water</td>
</tr>
<tr>
<td>Group IV</td>
<td>LV</td>
<td>LV</td>
<td>6</td>
<td>9mg + Water</td>
</tr>
</tbody>
</table>

Table 3. Grouping of animals (Analgesic study)
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 Cn 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 Kaalpana 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.
REFERENCES


