INVIVO ANTI - PYRETIC ACTIVITY OF *CORDIA MONOICA* (ROXB.) ETHANOLIC LEAF EXTRACT

Dr.A.Dhivya[1], Dr.D.Jayasheela[2] and Dr.R.Sivakumar[3]

[1,3]Assistant Professor, [2]Associate Professor,
[1,2]Department of Biotechnology, Sri Ramakrishna College of Arts and Science, (Autonomous), Coimbatore
[3]Department of Botany, L.R.G Government Arts College for women, Tirupur.

***ABSTRACT*: The Present study was carried out to evaluate the anti-pyretic activity of *Cordia monoica* (Roxb.) leaves. The anti-pyretic activity of *Cordia monoica* (Roxb.) leaves was assessed using Brewer's Yeast Induced Pyrexia Method in Wistar Albino Rats. The ethanolic extract of *Cordia monoica* (Roxb.) leaves at a dose of 100mg/kg bw and 200 mg/kg bw was used for the activity. The result was dose dependent. The ethanolic extract of *Cordia monoica* (Roxb.) leaves showed a statistically significant anti-pyretic activity in experimental rats. The present study justifies the use of *Cordia monoica* (Roxb.) in the treatment of fever and hence can be used for further experiments.**

***KEYWORDS*: *Cordia monoica* (Roxb.) leaves, ethanolic extract, anti-pyretic activity, Wistar Albino Rats, Brewer's Yeast.**

I. INTRODUCTION:

Since the dawn of civilization, people have used plant and plant extract for various purposes to treat diseases. Ethno-botanical preparations have been used by various cultures for various reasons around the world. Pyrexia is defined as the combination of indigestion, seasonal variations and significant alteration in daily routine in Ayurveda (Gupta *et al.,* 2008). Fever is associated with elevation of body temperature and its predicted aftermaths. It is related to behavioural features such as lethargy, depression, hyperalgesia, sleepiness, anorexia, etc. Fever has its base with a number of disease conditions such as infections, skin inflammation, tissue destruction, and cancer, disorders due to metabolism, immunological disorders and due to incompatible blood products (Emdad Hossain *et al.,* 2011). Cytokines, interleukins, interferon and tumor necrosis factor alpha are formed in large amount during fever. This in turn increases PGE 2 that will induce hypothalamus to increase body temperature (Rajani *et al.,* 2011). However, antipyretic medication can be effective in lowering the temperature. It may also include the affected person's comfort (Duraisankar and Ravichandran, 2012).

Many anti-pyretic drugs that have been used clinically for the treatment of fever, drowsiness, inflammation sometimes leads to adverse reactions and fulfilment can be minimal as such (Dhillon and Kaushik, 2009). There is a search for a safer antipyretic drug without any side effects still now (Bennett and Brown, 2003). Therefore, there is a need to search equally efficient herbal medicines that with less toxicity and also free from side effects.

Cordia monoica Roxb. belonging to Boraginaceae family is a multi-stemmed evergreen shrub or small tree. *Cordia monoica* Roxb. distributed worldwide is found mainly in India, Sri Lanka and Africa. In India, the distribution is widely in southern part of all districts of Tamil Nadu, Andhra Pradesh and Kerala (Nadkarni, 1976). *Cordia monoica* Roxb. have several uses in traditional medicine. The crushed leaves with a cup of water are orally given to treat a local illness termed as MICH. MICH is a febrile disease with symptoms such as sweating, headache and fever (Giday, 2001). The leaf preparations of several species of *Cordia* are used in traditional medicine as remedies for some tumoral formations (Hartwell, 1982; Rapisarda *et al.,* 1993). Based on the traditional use, the present study was carried out to evaluate the antipyretic activity of ethanolic extract of *Cordia monoica* Roxb. leaves.

II. METHODOLOGY

2.1 MATERIALS AND METHODS:

2.1.1 Collection of Plant Material:

Cordia monoica Roxb. belonging to Boraginaceae family is a shrub, broadly scattered in most districts of Tamil Nadu on gravel mount sides. The leaves of *Cordia monoica* were collected in the month of June from Maruthamalai Hills of Coimbatore, Tamil Nadu, India. Flowering shoots of the plants were also collected for identification. The collected plant material was identified and their authenticity was confirmed by comparing the voucher specimen at the Botanical survey of India, Coimbatore, Tamil Nadu, India (BSI/SRC/5/23/2014-15/Tech/512). The collected specimens were deposited in the Department of Biotechnology, Sri Ramakrishna College of Arts and Science, Coimbatore, Tamil Nadu, India.

2.1.2 Extraction Process:

Cordia monoica leaves were cleaned to eliminate dirt and then shade dried. Then the dried leaves were powdered in mechanical grinder fine enough to pass through a No.40 sieve for powder analysis. Coarse leaf powder was used for further extraction process

and pharmacological studies. 50gm air dried coarse leaf powder was mixed with 100 ml of ethanol, ethyl acetate and petroleum ether. The extraction was carried out in a closed macerated flask for 24 hours, shaking frequently during the first 6 hours and allowed to stand for 18 hours. Thereafter, the mixture was filtered in haste taking safety measures against loss of the solvent. 25ml of the filtrate was evaporated to aridness in a tarred flat bottomed shallow dish. The extract is stored and used for further analysis (Harborne, 1984; Kokate *et al.*, 1995).

2.1.3 Experimental Animals

Male Wistar Albino rats (150 g) used in the present study were procured from the small animals breeding station, Mannuthy, Kerala, India. They were housed in polypropylene cages (38 x 23 x 10cm) with not more than six animals per cage. The rats were maintained under standard environmental conditions (14h dark /10h light cycles; temp 25±2°C; 35-60% humidity, air ventilation) and were fed with standard pellet diet (M/s. Hindustan Lever Ltd., Mumbai, India) and fresh water *ad libitum*. The animals were acclimatized to the environment for two weeks preceding to experiment use. Animals were fasted over night ahead of the experimental schedule, but have free admittance for water *ad libitum*. The study was approved by ethics committee for animal experimentation (Ref No: ML-EA-CPCSEA/09-2014/07).

2.2 ANTIPYRETIC ACTIVITY

The antipyretic activity of the sample extract was tested against Yeast induced pyrexia in rat model. Wistar Albino Male rats were segregated into four groups of six animals each. The experiment was designed as follows:

Group I : Untreated control rats
Group II : Standard drug paracetamol (150 mg/kg bw.) treated rats
Group III : Ethanolic extract of *Cordia monoica* leaves (200 mg/kg bw p.o)
Group IV : Ethanolic extract of *Cordia monoica* leaves (400 mg/kg bw p.o)
The animals were selected for the experiment after confirmation of approximate constant rectal temperature for 7 days.

Pyrexia was induced by subcutaneous injection of 10 ml/kg of 15% w/v Brewer's yeast suspension below the nape of the neck (Jaiswal *et al.*, 2011). The rectal temperature of each rat was measured before and after 18 h of yeast induction using digital clinical thermometer. After 18 h, animals with temperature increase of 1°C were selected and grouped for the study. Group - I served as control and received normal water. Group II was administered with paracetamol (150 mg/kg bw p.o.) which served as standard reference group. Groups III and IV received the ethanolic extract of *Cordia monoica* leaves (200 and 400 mg/kg bw p.o.) respectively. After drug administration the rectal temperature of the animals was taken at 1h interval for 6h.

2.3 STATISTICAL ANLAYSIS:

All the data obtained in the present investigation were subjected to statistical analysis using SPSS 16 version. Values are expressed as mean ± S.E.M. (n=6). The significance level was set at 5% ($p<0.05$) and 1% ($p<0.01$) interval using student's t Test

III RESULT

By yeast induced pyrexia method, the present study has been carried out to assess and compare the *in-vivo* antipyretic activity of the ethanol extract of *Cordia monoica* leaves. It indicates the activity in a dose dependent manner. As shown in table 1, animals receiving drug paracetamol 150 mg/kg b.w and treated group receiving 200 mg/kg b.w and 400 mg/kg b.w of *Cordia monoica* leaf extract showed a highly significant difference in 0 to 360 min.

The mean initial basal rectal temperature of rats before yeast injection corresponds to 37º C in the present study. The initial rise of temperature after one hour of subcutaneous yeast injection was 39ºC. Administration of Baker's yeast produced an increase in temperature from normal to 39.5ºC within four hours of injection. Fig1 shows that the maximum temperature attained in the control group at one hour. Treatment with paracetamol decreased the temperature to normal within six hours. The oral treatment of rats with ethanolic extract of *Cordia monoica* leaves at two different doses (200 mg/kg bw and 400 mg/kg bw) revealed significant decrease in temperature. At 200 mg/kg the temperature was reduced to 38º C and at 400 mg/kg it was decreased to near normal as that of standard paracetamol. The result was dose dependent with increase in concentration increase in activity was obtained.

IV DISCUSSION

Herbal remedies with potent antipyretic activity received momentum as the synthetic drug paracetamol; nimesulide has toxic effects to various organs of the body. The body has the ability to maintain a natural balance of COX1 and COX2 that regulate all biological systems. A number of plant extracts modulate enzymes of cyclooxygenase pathway that inhibit leukotriene and prostaglandins synthesis, while COX1 and COX 2 was inhibited by crisittineol, apigenin, rasmarinic acid and eugenol of *Ocimum scantum* similar to ibuprofen naproxen and aspirin.

Herbal drugs are to be subjected for several processes such as identification isolation, purification, characterisation, structural elucidation and therapeutic evaluation. Chemometrics provides the scientists with useful tools in understanding the enormous

amounts of data generated by the analytical advances and it prove to be valuable for quality control, classification, modelling and discrimination between herbal fingerprints.

Fever is a complex process triggered by stimuli or infections. There will be elevation of body temperature, when the concentrations of prostaglandin increase. This will ultimately cause a variation in the rate of neurons that control the thermoregulation process in the hypothalamus. Vasopressin and arginine are the own antipyretic substances of the body. The extract may enhance the production of these compounds to decrease the effects of fever.

Antipyretics restrain fever by inhibiting prostaglandin synthetase resulting in the blockage of the synthesis of prostaglandin in the brain or suppressing the rise of IL-Iα production which is subsequent to interferon production. Flavanoids like baicalin suppress TNF-α and exert antipyretic activity (Adesokan *et al.,* 2008) and it is related compounds of prostaglandin levels, thus reducing fever and pain (Germain *et al.,* 2011).

The antipyretic activity of steroids, tannins, flavanoid, triterpenoids and coumarin glycosides have been taken up for research and reported in various studies conducted (Kim *et al.,* 2004; Tiwari *et al.,* 2010). Preliminary Phytochemical analysis of *C. monoica* Roxb. leaves were carried out with ethanolic extract and compounds such as flavanoid, phenol, tannin and steroid were determined (Dhivya and Sivakumar, 2014). The Gas Chromatography-Mass Spectroscopic analysis concluded the presence of bioactive phytochemical compounds in the plant. It was reported that the concentrated ethanol extract contains a variety of bioactive compounds such as Nonacosane, carotene, neophytadiene, Lycopene 7, n- Hexadecanoic acid, Octadecanoic acid, Phenol 3-pentadecyl, Heptacosane, Tetracosahexane hexamethyl (CAS), Benzofuran and Carotene (Dhivya and Sivakumar, 2014). Hence, the reported anti-pyretic property may be due to phenolic content and flavonoid content. The study justifies the use of *C. monoica* leaves as an anti-oxidant, anti-inflammatory and anticancer agent in herbal medicine.

V CONCLUSION:

The present study justifies the traditional use of *C. monoica* leaves to treat Pyrexia, which is a major symptom in MICH (a febrile disease). The antipyretic activity of *Cordia monoica* leaves may be attributed due to its content of steroids, tannins, flavanoid, triterpenoid, glycosides and coumarins. Further studies on characterisation of the novel compound responsible for the antipyretic activity may pave a way for the synthesis of safer drug.

VI ACKNOWLEDGEMENT:

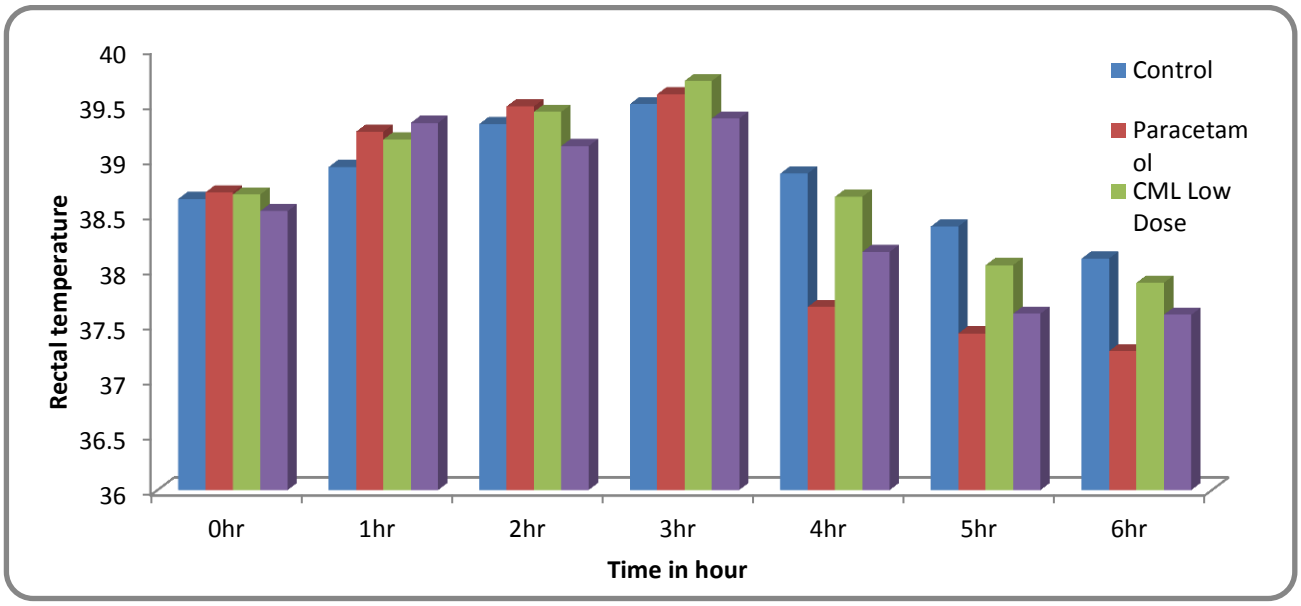
The authors are grateful to the Management, Principal and Faculty of Department of Biotechnology, Sri Ramakrishna College of Arts and Science for providing technical facilities.

TABLE: 1 Effect of Ethanolic extract of *Cordia monoica* Leaves on Yeast Induced Pyrexia

Group	Dose	Rectal Temperature (ºC)							
		Before	0 h	1h	2h	3h	4h	5h	6h
Control	-	37.11 ± 0.01	38.64 ± 0.02	38.93± 0.01	39.32 ± 0.02	39.50 ± 0.02	38.87 ± 0.02	38.39 ± 0.04	38.10± 0.05
Standard	150 mg/kg	37.04 ± 0.02	38.70 ± 0.02 *	39.25± 0.03 **	39.48 ± 0.01 **	39.59 ± 0.01 *	37.66 ± 0.06 **	37.42 ± 0.06 **	37.26± 0.06 **
CML Low Dose	200 mg/kg	37.10 ± 0.02	38.68 ± 0.03 *	39.18± 0.02 **	39.43 ± 0.03 **	39.71 ± 0.04 *	38.66 ± 0.03 **	38.04 ± 0.03 **	37.88± 0.10 **
CML High Dose	400 mg/kg	37.12 ± 0.01	38.53 ± 0.01 **	39.33± 0.04 **	39.12 ± 0.02 **	39.37 ± 0.02 **	38.16 ± 0.05 **	37.6 ± 0.04 **	37.59± 0.06 **

CML-*Cordia monoica* ethanolic leaf extract h-hour

Values are expressed as mean ± S.E.M. (n=6). P values vs. respective control by Student's t - test * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.



CML-*Cordia monoica* ethanolic leaf extract

Fig 1 Antipyretic Effect of *Cordia monoica* (ROXB.) Ethanolic Leaf Extract.

REFERENCES:

Adesokan, A.A. Yakubu, M.T. Owoyele, B.V. and Akanji, M.A. Soladoye, A.O. and Lawal, O. (2008). Effect of administration of aqueous and ethanol extracts of *Enantia chlorantha* stem bark on brewer's yeast induced pyresis in rats. African J of Biochemistry. 2(7): 165-169.

Bennett, P.N. and Brown, M.J. (2003). Clinical Pharmacology. Indian Reprint 2005. New Delhi: Churchill Livingstone, 287.

Dhillon, I. and Kaushik, J.J. (2009). Anti-inflammatory and effect on central nervous system of *Alseodaphne andersonii* in experimental animal models. Pharm. Res. 2: 8-15.

Dhivya, A. and Sivakumar, R. (2014). GC- MS Profiling on ethanolic leaf extract of *Cordia monoica* (Roxb). *International Journal of Advanced* Research. 2(9): 411-419.

Dhivya, A. and Sivakumar, R. (2014). Phytochemical analysis and *invitro* antioxidant evaluation of *Cordia monoica* (ROXB). Leaf extract. International Journal of innovative Pharmaceutical science and research. 2(12); 3001-3017

Duraisankar, M. and Ravichandran, V. Antipyretic Potential of Polyherbal Ayurvedic Products. Asian J Pharm Clin Res. 5(2), 146 – 150.

Emdad Hossain, Subhash C. Mandal and Gupta, J.K. (2011). Phytochemical Screening and In-vivo Antipyretic Activity of the Methanol Leaf-Extract of *Bombax Malabaricum* DC (Bombacaceae). Trop J Pharm Res.10 (1): 55-60

Germain, S. Taiwe, Elisabeth Ngo Bum, Theophile Dimo, Emmanuel Talla, Norbert Weiss Neteydji Sidiki, Amadou Dawe, Fleur Clarisse Okomolo Moto, Paul Desire and Michel Waard. (2011). Antipyretic and antinociceptive effects of *Nauclea latifolia* roots decoction and possible mechanisms of action. Pharm Biol. 49(1):15-25

Giday, M. (2001). An ethnobotanical study of medicinal plants used by the Zay people in Ethiopia. CBM:s Skriftserie, 3: 81 – 99.

Gupta, M. Shaw, B.P. and Mukerjee, A. (2008). Studies on Antipyretic Analgesic and Ulcerogenic activity of Polyherbal Preparation in Rats and Mice. Int. J. Pharm. 4(2): 88-94.

Harborne, J.B. (1984). Phytochemical Methods: A Guide to Modern Technique of Plant Analysis. 2nd ed. Chapman & Hall, London.

Hartwell J.L. (1982). Plant Used Against Cancer, Massachusetts, 67-68.

Jaiswal, A. Kumar, R. Abhinav, K. and Kumar, A. (2011). Antipyretic activity of *Platycladus orieantalis* leaves extract in rat. Int J Appl Biol Pharm. 2: 250-252.

Kim, H.P. Son, K.H. Chang, H.W. Kang, S.S. (2004). Antiinflammatory plant flavonoids and cellular action mechanisms. J Pharmacol Sci. 96: 229-245.

Kokate, C.K. Purohit, A.P. and Gokhale, S.B. (1995). Pharmacognosy, 3rd edition, Nirali Prakashan, Pune.

Nadkarni, A.K. and Nadkarni's Dr. K.M. (1976). Indian Materia Medica. With ayurvedic, unani- tibbi, siddha, allopathic, homeopathic, naturopathic & home remedie. Popular Prakashan, Bombay, India. 3rd ed, 1 & 2,

Rajani, G.P. Deepak Gupta, Sowjanya, K. and Sahithi, B. (2011). Screening of antipyretic activity of aerial parts of *Nelumbo nucifera* gaertn in yeast induced pyrexia. Pharmacologyonline. 1: 1120-1124.

Rapisarda, A. and Ragusa, S and De Pasquale, A. (1993). Brine shrimp bio-assay of the leaves of some *Cordia* species. Médicamentsetaliments:l'approche Ethnopharnlacologlqlje 1:328-330.

Tiwari V, Tiwari A, Madhavan V. Preliminary phytochemical analysis, HPTLC studies and antipyretic activity of alcohol and aqueous extract of *Helicteres isora* L. Root. Int J Pharmacy Pharm Sci 2010; 2(2): 74-79.