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STANDARDIZATION OF VEDANASTHAPANA GANA RASAKRIYA TO EVALUATE ITS ANALGESIC ACTIVITY PRECLINICALLY

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ABSTRACT

Vedanasthapan gana mentioned by *Acharya Charaka* in *Charaka Samhita Sutrasthana* 4/17 is prescribed for the painful condition in *Ayurveda.* But there are very few reports in the literature regarding the systematic evaluation of this *gana* to explore its analgesic potential. The analgesic efficacy Was evaluated by Eddy's hot plate method in Wister rats of either sex. In Eddy's hot plate method *Vedanasthapana gana* extract in the doses of low and high doses [50 and 100 mg/kg], significantly prolonged the reaction time (latency) in rats at 60 and 90 minutes as compared to control ($p<0.01$). While Pentazocine showed significant findings from 30 minutes onwards ($p<0.01$) when compared to control, which suggests that it elicits analgesic activity through its action on central pain receptors. The onset of its analgesic effect after administration was seen at 30 minutes, which peaked at 60 minutes and lasted beyond 90 minutes. It could be recommended as a supplemental add-on to drugs used to manage chronic pain conditions like arthritis. It may help to decrease the dose and associated dose-dependent adverse effects of other drugs.

Keywords: Vedanasthapan gana, analgesic, eddy's hot plate, pain.

INTRODUCTION

Pain is an unpleasant sensation no doubt, but on the whole, it is usually not beneficial to man and animal. It is a mainly protective mechanism for the body, occurs whenever any tissues are being damaged, and it causes an individual to react to remove the pain stimulus.

Typically, pain is a direct response to an untoward event associated with tissue damage, such as injury, or inflammation. But severe pain can arise independently of any obvious predisposing causes (e.g., Trigeminal neuralgia or persistent long after the precipitating injury has healed, Phantom limb pain). It can also occur as a consequence of brain or nerve injury (following a stroke or herpes infection). With many pathological conditions, tissue injury is the immediate cause of pain, and this results in the local release of a variety of chemical agents which are assumed to act on nerve terminals either activating them directly or enhancing their sensitivity to other forms of stimulation.

Chronic painful conditions are a few of the oldest known diseases of mankind and the majority of the population. No substantial progress has been made in achieving permanent relief of these conditions. Although a number of potent synthetic drugs are available, their toxic effects pose a limitation to continuous use. Modern medications for pain relief provide only symptomatic relief and are associated with adverse drug reactions. So there is a need for safe and effective agents to substitute or supplement modern medications.

Vedanasthapan gana mentioned by *Acharya Charaka* in *Charaka Samhita Sutrasthana* 4/17 is prescribed for the painful condition in *Ayurveda*. But there are very few reports in the literature regarding the systematic evaluation of this *gana* to explore its analgesic potential. Hence studies were undertaken to evaluate its analgesic efficacy by using experimental models of rats.

In this study, we have observed the effect of *Vedanasthapana gana rasakriya* in the therapy of painful conditions like arthritis, gout, etc., If proved effective, it may be possible to reduce the usage of modern medicines with the advent of alternative drugs like *Vedanasthapana gana*. Therefore, the search for a better analgesic agent is ongoing. More and more research is being focused on developing drugs from indigenous medicinal plants as well as developing safe and effective formulations to improve quality of life.

MATERIALS AND METHODS

Experimental animals:

The animals used in this study were procured from the animal house of Bombay Veterinary college & P.G. institute, Parel, Mumbai. The study was carried out on rats of either sex (male or female) weighing between 170-250 g.

The animals were randomly divided into 4 groups with 6 animals in each group. Animal identification was done by cage number and individual marking on the tail.

Accommodation and Feed

I. Experimental rats (6 per cage) were housed during acclimatization and treatment [approx. sized 1.290x W220 x 1+140 mm]. The cages were of stainless-steel top grill having facilities.

II. Animals were fed with commercially available rat pellet feed. The nutrition provided by the pellet feed was as follows:

Energy-3620 kcal, crude protein-22.15%, crude fiber-62.48%, ash-5.11%, sand silica-1.15%. Aqua guard pure water was provided to the rats through the feeding bottles with stainless steel nozzle in each cage. Food and water were replenished once daily.

Drug administration:

According to *Ayurveda, Vedanasthapana gana rasakriya* formulation is administered on a full stomach. The animals were fed by *Vedanasthapana gana* formulation only on a full stomach.

Routes of administration:

Vedanasthapana gana Raskriya formulation has been administered orally. It was dissolved in 0.5% Carboxy Methyl Cellulose (CMC) that was prepared by dissolving 100 mg of Carboxy Methyl Cellulose powder in 20 ml of distilled water.

The vehicle control group received Distilled water orally.

Pentazocine standard drug was given in the dose of 5.4mg/kg body weight, intraperitoneal (i. p.).

Dose levels:

The doses of which were computed from the doses documented in the Ayurvedic and standard textbooks. (Nayak B., 2010)

i. Doses of the trial group were listed below -

Vedanasthapan gana Raskriya formulation 1st dose- 50 mg/kg p. o. (10 mg/200g rat)

Vedanasthapan gana Raskriya formulation 2nd dose- 100 mg/kg p. o. (20 mg/200 g rat**)**

ii. Standard control: Pentazocine-

Dose in Rat- 5.4 mg/kg p. o (1.08 mg/200 g rat)

Study groups:

The experimental groups in each model were as follows:

[n =6 animals in each group.]

Group 1: Vehicle Control [Distilled Water]

Group 2: Standard Control [Pentazocine]

Group 3: *Vedanasthapana gana formulation* 1st dose [Low Dose]

Group 4: *Vedanasthapana gana formulation* 2nd dose [High Dose]

The samples of *Vedanasthapana gana* were obtained from the local market. The certificate of analysis was approved by the Yerala medical trust Department of *Dravya guna*.

Self-made preparation of *Vedanasthapana gana Raskriya* formulation was used.

Evaluation of analgesic activity

Eddy's Hot Plate Method [Vogel GH, 2002]

Wistar rats of either sex weighing between 170-250 g were used for each dose. The commercially available Eddy's hot plate consists of an electrically heated surface. The temperature is controlled at 55-56 °C. Each rat was individually placed on a hot plate and the time until either licking or jumping occurs is recorded by a stop watch, only those rats which were reacted in 5 seconds were selected. The latency was recorded before and after 20, 60, and 90 minutes following oral administration of the test compound and the standard drug. The rats should not be placed on a hot plate for more than 30 seconds [cut-off time] to avoid damage to the paw. The procedure was repeated at 30, 60, and 90 minutes.

The values of prolongation of latency time of experimental groups were compared with the control group for statistical analysis.

Statistical analysis

The data was compiled and analyzed by using the Statistical Package for Social Sciences (SPSS) for Windows version (16.0) was used to analyze the data (SPSS Inc., Chicago, IL). Results are expressed as Mean ± SD and statistical significance between means was analyzed using one-way analysis of variance (ANOVA). A value of $p<0.05$ was considered statistically significant.

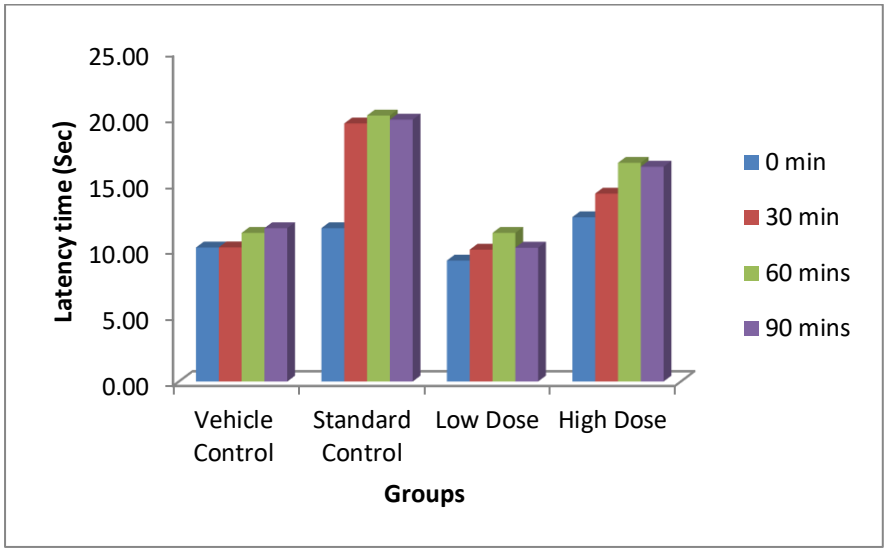
RESULTS

Vedanasthapan gana extracts in the doses of low and high doses [50 and 100 mg/kg], significantly prolonged the reaction time (latency) in rats at 60 and 90 minutes as compared to control ($p<0.01$). While Pentazocine showed significant findings from 30 minutes onwards ($p<0.01$) when compared to control.

Table 1: Eddy's hot plate method latency intervals:

	Latency time (seconds)			
Group	**0 min**	**30 min**	**60 min**	**90 min**
Vehicle Control	10.17± 0.08	10.18±0.07	11.28±0.26	11.64±0.50
Standard Control	11.64±0.50	19.58±0.38*****	20.18±0.74*****	19.87±0.52*****
Vedanasthapan gana formulation [Low dose]	9.18±0.20	10.00±0.31	11.28±0.26	10.16±0.76
Vedanasthapan gana formulation [High Dose]	12.47±0.62	14.26±0.78*****	16.60±0.54*****	16.30±0.47

*****$p<0.01$, when compared with the vehicle control group



Eddy's hot plate method latency intervals.

DISCUSSION

The present study was undertaken to evaluate the analgesic efficacy of *Vedanasthapan gana* to establish, its yet another therapeutic potential. This study involved the use of well-established animal models of pain to confirm its analgesic efficacy. Eddy's hot plate method for evaluating the central action is believed to be reliable and one of the most widely used. The results from the present study showed that *Vedanasthapan gana* has analgesic efficacy comparable to standard.

Vedanasthapan gana treatment significantly prolongs the reaction time on heat stimulus and mechanical stimulus; that suggests that the treatment of *Vedanasthapan gana* elicits analgesic activity through its action on central pain receptors. There was significant drowsiness observed in the test rats treated with the same. It can provide a sense of well-being like a central effect.

This work scientifically confirms the traditional, folk, and preliminary claims of *Vedanasthapan gana* for its analgesic activities. This is also a step ahead in the direction of increasing the number of marketable drugs with traditional backgrounds with modern and scientific standards. Like most *ayurvedic* drugs, it has been used for ages by *ayurvedic* physicians and no serious adverse effect or drug reaction has been reported so far. Additional advantages of being cheap and easily available are added benefits.

The burden of unwanted side effects with the various groups of drugs that are used to alleviate pain in allopathic medicine (as mentioned in the literature survey) could be reduced if *Vedanasthapan gana* is used supplemental to the present analgesic regime. The *Vedanasthapan gana* could be especially advantageous in treating painful conditions with inflammation like arthritis along with traditional allopathic analgesic regimens. Moreover, it's supplemental use with analgesics would also result in a reduction of dose and side effects of the primary analgesic agents leading to better patient compliance and tolerability. Thus, the results obtained in this study indicate that *Vedanasthapan gana* possesses potent analgesic properties, which are mediated via central inhibitory mechanisms. Moreover, if the present finding could be confirmed in a clinical situation, then there may be a possibility to develop a novel analgesic drug from the treasure of our traditional system of medicine. Future studies can be done by extracting the chemical components from *Vedanasthapan gana* (an individual component) responsible for its analgesic efficacy. However, further molecular pharmacological studies

to find out the specific receptors involved and other biochemical investigations are needed to unwind its cellular mechanisms.

CONCLUSION

From the present study, we can conclude that *Vedanasthapana gana* exhibited an analgesic effect at test doses of 50 mg/kg and 100 mg/kg which may be mediated by central receptors. The onset of its analgesic effect after administration was seen at 30 minutes, which peaked at 60 minutes and lasted beyond 90 minutes. It could be recommended as a supplemental add-on to drugs used to manage chronic pain conditions like arthritis. It may help to decrease the dose and associated dose-dependent adverse effects of other drugs. In addition, it has anti-ulcer properties comparable to Pentazocine so it can reduce the possibility of ulcers on chronic use. Moreover, the additional advantage of being cheap and easily available is an added benefit with *Vedanasthapana gana*.

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