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IN VIVO STUDY ON HEPATOPROTECTIVE POTENTIAL OF NAGDANTYADI GHRITA IN PARACETAMOL INDUCED HEPATOTOXICITY IN WISTAR RATS

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ABSTRACT

Background: In the literature of Ayurveda there is reference of *Gara Visha* which can be co- related to artificial poison as per modern science. As per Ayurveda, *Gara visha* hampers the normal functioning of *Yakrut* i.e. Liver. Hence *Acharya Charaka* have mentioned *'Nagdantyadi ghrita'*(Polyherbal Medicated butter) in context of management of *Gara visha* (Artificial poison). As per pharma industry estimate, India consumes nearly 1500 tons of paracetamol in a month. Paracetamol, which causes hepato-nephro toxicity with indiscriminate use, is selling without any proper dosage on the strips and bottles. **Material and Method:** Animals required for this study i.e. Wistar rats of both sexes will be taken from Animal house. The dose for the experimental study will be calculated by extrapolating the clinical human dose of *Nagdantyadi ghrita*, standard drug Silymarin and Paracetamol to an animal dose. The subjects will be assessed before and after treatment for liver function test. **Objective:** To examine the therapeutic potential of *Nagdantyadi Ghrita* by analytical study and hepatoprotective action of *Nagdantyadi Ghrita* against hepatotoxicity induced by Paracetamol. **Result:** The Sample of *Nagdantyadi Ghrita* will be subject to Phyto chemical screening and efficacy of Nagdantyadi ghrita as hepatoprotective will be studied.

KEYWORDS: Ayurveda, Artificial Poison, Gara, Visha, Yakrut.

INTRODUCTION

Paracetamol is a kind of drug which is being sold without any Prescriptions. Acetaminophen (Paracetamol) was the most commonly consumed medication worldwide in 2003.[1] Paracetamol, which is a analgesic and Antipyretic sold over the counter in high number in India, is being consumed by large crowd in improper doses to treat fever in both adults as well as children. As per pharma-industry estimate, India consumes nearly 1500 tons of paracetamol in a month. Paracetamol, which causes hepato-nephro toxicity with excess consumption, is selling without any proper dosage on the strips and bottles.[2]

Apart from *Sthawar* (Static) and *Jangam* (Animate) *Visha* (Poison) one more type of Poison is explained in classics of Ayurveda which is '*Gara Visha'* (Artificial poison). It is formed by combination of Non-poisonous substances or from Poisonous substances. Such kind of combinations are able to produce toxic effects/Diseases in the body after ingestion, but Metabolization of such poison takes time to interfere with the physiology of the body hence *Gara* visha poisoning does not kill the patient instantly.[3]

After elaborating *Gara visha* in detail, *Acharya Charaka* have mentioned *'Nagdantyadi ghrita*'(Polyherbal Medicated butter) in context of management of *Gara visha* (Artificial poison), Snake poison, Insect bite.[4] The content of *Nagdantyadi ghrita* are *Nagdanti* (Croton oblongifolius), *Nishoth* (Operculina turpethum linn.), *Dantimool* (Baliospermum montanum), *Dravanti mool* (Croton tinglum), Snuhi/Sehund (Euphorbia neriifolia), Mainfal/ *Madanfa l* (Randia dumetorum lam), *Gomutra* (Cows urine), *Maahish Sarpi* (Clarified Butter prepared from Buffalos milk).

The literature of *Nagdantyadi ghrita* explore about the mechanism of action of its content. Various drugs mentioned in this poly-herbal formulation are purgative, anti-inflammatory, digestive etc. in nature which helps to get rid of the poisons as soon as medication is given to sufferer. As mentioned earlier by *Acharya Charak* that Metabolization of *Gara visha* takes time hence above stated properties of this formulation helps to manage the overload of toxins on liver and preventing the sufferer from various diseases or harmful effects of *Gara visha*.

According to Acharya Sushruta, the *utpatti* (Origin) of *Yakrut* and *Pleeha* is by *Rakta* (Blood).[5] Its functions are mainly ascribed towards *Rakta*. *Yakrut* and *Pleeha* are considered as the *moola* of *raktavaha-srotas*. From the above description, one can infer that *Yakrut* and

Rakta have a (*Samavaya)* relation. Therefore, vitiation of *Rakta* will also result in derangement in the functions of *Yakrut* and vice versa.[6]

Liver plays a crucial role in regulation of physiological processes. The liver is the soft target organ for the effect of toxic compounds because of its structure, role in intermediary and xenobiotic metabolism, position and function. Indiscriminate uses of drugs like tetracycline, acetaminophen, anti-tubercular drugs, oral contraceptives of hormonal origin, food preservative and agrochemicals are threatening to the liver.[7]

MATERIAL AND METHOD

Nagdantyadi Ghrita (Test formulation)- *Nagdanti* (Croton oblongifolius), *Nishoth* (Operculina turpethum linn.), *Dantimool* (Baliospermum montanum), *Dravanti mool* (Croton tinglium), Snuhi/Sehund (Euphorbia neriifolia), Mainfal/ *Madanfa l*(Randia dumetorum lam), *Gomutra* (Cows urine), *Maahish Sarpi* (Clarified Butter prepared from Buffalos milk) and Paracetamol (Acetaminophen) etc. will be used in the proposed study.

Classical method of preparation of *nagdantyadi ghrita*

नागदन्ती त्रिव्रूतदन्ति द्रवन्ती स्नुकपय: फ़लॅ:।

साधितं माहिष सर्पिः सगोमुत्राढकं हितम॥

सर्पकिटविषार्तानां गरार्तानां च शान्तये।

च. चि. २३/२४१.

First of all *Nagdanti* root, *Trivrit* root, *Dravanti* root and *Madanphal* has to be taken in equal amount after that *Snuhi ksheer* is to be added to it to make paste of one *kudav* (192 gm) which later on need to be processed with one *prasth ghrit* (768 ml*)* and one *adhak gomutra* (3072ml) to obtain *Nagdantyadi ghrita.* Purification of drugs needs to be done if necessary before using for *Ghrita* preparation)

Sr. No.	Drug name	Useful parts	Quantity
1	*Nagdanti*	Root	Equal quantity (One Kudav (192gm) Paste is to be Prepared)
2	*Dravanti*	Root	
3	*Madanphal*	Root	
4	*Snuhi*	*Ksheer* (Milk)	
5	*Trivrit*	Root	
6	*Danti*	Root	

7	*Ghrita*	*Ghrita*	One *Prastha* (768ml)
8	*Gomutra*	*Gomutra*	One *adhak* (3072 ml)

All the crude drugs of *Nagdantyadi Ghrita* has to be taken in equal quantity *and Ghrita* has to be prepared as per *Ghrita Kalpana vidhi* by standard protocol and this prepared *Ghrita* is going to use for further analysis. Physico-chemical study and Phytochemical screening of *Nagdantyadi Ghrita* need to be carried out. These studies are useful for deciding the identity, purity and strength of the *Nagdantyadi Ghrit.*

Experimental study

This study is aim to be conducted as per OECD guideline. Animals required for this study i.e.

Inclusion criteria: Wistar rats of both sexes weighing between 150-250 gm needs to be taken from Animal house for the study.

Exclusion criteria: Pregnant wistar rats are not allowed to be taken for the present study

Grouping[8]

Group A (Control group)	Animals have to be treated with distilled water only. No intervention is in this group.
Group B (Toxic Group)	Animals have to be treated with PCM only.
Group C (Standard control group)	PCM along with standard drug Silymarin has to be given
Group D (Test group)	PCM along with test drug N.G.(Rat dose equivalent to therapeutic human dose) has to be given.
Group E (Test group)	PCM along with test drug N.G.(Rat dose double of the therapeutic human dose) has to be given.

Dose: The dose for the present study has to be calculated by extrapolating the clinical human dose of *Nagdantyadi ghrita*, standard drug Silymarin and Paracetamol to an animal dose based on body surface area ratio by using conversion.[9] Animal needs to be acclimatized for 7 days prior beginning of study with 12 hours of night and 12 hours of day exposure. Animals need to be fed with food supplies from animal house and tap water.

Treatment protocol: Test drug *Nagdantyadi ghrita* (N.G.), tap water and Reference drug (Silymarin) has to be given orally for 9 consecutive days and then one dose of toxicant i.e. Paracetamol (PCM) will be given po (per oral) to each group except water control group on 7^{th} day one hour after the test drug administration. Then after 48 hours of paracetamol dose, blood will be collected in the tubes and will be sent for further biochemical investigations after sedation of animal. After that animals in each group has to be sacrificed for histopathological examination.[8]

Study duration- 21 Days.

Screening parameters: all animals from all groups have to be screened for following parameters.

- Liver Function Test (SGPT, SGOT, ALP, Total Bilirubin, Direct Bilirubin).
- All investigations has to be done before and after Experiment.

Analysis plan (Statistical test)

Statistical analysis hast to be done by applying suitable tests. (T test, One way ANOVA test)

RESULTS AND DISCUSSION

The Sample of *Nagdantyadi Ghrita* has to be subject to Phytochemical screening. Organo leptic characters along with physicochemical parameters need to be studied. Many studies revealed that medicinal plants have potential to manage the extra workload of liver by decreasing the severity of toxic signs and symptoms. Very few Herbal medications are available to use for the purpose of Hepatic protection. *Nagdantyadi Ghrita* could be the best remedy for it. As drugs of *Nagdantyadi Ghrita*, being easily available, they are widely mentioned in many antitoxic classical preparations. And when one see the individual drugs of *Nagdantyadi Ghrita*, these drugs are beneficial to counteract the harmful workload of liver i.e hepato-protective activity. But there is no work found in reference of *Nagdantyadi Ghrita* w.r.t. Hepato-protective activity. Hence Present study is preferred to validate the Statement of *Acharya* Charaka.

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