Assessment of *Trisama*, an ayurvedic formulation on intestinal transit time in swiss albino mice

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Abstract

Background: *Trisama* is an Ayurvedic formulation that can be prescribed for wide range of disorders, especially abdominal disorders such as indigestion, constipation and flatulence. *Trisama* is prepared by mixing an equal quantity of powder of *Shunthi* (*Zingiber officinale* Linn.), *Haritaki* (*Terminalia chebula* Retz.) and *Guduchi* (*Tinospora cordifolia* [Willd.] Miers.). As a single ingredient, *Haritaki* is an alternative to prokinetic drugs, *Guduchi* for intestinal motility and *Shunthi* for digestion-related problems. **Materials and Methods:** The present study aims to evaluate the effect of *Trisama* dosage forms on intestinal motility by adopting kaolin expulsion test in Swiss albino mice. *Trisama* powder (0.65 and 1.3 g/kg) and *Trisama* decoction (12.48 ml/kg) were administered and intestinal transit time of kaolin and latency of onset of kaolin expulsion in fecal matter was assessed. **Results:** Both the dosage forms of *Trisama* shortened the intestinal transit time of kaolin. However, the observed effects were statistically significant in *Trisama* powder at higher dose and *Trisama* decoction in comparison to control group. The behaviors of mice and consistency of fecal pellet were almost the same as observed in normal control group. **Conclusion:** From the present study, it is concluded that *Trisama* has significant intestinal motility-enhancing property in mice which may be useful in gastric problems without affecting the general physiology.

Keywords: Intestinal transit, kaolin, purgative, *Trisama* decoction, *Trisama* powder

Introduction

The sages in olden days were mainly involved in experimenting the different kinds of herbs and then the preparation of Ayurvedic formulations as per the specific methods. Ayurvedic pharmaceutics named *Bhaishajya Kalpana* is quite extensive. These concepts are not receiving sufficient consideration while formulating Ayurvedic drugs. The study on each medicinal plant in depth, along with its Ayurvedic properties, should be taken into account for designing the Ayurvedic formulations. The herbal drugs are characterized for polyvalent actions through active phytochemical constituents of individual plants. When combining the multiple herbs in a particular ratio, interpreted additives or in some cases they synergistically produce the observed therapeutic effect rather than insufficient to achieve the desirable therapeutic effects by a single drug.[1] *Trisama*[2] is one of such polyherbal Ayurvedic formulations and can be prescribed for a wide range of disorders, especially metabolic disorders, abdominal problems such as indigestion, constipation and flatulence. *Trisama* is prepared by mixing an equal quantity of powder of *Shunthi* (*Zingiber officinale* Linn), *Haritaki* (*Terminalia chebula* Retz.) and *Guduchi* (*Tinospora cordifolia* [Willd.] Miers.). *Trisama* is credited with diverse beneficial properties and has been reported to possess many pharmacological properties which may be due to *Ushna Virya* (warm potential) and *Madhura Vipaka* (postdigestive effect in sweet taste) of the ingredients. The drugs with such properties may have the effects such as *Dahana* (heat), *Virechana* (therapeutic purgation), *Pachana* (digestion of food), *Vilayana* (solution or internal mixing) and *Srishtavinmutra* (easy release of feces and urine).[3]

According to an ethnopharmacological activity of a single ingredient, *Haritaki* can serve as a useful alternative to prokinetic drugs.[4] *Guduchi* is proved effective on intestinal motility[5] and *Shunthi* also has an effect on

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Quick Response Code:

Website: www.ayujournal.org

DOI: 10.4103/ayu.AYU_33_18

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How to cite this article: Patel AG, Patel MR, Nariya MB. Assessment of *Trisama*, an Ayurvedic formulation on intestinal transit time in Swiss albino mice. Ayu 2018;39:46-9.

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digestion-related problems.[6] Ingredients of *Trisama* possess wide range of pharmacological properties, such as antioxidant, anti-inflammatory, antipyretic, analgesic, antimicrobial, hypolipidemic and gastroprotective activity.[7] Although there is a very wide use of *Trisama* formulation in GI tract related disorders but, till date, no any pharmacological study is reported on *Trisama* formulation. Therefore, the present experimental study was designed to evaluate the effects on intestinal motility of *Trisama* powder and decoction dosage forms in Swiss albino mice. It is well established that the drugs having purgative property are supposed to increase intestinal motility;[8] hence, the effect of test drug on intestinal transit time of kaolin was evaluated in mice.

Materials and Methods

Test drugs and chemicals

The fresh cultivated ingredients of *Trisama* (*Shunthi, Haritaki,* and *Guduchi)* were collected from Mangrol and near places, Surat, Gujarat, India, during October to November 2017 after careful identifications. The plant materials were authenticated, and voucher specimens of each drug is submitted to the pharmacognosy laboratory of the institute. Drugs were dried properly by shade drying and stored in an airtight container. The powders of dried rhizome of *Shunthi*, fruit of *Haritaki*, and stem of *Guduchi* were prepared separately as per the classical procedure[9] and passed through a mesh sized 120, to get fine powder of *Trisama*. The *Trisama* powder (*Churna*) was prepared by mixing these three ingredients in equal proportion. *Trisama Kwatha* (decoction) was prepared by mixing coarse powder of *Z. officinalis, T. chebula* and *T. cordifolia* in equal proportion. Coarse powder (48 g) of mixture was taken and 768 ml of water was added and was boiled on low-to-medium heat till the water portion was reduced to 1/8th of the original volume (96 ml) and was filtered.[10]

Animals

Swiss albino mice of either sex weighing 30 ± 5 g were procured from the Animal house attached to Pharmacology Laboratory of the Institute. Animals were housed in polypropylene cages with standard husbandry conditions and reared under a standard condition of temperature and humidity, and exposed to 12 h light and dark cycles. They were fed with standard pellet feed of "Amrut brand" supplied by Kewal Sales Cooperation, Vadodara, Gujarat, India, and drinking water was given *ad libitum*. The mice were acclimatized for 1 week before commencement of the experiment. The institutional animal ethics committee had approved the experimental protocol (Approval number; IAEC/22/2017/10) as per the guideline of committee for the purpose of control (CPC) and supervision of experiments on animals (SEA), India.

Dose fixation

The dose of *Trisama* has not been given in literature; therefore, standard dose of powder (5 g) and decoction (96 ml) as per the classical literature was selected as therapeutic dose,[11] and the dose for the mice was calculated on the basis of body surface area ratio by referring the standard table of Paget and Barnes.[12] The mouse dose was calculated as 0.65 g/kg as therapeutic equivalent dose [TED] and 1.3 g/kg (TED × 2) for *Trisama* powder and 12.48 ml/kg (TED) for *Trisama* decoction. The *Trisama* powder was suspended in distilled water with suitable concentration depending on the body weight and was administered orally with the help of an oral catheter.

Experimental design

The selected animals were divided into four groups of six each comprising three male and three female animals.

The Group I served as control and received distilled water (10 ml/kg, po). Groups II and III were administered with *Trisama* powder orally at the two dose levels of 0.65 and 1.3 g/kg, respectively. Group IV was administered with *Trisama* decoction orally at the dose of 12.48 ml/kg. The test formulations were administered to overnight-fasted animals. The effect of the formulation on intestinal transit time was carried out based on the previous study.[13] One hour after drug administration, 0.1 ml of 40% (w/v) kaolin solution was administered to all the animals with the help of an oral catheter. The animals were placed in a transparent arena and were carefully observed for the beginning of the kaolin expulsion which begins in the form of white-colored fecal pellets. The onset time of kaolin expulsion in fecal pellet was recorded for each mouse.

Statistical analysis

The data were expressed as mean ± standard error of mean. The significance of differences among the groups was assessed using one-way analysis of variance followed by Dunnett's multiple *t*-test. $P < 0.05$ was considered statistically significant.

Results and Discussion

Trisama powder at a higher dose (17.14%) and *Trisama* decoction (11.71%) shortened the intestinal transit time of kaolin in mice compared to control group, which indicates the increase in intestinal motility in treated groups of mice [Table 1]. Observed effects were statistically significant in *Trisama* powder at a higher dose (1.3 g/kg) and *Trisama* decoction (12.48 ml/kg) compared to control group. The consistency of fecal pellet was almost the same as observed in normal control group. Further, the drug did not affected the general behavior of Swiss albino mice compared to control group.

Table 1: Effect of different dosage forms of *Trisama* on intestinal transit time

Groups	Dose	Kaolin pellet expulsion time (min)	Percentage change
Control	-	402.50±21.51	--
Trisama Churna	0.65 g/kg	395.60±13.50	01.71↓
Trisama Churna	1.3 g/kg	309.20±15.48*	17.14↓
Trisama Kwatha	12.48 ml/kg	346.40±06.25*	11.71↓

Data: Mean±SEM; ↓: Decrease; *P<0.05 when compared with control group (ANOVA followed by Dunnett's multiple *t*-test). SEM: Standard error of mean, ANOVA: Analysis of Variance

A number of methods are available to check intestinal transit time of drugs such as red phenol, dye and movement of charcoal, which have been instilled into the stomach or intestinal lumen of conscious animal to travel along the length of small intestine. For checking of traveling time of charcoal, it is necessary to sacrifice the animals at different time intervals. As it was difficult to assess *in vivo* movement of the drug, it was thought useful to administer a marker, which causes color change of fecal matter and does not alter the effect of drug. Further, to avoid the sacrifice of animals as per the ethical guideline, noninvasive method previously developed in the department is used known by kaolin expulsion which is used to test the effects of test drugs on intestinal transit in mice. Kaolin is a native aluminum silicate and has traditionally been used internally to control diarrhea; it is reported that kaolin is insoluble and it is not absorbed into bloodstream. Instead, it acts locally in the intestines, where it absorbs toxins and relieves mild diarrhea.[14] Therefore, it is not generally associated with toxicity.

In the classical literature, it has been clearly mentioned that *Virechana* (purgation) can be given as a curative, preventive, and health promotion measure.[15] This may be brought about by subtle changes in physiological, biochemical and immunological activities at molecular level. There are three types of *Virechana* (purgative) drugs described in literature,[16] viz., *Mridu Virechana* drugs, which cause lesser degree of purgation, e.g., *Trivrit* (*Operculina turpethum* R. Br.); *Madhyama Virechana* drugs, which cause moderate degree of purgation, e.g., *Aragvadha* (*Cassia fistula* Linn.) and *Tikshna Virechana* drugs which cause drastic purgation, e.g., *Snuhi* (*Euphorbia nerifolia* Linn.). In pharmacology, the drug action is quite often correlated with its chemical structure or active principle. In Ayurveda, the drug action is attributed to certain principles/doctrines, namely *Rasa* (taste), *Guna* (properties), *Virya* (potency), *Vipaka* (postdigestive effect) and *Prabhava* (action) of the active principles of the drug. These five basics are known as *Rasapanchaka* (Ayurvedic properties). The substances, such as food or drug (*Dravya*), act by its innate qualities of *Rasapanchaka* (Ayurvedic properties) and each Ayurvedic property of drug has its unique effects. *Acharya Charaka* described *Rasapanchaka* (Ayurvedic properties) and their importance in therapeutics in detailed while; *Acharya Sushruta* described few properties and importance of *Madhura Vipaka* and *Ushna Virya* and their actions with their therapeutic uses.

Both *Madhura Vipaka* and *Ushna Virya* have their own effect while mutually have a common action of *Virechana* (therapeutic purgation). *Ushna Virya* pacifies *Kapha* and *Vata* and aggravates *Pitta Dosha* which causes the effects such as *Pachana* (digestion of food), *Virechana* (therapeutic purgation) and *Vilayana* (solution or internal mixing). *Madhura Vipaka* is *Snigdha* (unctuous) and *Guru* (heavy) and acts as *Kapha Vardhaka* (increases Kapha), *Shukrala* (aphrodiasic) and *Srishtavinmutra,* i.e., easy release of *Mala* (excreted feces) and *Mutra* (urine).[12]

As per the modern concept, the observed effect may be due to interference with local stimulant effect on motility or acceleration of gastric emptying. The neural regulation of gastric motility involves stimulation by cholinergic neuron inhibition by adrenergic neurons. Antagonist of D2 and 5-HT3 receptors as well as agonists of 5-HT4 receptors can stimulate gastric motility.[17,18] Some drugs increase the motility of intestine by modifying fluid dynamics of the mucosal wall and may cause fluid accumulation in lumen.

In the present study, *Trisama* powder and *Trisama* decoction shortened the duration of expulsion of kaolin in mice. The observed shortening of duration may be due to the properties of *Ushna Virya* and *Madhura Vipaka* Ayurvedic properties of *Trisama*. Further, as per the modern concept, *Trisama* enhancing the intestinal motility may be due to cholinergic stimulation or stimulation of 5-HT4 receptors; it is also possible that it may be antagonizing the effect of sympathetic system. Another probable mechanism is stimulation of the enteric nervous system. It may not be affecting the fluid dynamics because the test drug did not change the consistency of the expelled fecal matter to a significant extent.[19]

Conclusion

Trisama powder at 2 times human therapeutic equivalent dose, i.e., 10 g/d and *Trisama* decoction 96 ml/d (human dose) have significant intestinal motility-enhancing property in mice which may be useful in gastric problems such as constipation and abdominal pain, without affecting the general physiology.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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