Ancient Science of Life, Vol No. XV No .1 July 1995, Pages 7-14

ANTIPYRETIC ACTIVITY OF TBR-002, A HERBAL FORMULATION

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Received: 27 March, 1995 **Accepted: 12 May, 1995**

ABSTRACT: *The antipyretic activity of a herbal formulation, TBR-002 was compared with that of andrographis paniculata, andrographis elongate and paracetamol in yeast-induced pyrexia in male albino rats, TBR-oo2 was found to be effective at an oral dose of 100 mg/kg in the inhibition if pyrexia. Its efficacy was almost comparable to that of paracetamol as well as andrographis elongate, the antipyretic activity of andrographis paniculata, the well known antipyretic herb, was found to be less than that of the above drugs.*

INTRODUCTION

Many herbal drugs are used in Indian system of medicines as well as in folk and tribal medicines for common ailments. To reactivate these invaluable medical practices, Tropical Botanic Garden and research Institute, Palode (Trivandrum District, Kerala), among other things, has developed a herbal health care kit for common ailments. An antipyretic herbal formulation for common fever known a s TBR-002 is included in the herbal health care kit. It was of interest to determine the efficacy of this formulation in experimental animals.

In the treatment of intermittent and remittent fevers, herbal drugs such as androgaphis paniculata, andrographis alata Nees and Andrographis lineate Nees are used by traditional medical practitioners (Kirtikar and Basu[1], Tomar et al[2]). The antipyretic effects of *A. paniculata* have been scientifically validated and an active principle andrographolide ($C_{20}H_{30}O_5$) has been isolated (Vedawathy et al[3], Roych oudhury and Poddar[4]; Quadrat-i-khuda et al[5]). In a recent study, the antipyretic activity of *A. Paniculata, A. lineate* and *A. alata* was compared and the efficacy of *A. paniculata* (Balu et al[6]). However, *A. elongata*, a related species has not been studied.

Paracetamol is an effective antipyretic agent commonly used in the modern system of medicine. Excess of paracetamol (Over dose) causes liver damage (Chattopathyay et al[7]; Wendel et al[8]).

The present study was undertaken to determine and compare the antipyretic efficacy of TBR-002 with that of *A. paniculata, A. elongata* and paracetamol against yeast-induced pyrexia in male rats.

MATERIALS AND METHODS

Samples of Andrographis elongata and *A. paniculata* were collected during their pre-flowering period from the campus of tropical botanic garden and research Institute, Palode and identified by

comparing with the herbarium specimens of the Institute.

The leaves of the plant materials were dried shade and powdered. A suspension of the powder was prepared in 2% gum acacia and used. TBR-002 formulation, in powder form was suspended in 2% gum acacia, Paracetamol (Calpol) Burroughs Welcome (India) Ltd., was purchased from local medical store within its expiry date.

Male albino rats of wistar strain weighing 100-120g were used for the experiments. Pyrexia was induced in rats by subcutaneously injecting a suspension of 12% yeast in water at a dose of 1 ml /100g body weight. The test was carried out in an air conditioned room ($26^{o}C$ and 50% humidity). Food was with held during the experiment, the initial rectal temperature was taken and then pyrogen was injected. After the injection the temperature readings were taken at one hour interval till 5^{th} hour.

To study the effect of the drugs each drug suspension in water containing 2% gum acacia was given orally in one ml at a dose of 500 or 100mg/kg body wt.1 hr prior to yeast injection or 2 hrs after yeast injection.

The % of pyrexia was calculated for control, herbal drug treated and standard groups.

To determine acute toxicity, if any, rats weighing 200-220g. Were divided into 3 groups of 6 rats in each group. Group I received an oral dose of 3 ml of 2% gum acacia and served as control. Groups II and III were given orally TBR-002 powder suspended in 2% gum acacia (3ml/rat) at a dose of 5 and 10g/kg respectively. Survival, gross behaviour, food intake and faecal droppings were observed.

Toxcity study of repeated doses was carried out in mice. Mice weighing 20-22g. Were divided into 2 groups of 6 mice in eash group. One group received daily oral dose of 1g/kg (1ml/mouse) of TBR-002 powder (suspended in 2% gum acacia) for 10 days. The control group received gum acacia in an identical manner, Gross behaviour, food intake and faecal droppings of mice were observed during the experimental period, On day 11, animals were killed, organs were removed, weighed and observed for grass pathological lesions, Haemoglobin content and total blood leucocyte content were determined.

RESULTS

Subcutaneous injection of 15% yeast suspension to rats induced pyrexia which reached a peak in about 3 hrs, The antipyretic actions of various drugs, when administered 2 hrs after yeast injection, are given in Table 1. Oral administration of TBR-002 or *A. elongata* or paracetamol at a dose of 500 mg/kg body weight brought down the rectal temperature to normal levels within one hour, However, at this dose *A. paniculata* was not as effective as the other drugs, it showed less than 50% restoration of normal temperature, The antipyretic activity of the drugs tested was found to be dose dependent, At a lower dose (100mg/kg) although the drug could not completely restore the normal levels of temperature they were very effective in controlling the pyrexia, except *A. Paniculata* which showed only marginal activity (Table 1)

The effect of the drug pretreatment 1 hr prior to pyrogen administration is given in Figure 1. In this case also TBR -002 is almost as effective as paracetamol in preventing the pyrogenic effect of yeast, whereas *A. paniculata* showed only moderate antipyretic activity (Fig1). The drugs showed a concentration dependent

activity and a dose of 100 mg/kg of TBR-002 was found to be effective.

Acute toxicity study in rats showed no mortality when TBR -002 was given at a single dose o f5 or 10g/kgbody weight. In addition, there were no noticeable changes in behaviour, food and water intake, faecal droppings and morphology of viscera, Similarly repeated administration of the drug (1g/kg) for 10 days to mice did not influence the above parameters. The weight of body, liver and kindneys was not significantly alterted by the treatment. Further, haemoglobin content and total leucocyte count in blood were found to be unchanged as compared to control (Table 2)

DISCUSSION

The antipyretic property of the herbal formulation TBR-002 was found to be almost equal to that of paracetamol, This herbal formulation may form an alternative to paracetamol in combating common fever. Accidental over dose of paracetamol may result in liver damage (Chattopadhyay et al7; Wendel et al 8). The herbal formulation is a non toxic drug.

In a recent study, it was found that A. alata has better antipyretic activity as compared to *A. paniculata* (Balu et al[6]). In the present study, it has been observed for the first time that *A elongata* taxonomically very close to *A.alata*, is a superior antipyretic agent as compared to *A. paniculata*. studies are in progress in this laboratory to isolate the active principles involved from *A. elongata* and compare it with that from *A. paniculata*, *A paniculata* is readily available even as a weed, in many places in south India whereas *A. elongata* as well as *A.alata* have restricted distribution and availability. Although TBR-002 dose not contain both these drugs it has very potent antipyretic activity. This formulation has been developed from easily available herbs used in ethnomedicine.

ACKNOWLEDGEMENT

The authors thank Mrs. J. Usha Kumar and Mr. S. Radhakrishna Pillai for laboratory assistance.

Table 1
Effect of TBR-002 and other antipyretic drugs on yeast –induced Pyrexia in male albino rats

		Temperature in of after pyrogen treatment (hrs)			
Drug Treatment	Drug dosage (mg/kg)	0 (initial)	2	3 (1)	5 (3)
Control	0	100.4 ± .50	103.8 ± .42	105.1 ± .61	103.6 ± .41
TBR-002	500	100.1 ± .40	103.5 ± .41	100.2 ± .62*	100.9 ±.59*
TBR-002	100	100.0 ± .38	103.2 ± .39	101.2 ± .60*	102.0 ± .63**
A.Paniculata	500	100.4 ± .34	103.7 ± .43	102.8 ± .62*	102.8 ± .60**
A.Paniculata	100	100.3 ± .48.	103.8 ± .34	104.0 ± .63*	103.2 ± .59
A. elongata	500	100.3 ± .42	103.6 ± .40	100.8 ± .49*	100.8 ± .50*
A. elongata	100	100.2 ± .42	103.5 ± .50	101.6 ± .51*	101.8 ± .61*
Paracetamol	500	100.0 ± .49	103.4 ± .43	099.8 ± .45*	100.2 ± .48*
Paracetamol	100	99.8 ± .45	103.5 ± .46	101.1 ± .51*	101.1 ± .59*
Paracetamol	20	100.1 ±.38	103.3 ± .37	102.6 ± .61*	102.4 ± .62**

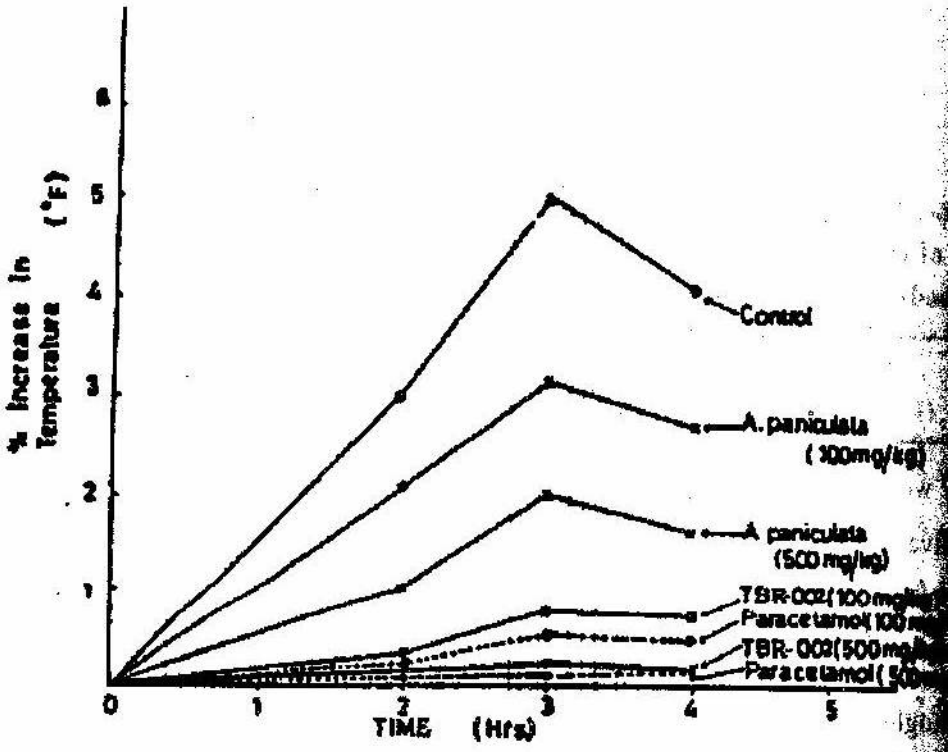
Drugs were administered 2 hrs after pyrogen administration. Time after drug administration is given within parantheses.

4 animals were used in each group. Values are mean ±SD. *P<.001, **P<.05

Table 2
Effect of repeated administration of TBR-002 to mice on the weight of body, liver and kidney and on haematological parameters.

	Control	TBR-002 Treated (1g/kg)
Body weight (g)	26.9±2.52	25.1±3.32
Relative organ weight		
Liver	4.48 ±0.42	4.42 ± 0.52
Kidneys (Two)	1.28 ± 0.06	1.30 ± 0.07
Haemoglobin (g/100ml blood)	14.2 ± 1.1	13.8 ± 0.9
Total blood leucocytes (Cells/mlx10-6)	08.1 ± 0.9	08.3 ±1.2

Drug was orally administered daily for 10 days. Relative organ weight = (Weight of organ/weight of bodyx100). Initial body weight was 20-22g in both the groups. Values are mean ± S.D. n=6.



(After pyrogen administration)

Figure . 1. Effect of pretreatment with TBR 002 and other anti drugs on yeast-induced pyrogenesis in rats. Drugs were orally hr. Before pyrogen administration.

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