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Evaluation of antipyretic activity of "Anjanavaerathichooranam" in yeast induced pyrexia: A critical analysis

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Abstract
The practice of herbal medicine dates back to the very earliest period of known human history - There is evidence of herbs used in the treatment of diseases and for revitalizing body system in almost all ancient civilization. Ayurveda, the Science of Life, has provided a rational basis for treatment of various ailments. Pain, inflammation and fever are common complications in human beings – In this paper, the autors have analysed how antipyretic activity of "Anjanavaerathichooranam" in yeast induced pyrexia are used in curing the disease.

Keywords: herbal medicine, anjanavaerathichooranam, pyrexia, antipyretic, activity

Introduction

The practice of herbal medicine dates back to the very earliest period of known human history. There is evidence of herbs have been used in the treatment of diseases and for revitalizing body system in almost all ancient civilization. Ayurveda, the Science of Life, has provided a rational basis for treatment of various ailments. Pain, inflammation and fever are common complications in human beings.

Pyrexia or fever is caused by a secondary impact of infection, malignancy or other diseased states; wherein there is abrupt increase the core temperature above the normal level (Math *et al*., 2011) [20]. It is the body's natural defence to create an environment where the infectious agent or damaged tissue cannot survive (Chattopadhyay *et al*., 2005) [7, 21]. Normally the infected or damaged tissue initiates the enhanced formation of pro-inflammatory mediator's (cytokines like interleukin 1a and TNF- a) which increase the synthesis of prostaglandin E2 (PGE2) near peptic hypothalamus area and thereby triggering the hypothalamus to elevate the body temperature (Spacer and Breder, 1994) [8]. The regulation of body temperature requires a delicate balance between the production and loss of heat. As the temperature regulatory system is governed by a nervous feedback mechanism, so when body temperature becomes very high, it dilates the blood vessels and increases sweating to reduce the temperature; but when the body temperature becomes very low hypothalamus protect the internal temperature by vasoconstriction. The hypothalamus regulates the set point at which body temperature is maintained. In fever, this set point is elevated and a drug like paracetamol does not influence body temperature when it is elevated by factors such as exercise or an increase in ambient temperature (Ashokkumar *et al*., 2010).

Several plants and their products are claimed and proved to possess antipyretic property (Nanda *et al*., 2009) [27, 42]. Although the body surface temperature is ordinarily measured in clinical practice, it is the body core temperature which is physiologically important. The rectal temperature (which reflects the core temperature closely) is about 0.6ºC higher than oral temperature and about 1.4ºC higher than axillary temperature. The accepted normal limits of rectal temperature in adults are 36.1ºC and 37.8ºC; the body temperature is higher in infants. If the core temperature rises by more than a few degrees in man, mental changes occur. It is well known that an individual with the high fever is often confused and delirious. The working of many tissue enzymes is also adversely affected and, hyperpyrexia may result in death. However, core temperature below 40.5ºC is tolerated by most individuals (Satoskar *et al*., 2010) [28, 43].

A natural antipyretic agent with reduced or non- toxicity is essential. Further, as health care costs continue to escalate, the attraction for low-cost remedies has stimulated consumers to re-evaluate the potential of alternatives (Chattopadhyay and Arunachalam, 2005; Valarmathi *et al*. 2010; Jaiswal *et al*., 2011) [7, 21, 22, 23]. Therefore the present study was undertaken to investigate the antipyretic properties of the Anjanavaerathichooranam.

Requirements

Animal: Wistar albino rats weighing 180-200 g
Drugs and chemicals: Injection of 20 % w/v of brewer's yeast (10 ml/kg) Anjanavaerathichooranam.

Experimental animals

Wistar albino rats were weighed (180-200 g) were procured from K.M.College of Pharmacy, Madurai. The animals were housed in the departmental animal house under standard conditions (26 ± 2°C and relative humidity 30-35%) in 12 hours light and 12 hours dark cycle respectively for 1 week before and during the experiments. Animals were provided with standard rodent pellet diet and had the free excess of water. The composition of diet is 10% protein, 4% Arachis oil, 1% fibres, 1% calcium, 1000 IU/gm vitamin A and 500 IU/gm vitamin D. All the animals were acclimatized to the laboratory conditions prior to experimentation. All the experiments were conducted between 10.00 and 17.00 hr and were in accordance

with the ethical guidelines of the CPCSEA.

Treatment protocol

Body weights of the animals were recorded, and they were randomly divided into five groups of 6 animals each as follows:

- Group I: Animals served as control normal saline 10 ml/kg)
- Group II: Animals were treated with yeast via subcutaneous injection (10 ml/kg).
- Group III: Animals were administered with yeast (10 mL/kg) and the standard drug paracetamol 150 mg/kg b.w.), orally
- Group IV: Animals were administered with yeast (10 mL/kg,) and received 200mg/kg of Anjanavaerathichooranam dissolved with 2ml sterile water and administered through orally.
- Group-V Animals were administered with yeast (10 mL/kg,) and received 400mg/kg of Anjanavaerathichooranam dissolved with 2ml sterile water and administered through orally.

Antipyretic Activity: (**Yeast induced pyrexia method)**

A suspension of Brewer's yeast (15%) in saline (0.9%) was prepared. Five groups, each containing six rats of either sex were taken. The thermocouple was inserted 2 cm deep into the rectum and the rectal temperatures were recorded. Pyrexia was induced by subcutaneous injection of 20% w/v of brewer's yeast (10 ml/kg) in distilled water. The basal rectal temperature was measured before the injection of yeast, by inserting the digital clinical thermometer to a depth of 2 cm into the rectum. The sight of injection was massaged in order to spread the suspension beneath the skin. The room temperature was kept at 22-24°C, immediately after yeast administration, food was withdrawn and the rise in rectal temperature was recorded. The measurement was repeated after 30 minutes. The dose of the test compound and standard drug was given orally. The rectal temperature was recorded again after 1, 2 and 4 hours. Paracetamol (150 mg/kg) was selected as a standard drug. The Anjanavaerathichooranam were dissolved in sterile water. The data were analyzed for significance using the one-way ANOVA followed by Newmann keuls multiple range tests.

Results

The antipyretic potential of Anjanavaerathichooranam was evaluated by determining its effect on yeast-induced pyrexia in albino rats. Table.1 shows that animals treated with Anjanavaerathichooranam possess significant antipyretic property when compared with group 2 and also provided the highest marked antipyretic activities. The result showed the Anjanavaerathichooranam at a dose of 200 and 400 mg/kg caused lowering of the body temperature induced by injection of Brewer‟s yeast in the experimental animals significantly from 1 to 3 hours following its administration. The effect of Anjanavaerathichooranam on yeast-induced pyrexia showed that the rectal temperature was markedly elevated to 39.19°C, 3 hours after the subcutaneous injection of yeast suspension, decreased to 38.67°C within 3 hours of Anjanavaerathichooranam treatment respectively, and reduced till 3 hrs showing a sizeable decrease and was comparable to paracetamol at 150 mg/kg marked antipyretic activity detected which were significantly different than the controls ($p<0.01$). The antipyretic activity was equal to that of the standard drug paracetamol. This result reveals that the Anjanavaerathichooranam has marked the antipyretic activity as compared with standard paracetamol**.**

Table 1: The Effect of Anjanavaerathichooranam on body temperature in yeast induced pyrexia.

Group	Rectal Temperature			
	0hr	1hr	2hr	3hr
Group I (Control)	38.28 ± 0.5	37.42 ± 0.65	37.75 ± 0.78	37.48 ± 0.46
Group II (10 ml/kg)	41.38 ± 0.20	42.27 ± 0.26	39.24 ± 0.18	39.26 ± 0.52
Group III (150 mg/kg)	41.25 ± 0.20	39.48 ± 0.20	38.36 ± 0.25*	37.60 ± 0.42 *
Group IV (200 m/kg)	41.45 ± 0.18	39.64 ±0.25	39.30 ± 0.21*	38.50 ± 0.40 *
Group V (400 m/kg)	41.28 ± 0.20	39.40 ±0.20	39.23 ± 0.20*	38.54 ± 0.44 *

Values are expressed as Mean ±SEM. n = 6 in each group,

*values are significant ($P < 0.01$) different from pyrexia control (G2)

Discussion

The Anjanavaerathichooranam showed significant antipyretic activity. The animals were also fevered by injection of Brewer's yeast suspension (10 mL/kg) subcutaneously in back below the nape of the neck for the antipyretic activity. The Anjanavaerathichooranam showed significant decrease in elevated body temperature as compared to standard drug paracetamol. The possible mechanism of antipyretic action may be due to the inhibition of prostaglandin as that of paracetamol by blocking the cyclo-oxygenase enzyme activity (Chandrasekharan and Simmons, 2004). There are several mediators for pyrexia, and the inhibition of any one of these can be responsible for the antipyretic effect (Rawlins and Karger, 1973). Inhibition of any of these mediators may bring about antipyresis.

Antipyretics have been shown to suppress fever by inhibiting prostaglandin synthetase, resulting in the blockade of the synthesis of prostaglandin in the brain or suppressing the rise of interleukin-1α production subsequent to interferon production. The oral administration of Anjanavaerathichooranam were significantly attenuated rectal temperature of yeast induced pyrexia in rats and comparable to that of standard drug paracetamol. So, inhibition of prostaglandin synthesis could be the possible mechanism of antipyretic action as that of paracetamol. Also, there are several mediators or multi processes underlining the

pathogenesis of fever.

Inhibition of any of these mediators may bring about antipyresis (Akil *et al*., 1998). Thus, it can be postulated that the Anjanavaerathichooranam contains pharmacologically active principles that interfere with the release of prostaglandins. This may be attributed to the presence of the various bioactive compound present in the Anjanavaerathichooranam which may be involved in inhibition of prostaglandin synthesis. Also, there are several mediators or multiprocessors underlining the pathogenesis of fever. Inhibition of any of these mediators may bring about antipyresis. Flavonoids like baicalin have been shown to exert the antipyretic effect by suppressing TNF-α (Adesokan *et al.*, 2008) [56] and its related compounds also exhibit inhibition of arachidonic acid peroxidation, which results in the reduction of prostaglandin levels thus reducing the fever and pains (Germain *et al*., 2011) [47].

The present study also correlates with the study of Zakaria *et al.,* (2007) [35, 50, 58] that the compounds like flavonoids and saponins are suggested to act synergistically to exert the observed pharmacological activity. Flavonoids are known to target prostaglandins which are responsible for pyrexia (Rajnarayanan *et al*., 2006) [26]. The presence of flavonoids in the Anjanavaerathichooranam may be contributory to its antipyretic activity. This potentiality supports the earlier traditional claims as a pediatric antipyretic remedy.

Conclusion

Herbal medicines derived from the plant extracts are being increasingly utilized to treat a wide variety of clinical diseases, though relatively little knowledge about their mode of action is available. In conclusion, the present study provides evidence for the Anjanavaerathichooranam shows significant antipyretic activity which could partly contribute to its ethno medical use.

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