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Testing of Polyherbal extract of Ficus Species as an antipyretic agent in fever of unknown origin (FUOs)

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ABSTRACT
The present pharmacological investigation was undertaken to study the anti-pyretic activity of Ficus benghalesis, Ficus glomerata and Ficus religiosaleaves extract in wistar rats against 4-Dinitrophenol (DNP)-induced pyrexia, Lipopolysaccharide Induced Pyrexia Model, turpentine induced pyrexia. Four groups of six animals each were used for the experimental study. The pyrexia induced methods were standardized first by injecting the irritants followed by recording the rectal temperature at regular intervals. Then the evaluation of anti-pyretic activity of Ficus speciesleaves extractwas carried out by using this standard procedure. TheFicus species leaves extract samples significantly attenuated the raise in temperaturein a highly significant manner in comparison to control groups. The data generated during study shows that herbal extract having significant anti-pyretic activity. These plants has been traditional medicine used for treating inflammatory conditions and is use by tribal people in India. Its anti-inflammatory effect must be related to the arachidonate cascade and inhibition of cyclo-oxygenase. After conduction of this study we can putforthits use treat her symptoms and may thus be a suitable treatment for patients with undiagnosed fever of unknown origin.

Keywords – FUO, polyarthritis, pyrogen free, parasitic etc.

I. INTRODUCTION

Fever of unknown origin (FUO)is defined as a temperature of 101 degrees Fahrenheit (38.3 degrees Centigrade) or higher with a minimum duration of three weeks without an established diagnosis despite at least one week's investigation in the hospital

It is a fever at or above 101°F (38.3°C) for 3 weeks or more that remains undiagnosed after 3 days of in-hospital testing or during two or more outpatient visits. For diagnostic purposes, FUOs may be grouped into four separate categories.

1. Infectious
2. Neoplasm/Malignant
3. Rheumatic/Inflammatory
4. Miscellaneous

Causes of fever are numerous. Possibilities include viral, bacterial, parasitic and fungal infections. Immune-mediated diseases such as immune-mediated polyarthritis and lupus may include fever as a clinical sign. Various neoplastic diseases (tumours) and reactions to some drugs may cause fever. Inflammation or infection of organs in the abdomen or chest can also be associated with fever. So by checking antipyretic activity in different models having different origin of fever can give us idea to use these plants together for FUOs

Treatments

1. Medical Treatments like antipyretics including NSAIDS
2. Traditional Medicine

Long term use of NSAIDS also leads to determinant effects on vital organs if used for prolonged time, in contrast herbal medicine has much better effect and heal the route cause

II. MATERIALS AND METHODS

The medicinal plants used in the study were Ficus benghalesis, Ficus glomerata and Ficus religiosa. Fresh leaves of above mentioned plants has collected, washed and shade dried Plants have been authenticated by Shri Shivaji Science college, chikhli. (MS)

Preparation of Plant extract

The shade dried leaves of plantscrushed by a mechanical grinder. The powdered of leaves of each plants in proportion of 1:1:1 portionwas

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combined. The alcoholic extract of powder obtained by soxhlet extraction method. The extracts were successively separate by filtration using Whatman filter paper and concentrated it at an appropriate temperature (40 °C) on a rotary evaporator and dried under freeze drier. The percentage yield was found between 25-30% (w/w) respectively, and the final dried powder was stored in a closed container at a cool place.

Animal studies:

Animal sprocured from P.Wadhwani College of pharmacy Yavatmal (MS) and protocol was approved by IAEC of institute. LD50 was determined by OECD guideline and Safe dose has been determined.

Animal Models:

1. 4-Dinitrophenol (DNP)-induced pyrexia:

The modified method by Okokon and Nwafor (2010) and Essien et al. (2015) was adopted. After 24 hour fast with free access to water, twenty-four (24) rats were divided into four groups of six rats per cage. Their basal rectal temperature was recorded before inducing pyrexia intraperitoneally, with 10 mg/kg of DNP. Thirty minutes post DNP administration with pyrogen free sterile water, rectal temperature was measured to confirm the state of pyrexia and to disregard rats without temperature elevation above 0.5°C. Thereafter, 200 and 400 mg/kg Polyherbal extract were administered orally to Group IIand Group III respectively; while control Group I and IV received pyrogen free sterile water (5 ml/kg) and aspirin (150 mg/kg) respectively. Thereafter, the rectal temperature was measured by inserting a small thermoprobe and recorded at 1 h interval and for 6 h.

Treatment	**0 hr**	**1 hr**	**2 hr**	**03 hr**	**04 hr**	**05 hr**	**06 hr**
Control-I (5ml/kg)	37.55±0.06	37.61±0.09	37.42±0.08	37.43±0.03	37.85±0.09	37.70±0.05	37.43±0.03
Group-II (200 mg/kg)	37.61±0.08	36.34±0.07	36.43±0.10	36.89±0.09	36.56±0.11	35.71±0.04	35.49±0.04
Group-III (400 mg/kg)	37.42±0.04	36.23±0.01	35.58±0.05	35.26±0.08	35.77±0.09	35.82±0.11	35.91±0.08
Group-IVStnd. (150 mg/kg)	37.73±0.01	35.66±0.02	35.61±0.06	35.45±0.1	35.45±0.10	35.55±0.8	35.55±0.11

Table no. 1: Rectal temperature measures by 4-Dinitrophenol (DNP)-induced pyrexia

Lipopolysaccharide Induced Pyrexia Model –

Wistar Rats were selected to perform this study. Animals were divided in a four group six animals in each group. Animals group were injected intraperitoneally with LPS (500ug/kg) in pyrogen free sterile water. Thirty minutes post LPS (500ug/kg) administration with pyrogen free sterile water, rectal temperature was measured to confirm the state of pyrexia. Thereafter, 200 and 400 mg/kg Polyherbal extract were administered orally to Group IIand Group III respectively; while control Group I and IV received pyrogen free sterile water (5ml/kg) and aspirin (150 mg/kg) respectively. Thereafter, the rectal temperature was measured by inserting a small thermoprobe and recorded at 1 h interval and for 6 h.

Treatment	**0 hr**	**1 hr**	**2 hr**	**03 hr**	**04 hr**	**05 hr**	**06 hr**
Control-I (5ml/	37.65±0.07	37.61±0.09	37.42±0.09	37.43±0.03	37.85±0.09	37.70±0.05	37.43±0.03

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kg)							
Group-II (200 mg/kg)	37.60±0.09	36.35±0.09	36.73±0.10	36.80±0.09	36.50±0.11	35.65±0.04	35.50±0.04
Group-III (400 mg/kg)	37.42±0.05	36.20±0.04	35.50±0.04	35.25±0.08	35.65±0.09	35.73±0.11	35.89±0.08
Group-IVStnd. (150 mg/kg)	37.63±0.02	35.66±0.03	35.61±0.06	35.45±0.1	35.45±0.10	35.55±0.8	35.55±0.11

Table no. 2: Rectal temperature measured by Lipopolysaccharide Induced Pyrexia Model

3) Turpentine-induced pyrexia: Wistar Rats were selected to perform further study. Animals were divided in a four group six animals in each group. Animals group were Turpentine(15ml/kg) injected intraperitoneally in pyrogen free sterile water. Thirty minutes after administration of Turpentine with pyrogen free sterile water, rectal temperature was measured to confirm the state of pyrexia. Thereafter, 200 and 400 mg/kg Polyherbal extract were administered orally to Group IIand Group III respectively; while control Group I and IV received pyrogen free sterile water (15ml/kg) and aspirin (150 mg/kg) respectively. Thereafter, the rectal temperature was measured by inserting a small thermoprobe and recorded at 1 h interval and for 6 h.

Treatment	**0 hr**	**1 hr**	**2 hr**	**03 hr**	**04 hr**	**05 hr**	**06 hr**
Control I (5ml/kg NS	37.66±0.06	37.62±0.09	37.45±0.08	37.47±0.03	37.88±0.09	37.79±0.05	37.53±0.03
Group II (200 mg/kg)	37.61±0.08	36.30±0.07	36.70±0.10	36.80±0.09	36.50±0.11	35.60±0.04	35.50±0.04
Group III (400 mg/kg)	37.65±0.04	36.60±0.01	35.51±0.05	35.44±0.08	35.33±0.09	35.23±0.11	35.29±0.08
Group IVStnd. (150 mg/kg)	37.60±0.01	35.60±0.02	35.61±0.06	35.45±0.1	35.45±0.10	35.55±0.8	35.55±0.11

Table no. 3: Rectal temperature measured Turpentine-induced pyrexia model

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4) Yeast-induced pyrexia:

Wistar rats were randomly selected and divided into four groups of six rats in each group. Clinical thermometer was used in measuring their initial basal rectal temperature. Thereafter, pyrexia was induced in rats by injecting subcutaneously 20 ml/kg of 15% brewer's yeast, suspended in 0.5% methylcellulose solution.After 24 h, rectal temperature was again measured and any rats without elevated temperature above by 0.5°C was disregarded for the study. Thereafter, 200 and 400 mg/kg polyherbal extract were administered orally to groups II and III respectively; while control groups Iand IV received pyrogen free sterile water (5ml/kg) and aspirin (150 mg/kg) respectively. Their rectal temperature was again recorded at 1h interval and for 6 h after drug administration.

Treatment	0 hr	1 hr	2 hr	03 hr	04 hr	05 hr	06 hr
Control I (5ml/kg NS	37.60±0.06	37.60±0.09	37.40±0.08	37.35±0.03	37.90±0.09	37.70±0.05	37.57±0.03
Group II (200 mg/kg)	37.62±0.08	36.34±0.07	36.72±0.10	36.81±0.09	36.52±0.11	35.61±0.04	35.50±0.04
Group III (400 mg/kg)	37.65±0.04	36.63±0.01	35.57±0.05	35.39±0.08	35.38±0.09	35.28±0.11	35.30±0.08
Group IVStnd. (150 mg/kg)	37.65±0.01	35.60±0.02	35.63±0.06	35.43±0.1	35.45±0.10	35.45±0.8	35.55±0.11

Table no. 3: Rectal temperature measured Yeast-induced pyrexia model

III. RESULT:

According to test model it seen that the oral administration of polyherbal extract to the wistar rat at test dose clearly demonstrate antipyretic effect by decrease in the body temperature.It is highly possible bioactive compounds present in these plants combinely may inhibiting the production of prostaglandins (PGE2). Further study needed to isolate those compounds and more advanced research has to be done.

IV. CONCLUSION:

The antipyretic activity of polyherbalextract of Ficus speciesshowed antipyretic action in various antipyretic models suggesting this extract can be supplement or alternative to modern medicine especially in few cases of FUOs not related to HIV

REFERENCES:

[1]. Petersdorf, Robert G. "Fever of unknown origin." Annals of Internal Medicine 70.4 (1969): 864-866

[2]. Durack, D. T. "Fever of unknown origin-reexamined and redefined." Current Clinical Topics in Infectious Disease 11 (1991): 35-51.

[3]. Ravikumar, Sundaram, et al. "Antiplasmodial activity of two marine polyherbal preparations from Chaetomorphaantennina and Aegicerascorniculatum against Plasmodium falciparum." Parasitology research 108.1 (2011): 107-113.

[4]. Arnow, Paul M., and John P. Flaherty. "Fever of unknown origin." The Lancet 350.9077 (1997): 575-580.

[5]. Okokon, Jude E., and Paul A. Nwafor. "Antiinflammatory, analgesic and antipyretic activities of ethanolic root extract of Croton zambesicus." Pak J Pharm Sci 23.4 (2010): 385-392.

[6]. Essien, A. D., et al. "Evaluation of antipyretic potential of the ethanolic leaf extract of Salacia lehmbachiiLoes." Asian Journal of Medical Sciences 7.2 (2015): 22-25.

[7]. Adejoh, IDAKWOJI Precious, et al. "Effect of Aqueous Leaf Extract of Anogeissusleiocarpus against Experimental

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Models of Pain and Pyrexia." Int. J. Adv. Res. Biol. Sci 6.6 (2019): 181-188

[8]. Alolga, Raphael Nammahime, et al. "Anti-inflammatory and antipyretic properties of Kang 601 heji, a traditional Chinese oral liquid dosage form." Asian Pacific Journal of Tropical Biomedicine 5.11 (2015): 921-927.

[9]. Koech, S., et al. "Anti-pyretic potential of dichloromethanolic root extract of Clutiaabyssinica in Wistar Albino Rats." Med Aromat Plants 6.281 (2017): 2167-0412

[10]. Nthiga, P. M., et al. "Antipyretic Potential of Methanolic Stem Bark Extracts of HarrisoniaAbyssinicaOliv and LandolphiaBuchananii (Hallier F.) Stapf in Wistar Rats." Journal of Applied Pharmacy 8.3 (2016): 1-7.

[11]. Yao, Xiu-Juan, et al. "Puerarin exerts antipyretic effect on lipopolysaccharide-induced fever in rats involving inhibition of pyrogen production from macrophages." Journal of Ethnopharmacology 141.1 (2012): 322-330.

[12]. Romanovsky, Andrej A. "Thermoregulation: some concepts have changed. Functional architecture of the thermoregulatory system." American journal of Physiology-Regulatory, integrative and comparative Physiology 292.1 (2007): R37-R46.

[13]. Liu, Shumin, et al. "Effect of Huanglianjiedu Tang on fever in rats induced by 2, 4-dinitrophenol." Journal of traditional Chinese medicine 33.4 (2013): 492-499

[14]. Liu, Shumin, et al. "Metabolomic study of a rat fever model induced with 2, 4-dinitrophenol and the therapeutic effects of a crude drug derived from Coptischinensis." The American Journal of Chinese Medicine 39.01 (2011): 95-109.

[15]. Essien, A. D., et al. "Pharmacological evaluation of the aqueous stem bark extract of Bombaxbuonopozense in the relief of pain and fever." African Journal of Pharmacy and Pharmacology 10.5 (2016): 59-65.

[16]. McCann, Margaret E., et al. "In vitro effects and in vivo efficacy of a novel cyclooxygenase-2 inhibitor in cats with lipopolysaccharide-induced pyrexia." American journal of veterinary research 66.7 (2005): 1278-1284.

[17]. Khan, Ashrafullah, et al. "Anomalin attenuates LPS-induced acute lungs injury through inhibition of AP-1 signaling." International immunopharmacology 73 (2019): 451-460.

[18]. Antwi, Aaron O., et al. "Stigmasterol inhibits lipopolysaccharide-induced innate immune responses in murine models." International Immunopharmacology 53 (2017): 105-113.

[19]. Horai, Reiko, et al. "Production of mice deficient in genes for interleukin (IL)-1α, IL-1β, IL-1α/β, and IL-1 receptor antagonist shows that IL-1β is crucial in turpentine-induced fever development and glucocorticoid secretion." The Journal of experimental medicine 187.9 (1998): 1463-1475.

[20]. Horai, Reiko, et al. "Production of Mice Deficient in Genes for Interleukin (IL)-1 , IL-1 , IL-1, and IL-1 Receptor Antagonist Shows that IL-1 Is Crucial in Turpentine-induced Fever Development and Glucocorticoid Secretion." Journal of Experimental Medicine 187 (1998): 1463-1476.

[21]. Kozak, Wieslaw, et al. "IL-6 and IL-1β in Fever: Studies Using Cytokine-Deficient (Knockout) Mice a." Annals of the New York Academy of Sciences 856.1 (1998): 33-47.

[22]. Kluger, Matthew J., et al. "Cytokines and fever." Neuroimmunomodulation 2.4 (1995): 216-223.