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ORIGINAL RESEARCH ARTICLE

Anti-Pyretic Activity of *Madhukadi Kwatha* and *Madhukadi Ghana* - An Experimental Study

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ABSTRACT

The present study was carried out to evaluate the anti-pyretic activity of *Madhukadi Kwatha* (decoction) and it's *Ghana* (aqueous extract) in Brewer's yeast induced pyrexia method in Wistar strain albino rats. Selected animals were randomly divided into four groups of 6 animals each. The Trial drug 1 (*Madhukadi* decoction) was administered orally at a dose of 4.5ml/Kg body weight and Trial drug 2 (*Madhukadi* aqueous extract) at a dose of 9mg/Kg body weight. Paracetamol suspension (100mg/kg body/weight) was used as a Standard anti-pyretic drug for comparison and Distilled water as Control drug. Both the trial drugs showed almost equal significance in condition of Pyrexia compared to Paracetamol. Thus *Madhukadi* decoction and its aqueous extract can be considered as a safe and can be potentially used in treating Pyrexia.

Key words: Pyrexia, *Madhukadi* decoction, Aqueous extract, Paracetamol, Brewer's yeast

INTRODUCTION:

Pyrexia is a condition wherein there is abrupt increase in core temperature above the normal level. Many a times it is equated with a condition of Hyperthermia but both are completely different entities. In modern system of medicine it has been considered more as a symptom rather than a disease but certain conditions like Dengue, Malaria, Chikungunya etc drawn attention towards the strength of Pyrexia even as a disease proper. Usage of the potent anti-pyretic drugs being the prime line of treatment, most of the antipyretic used in modern system are not devoid of complications or untoward effects[1]. Hence there is a strong need to find out such a formulation which not only cures the condition but won't produce any such complications.

Madhukadi decoction[2] mentioned in *Jwararogaadhikara* of *Bhaishajya Ratnaval i*(*Ayurvedic* classical book) has been indicated specifically in all conditions of Pyrexia. The component drugs of *Madhukadi* decoction (Table –I) are individually having the potent anti-pyretic activity. So the poly herbal formulation prepared from these drugs can be a potent antipyretic. Liquid dosage form (*Kwatha Kalpana)* mentioned under the five basic fundamentals of *Ayurvedic* Pharmaceutics (*Bhaishajya Kalpana)* is having its own limitations like short shelf life (*Sadyosevana*) and unpalatability (*Kashayarastawa*) which made the Seers (*Acharyas*) to mention about the secondary (*Kalpanas*) dosage forms so that the advantages of these dosage forms can be achieved by overcoming these limitations and which is the need of the present era. Thus, keeping in mind the importance of drug dosage form and the

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limitations of decoction like the formulation is converted into a *Ghana*[3](Dried aqueous extract). Both of the formulations *Madhukadi* decoction and its aqueous extract are evaluated for their antipyretic activity against Control (Distilled water) and Standard (Paracetamol).

MATERIALS AND METHODS:

Wistar strain albino rats of either sex weighing 150-200gm were used for the study. The animals were obtained from the animal house attached to the Institute. Animals were housed in poly-propylene cages and were provided certified rodent pellet diet and water *ad libitum*. They were maintained at 25°C and Humidity (50-60%) with 12h light and dark cycle. All animal experiments were performed in accordance with the strict guidelines prescribed by Institutional Animal Ethical Committee (IAEC) after getting necessary approval. (Approval Number; A.E.B.K. 05/07)

Trial Drugs:

The raw materials of the trial drug (*Madhukadi* decoction) containing 8 drugs (**Table-I**) were collected freshly from their natural habitat after proper identification taxonomically in field with various floras. The collected drugs were dried under shade with proper precautions. These drugs were subjected to pharmacognostical studies to evaluate the quality. From the raw materials both the trial drugs *Madhukadi* decoction and aqueous extract were prepared by following the classical guidelines in the Pharmacy attached to the institute.

Table- I - Drug composition of *Madhukadi* Decoction and *Madhukadi* Aqueous extract

S. No.	*Ingredients*	*Botanical Name*	*Parts used*	*Proportion*
1.	*Yastimadhu*	*Glycyrrhiza glabra Linn.*	*Rt.*	*1 part*
2.	*Chandana*	*Pterocarpus santalinus Linn.*	*Hrt wd.*	*1 part*
3.	*Musta*	*Cyperus rotundus Linn.*	*Rz.*	*1 part*
4.	*Amalaki*	*Emblica officinalis Gaertn.*	*Fr.*	*1 part*
5.	*Ushira*	*Vetiveria zizanioides (Linn) Nash.*	*Rt.*	*1 part*
6.	*Dhanyaka*	*Coriandrum sativum Linn.*	*Fr.*	*1 part*
7.	*Guduchi*	*Tinospora cordifolia Miers.*	*St.*	*1 part*
8.	*Patola*	*Trichosanthes dioica Roxb.*	*Wh. Pt.*	*1 part*

Dose fixation:

The generalized dose for the rats was calculated based on the conversion formula, referring to the table of Paget & Barner's formula[4]

Animal grouping:

Wistar strain albino rats of body weight ranging from 150g – 200 g were used as experimental animals. They were divided in to 4 different groups shown in (**Table -2**).

Table 2: Showing the Grouping of Animals

S.No.	Grouping	No. of Rats	Drug administered	Dose/200 g body/ wt.
01	Control group	6	Distilled water	2 ml
02	Standard group	6	Paracetamol Suspension	20mg
03	Trial group I	6	Madhukadi Decoction	0.9 ml
04	Trial group II	6	Madhukadi Aqueous extract	9 mg

Experimental Design:

The experimental module selected for the present study was Brewer's yeast induced pyrexia method in Wistar strain albino rats[5]. Animals of either sex were divided in to four groups containing six in each group for this experiment. The animals were kept on fasting for 18 hours before the commencement of experiment, but drinking water was provided. Rectal temperature (T_R) was recorded by using digital thermometer. Immediately after measuring the initial basal rectal temperature, the animals were injected with baker yeast (20%, 1 ml/100g body weight, subcutaneously) in normal saline. After 1hour of the yeast injection initial rectal temperature was recorded and the test drugs and reference standard were administered to respective groups. The rectal temperature changes were recorded at 2^{nd}, 5^{th}, 8^{th}, 11^{th} and 14^{th} hour. The rectal temperature of control groups (yeast control) was compared with rectal temperature of the test drugs administered groups.

Statistical analysis:

Results were presented as Mean ± SEM, difference between the groups was statistically determined by unpaired student's t test and

analysis of variance (ANOVA) with the level of significance set at P<0.05. The level of significance was noted and interpreted accordingly.

RESULTS:

Yeast injection to experimental animals caused significant raise in body temperature at various time intervals (**Table – 3**). Paracetamol, a well known antipyretic drug attenuated the raise in temperature to significant extent at 8h and non-significantly at all other time intervals. Treatment with *Madhukadi* decoction significantly protected yeast induced pyrexia at almost all time intervals. The observed activity is rapid onset as well as long lasting. *Madhukadi* aqueous extract also showed significant anti-pyretic activity at 11h and 14h. Further, the observed anti-pyretic activity of both formulations is significant in comparison to standard anti-pyretic drug. Among both formulations *Madhukadi* decoction had shown better anti-pyretic activity than that of *Madhukadi* aqueous extract in terms of onset but overall both are having equal efficacy in treating pyrexia.

Table 3: Effect of Trial drugs on yeast induced pyrexia at various time intervals (albino rats)

Groups	Actual change in rectal temperature (°C)				
	2 h	5 h	8 h	11 h	14 h
Yeast control	2.17 ± 0.52	3.00 ± 0.26	3.67 ± 0.38	3.17 ± 0.32	2.33 ± 0.45
MK	0.64 ± 0.27*$^{\#\#A}$	1.89 ± 0.42$^{\#A}$	1.96 ± 0.55*	2.45 ± 0.59	1.53 ± 0.36
MG	1.78 ± 0.28	3.35 ± 0.33	3.04 ± 0.44	1.78 ± 0.44*	0.93 ± 0.26*$^{\#}$
Paracetamol	2.10 ± 0.33	2.23 ± 0.25	2.74 ± 0.23*	2.60 ± 0.22	1.98 ± 0.29

Data: Mean ± SEM;*P<0.05 (Compared with yeast control),
$^{\#}$P<0.05, $^{\#\#}$P<0.01 - (Compared with paracetamol); ^{A}P<0.05 (Compared with MG)

DISCUSSION:

Fever may be a result of infection or one of sequelae of tissue damage, inflammation, graft rejection, or other disease states. Antipyretics are drugs which reduce an elevated body temperature. The regulation of body temperature requires a delicate balance between the production and loss of heat. 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[6].

Regulation of body temperature requires a delicate balance between production and loss of heat and the hypothalamus regulates the set point at which body temperature is maintained. Most of the antipyretic drugs inhibit COX-2 expression thus inhibiting PGE2 biosynthesis to reduce elevated body temperature

There is an extensive evidence to implicate free radicals in the development of diseases. Free radicals have been implicated in the causation of ailments such as fever, diabetes, liver cirrhosis etc. The antioxidant activity of Ascorbic acid, Riboflavin, Tannin, Tannic acid etc. may be helpful in either inhibiting or scavenging radicals. Reactive oxygen damages the important cellular components by causing tissue injury, through covalent binding and lipid peroxidation. In a previous study, the increase in the body temperature intensified the lipidperoxidation process, which indicates that pyrexia is associated with increased oxidative stress. The antioxidant supplementation decreased the lipid-peroxidation processes.[7] The composite drugs of the formulations have been reported to have antioxidant activity[8, 9, 10, 11,12,13,14]. Hence, antioxidant activity may be one of the possible mechanisms by which it reduces the elevated body temperature.

Yeast-induced pyrexia is called pathogenic fever and its aetiology involves production of prostaglandins. The effect of the composite drugs may be due to inhibition of prostaglandin synthesis. Formulation containing alkaloids, tannins, carbohydrates and flavonoids has been reported antipyretic potential in various studies[15]. Therefore, the activity may be due to the presence of the above group of phytoconstituents. Upon analysing the both the trial drugs the qualitatively phyto-chemicals such as flavnoids, steroids, glycosides, alkaloids, saponins and anthroquinones have been reported which are proved to exhibit anti-pyretic activity[16,17]. In many earlier studies flavonoids compounds have been

reported to exhibit antipyretic effect[18,19], as some flavonoids are predominant inhibitors of cyclooxygenase or lipooxygenase. [20, 21, 22]
Moreover the individual drugs of the formulations are already proved for their antipyretic activity[23,24,25,26] but no work has been carried out to evaluate the combined effect of these drugs as in the form of formulation either in decoction or aqueous extract form, to overcome the unsuitable dosage forms for the different age groups of patients.

CONCLUSION:

Madukadi Decocotion *(Kwatha)* showed significant action in attenuating the pyrexia, with early onset of action and for prolonged duration whereas *Madhukadi* Aqueous extract *(Ghana)* showed delayed but significant action in treating pyrexia. Hence both the formulations are found to be safe and effective in comparison to Paracetamol.

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