Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 5, Issue, 5, pp.1202-1205, May, 2013

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

ANTIPYRETIC ACTIVITY OF *Caesalpinia crista* LINN. SEEDS EXTRACT IN EXPERIMANTAL ANIMALS

[1]Sharma Ishan, [2,*]Gupta Nakul, [3]Mohammed M. Safhi, [4]Meetu Agrawal and [5]Chauhan Prerna

[1]Department of Pharmacology Om Institute of Technology, Near Patanjali, Roorkee, Haridwar, India
[2,3]Department of Pharmacology College of Pharmacy, Jazan University, Jazan, Kingdom of Saudi Arabia
[4]Department of Anatomy College of Pharmacy, Jazan University, Jazan, Kingdom of Saudi Arabia
[5]Department of Pharmacology NIMS Institute of Pharmacy, NIMS University, Shobha Nagar, Jaipur, India

ARTICLE INFO

Article History:
Received 27th February, 2013
Received in revised form
16th March, 2013
Accepted 18th April, 2013
Published online 12th May, 2013

Key words:
Caesalpinia crista linn.
Fever Nut
Brewe's yeast induced pyrexia
Bolied milk induced pyrexia
TAB vaccine induced pyrexia

ABSTRACT

Objective: The study was designed to evaluate antipyretic activity of ethanolic and aqueous extracts of seeds of Caesalpinia crista linn. in various experimental animal models. Material and methods: After collection of seeds, ethanolic and aqueous extract were prepared and the phytochemical screening was performed. Then ethanolic and aqueous both extracts of Caesalpinia crista linn. were evaluated for antipyretic activity using Brewer's yeast induced pyrexia in rats, TAB-vaccine induced pyrexia in rabbits and Boiled milk induced pyrexia in rabbits models. The differences between the temperatures were recorded. Results and Discussion: The preliminary phytochemical screening of the ethanolic and aqueous extracts of the plant Caesalpinia crista linn. showed the presence of phytoconstituents such as Flavonoids, Tannins, Proteins, Alkaloids, Carbohydrates Reducing Sugars, Phytosterols, Saponins and Triterpenoids. After the administration of extracts, when the rectal temperatures were compared with 0 hour temperature at a time interval of 1 hour for six hours, there was a significant decrease in the temperature by the plant extracts and the standard drug (Paracetamol). Flavonoids are known to target prostoglandins which are involved in the late phase of acute inflammation, pyrexia and pain perception. Flavonoids reduce lipid peroxidation by preventing or slowing the onset of cell necrosis and by increasing the vascularity. The anti-pyretic action of Caesalpinia crista linn. may be due to the inhibition of prostaglandin synthesis. Conclusion: The study shows that ethanolic and aqueous extracts have antipyretic activity, but the ethanolic extract shows more significance then aqueous extract.

INTRODUCTION

Pyrexia/Fever

Pyrexia or Fever is an elevation of core body temperature that exceeds the normal daily variation and occurs in conjunction with an increase in the hypothalamic set point.[(1)] In normal adults, the average oral temperature is 37°C (98.6°F). Body temperature above the usual range of normal, can be caused by abnormalities in the brain itself or by toxic substances that affect the temperature-regulating centers.[(2)] Causes of fever may also include some disease like liver disease, solid tumors, fungle infection or sometime caused by drug reactions.[(3)] 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. 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. Today it has become essential to screen plant drugs for its efficacy. *Caesalpinia crista* is a medicinal plant belonging to family Fabaceae, growing wildly throughout India and tropical countries of the world. Each and every part of the plant is claimed to possess some therapeutic property but seed kernel is the most widely used part all-over the world in various systems of medicine. Seed are extremely bitter, commercially available in plenty at a very low cost and are widely used for a variety of disease, especially in cases of all types of fever including malaria. In Ayurveda the seeds, the leaves and the bark all three parts are used. The herb is useful for treatment of amenorrhoea, dysmenorrhoea, diabetes and intermittent fevers.

***Corresponding author:** drnakulmgupta76@gmail.com

Also, used as febrifuge, anthelmintic and expectorant. [(4, 5, 6)] Its Anthelmintic activity [(7)], Nootropic Activity [(8)], Antioxidant and Reactive Oxygen Species Scavenging Activity[(9)] was already reported. Its antipyretic potential has not been explored yet. In the present study an attempt has been made to establish the antipyretic effect of Ethanolic and aqueous extract of the seeds of *Caesalpinia crista.*

MATERIALS AND METHODS

Plant Material

Plant part (seed) were collected from the local market of Ropar (Punjab) and authenticated by Mr. Madan Pal, Executive Engineer, Horticulture Division No.-2 (Chandigarh) and the plant part (seeds) were shade dried and grinded and made a coarse powder and the coarse powder were used for further studies.

Preparation of Extract

Shade dried part (seeds) of plant were powdered (250g) coarsely and firstly extracted with petroleum ether for defatting and then ethanol (99.99%) by Soxhlet apparatus for 72 hr. and aqueous extracted was prepared by maceration process. The extracts were then concentrated until dryness under reduced pressure and controlled temperature (40-50ºC) and then Preliminary Phytochemical screening was performed. [(10)] Percentage yield of all extracts were calculated. The % yield of ethanolic and aqueous extracts was found to be 8.1% and 13.3%. The

LD_{50} determination of *Caesalpinia crista*linn. seed extract was reported by Sunil N Kshirsagar.[8]

Preliminary Phytochemical Screening:[11]

The extracts were subjected to preliminary phytochemical qualitative screening to evaluate the presence of various primary or secondary metabolites following standard procedures.The preliminary phytochemical screening of the ethanolic and aqueous extracts of the plant *Caesalpinia crista* linn. showed the presence of phytoconstituents such as Flavonoids, Tannins, Proteins, Alkaloids, Carbohydrates Reducing Sugars, Phytosterols, Saponins and Triterpenoids.

Test Animals

The following study was done in three different antipyretic models in which Albino Rabbits and Wistar rats were used and the animals were maintained under standard laboratory conditions with access to standard commercial diet and water *ad libitum*. The experiment was carried out according to the Committee for the purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines.[12] Institutional animal Ethics Committee's permission was obtained before starting the experiments on animal.

Brewer's Yeast Induced Pyrexia in Rats:[13]

In this study wistar rats of either sex weighing 150–250 g were used and fed standard animal feed and tap water ad libitum. Pyrexia was induced in rats by subcutaneous injection of 10 ml/kg of a 20% aqueous suspension of dried yeast in the back below the nape of the rat. Animals were kept on fasting for 16h before experiment but allowed to free access to water. Rats were divided into 5 groups, each having 6 animals.

Group I - Treated with saline only (i.p.- 2ml/kg)
Group II - Brewer's yeast + Saline (i.p. – 2 ml/kg)
Group III - Brewer's yeast + Ethanolic extract of C. *crista* (100mg/kg)
Group IV- Brewer's yeast + Aqueous extracts of C. *crista* (100mg/kg)
Group V - Brewer's yeast+ Standard drug Paracetamol (150 mg/kg)

All drugs were given as freshly prepared aqueous suspension in 0.9% saline. The initial rectal temperatures of the rats were recorded using an electric telethermometer. Rats were made hyperthermic by a subcutaneous injection of 20% brewer's yeast suspension dried brewer's yeast in 0.9% saline at a dose of 1 mL/100 g body weight on the back below the nape of the rat. When the temperature was at a peak (18 h after yeast injection) the rectal temperature was recorded again. Those animals that showed a rise in rectal temperature of more than 1.2 °C were used. Test substances and control vehicle were given i.p. and rectal temperature of animals was recorded at 1 h intervals for 6 h after the administration of different extracts.

Statistical Analysis

The significance of difference among the various treated groups and control group was analyzed by means of one-way ANNOVA followed by Dunnett's multiple comparison tests. The experimental results are represented as ± SEM (standard error mean).

TAB-Vaccine Induced Pyrexia in Rabbits: [14]

The following study was performed in rabbits (1.5-1.6 kg). The animals were maintained in the laboratory for 24 hours prior to the experiment. In this method the rabbits were divided into 5 groups, each group consist 6 animals.

Group I - Treated with saline (i.p. - 2 ml/kg)
Group II - TAB vaccine + Saline (i.p. - 2ml/kg)
Group III - TAB vaccine + Ethanolic extract of C. *crista* (100 mg/kg)
Group IV - TAB vaccine + Aqueous extract of C. *crista* (100 mg/kg)
Group V - TAB vaccine + standard drug Paracetamol (150 mg/kg)

The normal rectal temperature of a group of rabbits were recorded by a telethermometer at hourly intervals for a period of 4 h. TAB vaccine will be administered intravenously into the marginal ear vein of rabbits at a dose of 0.5 mL/ rabbit C. *crista* were administered orally after 60 min of TAB vaccine when there was significant pyrexia. The rectal temperature of groups of rabbits were recorded every 60 min. upto 6hours by six lead electro-telethermometer.

Statistical Analysis

The significance of difference among the various treated groups and control group was analyzed by means of one-way ANNOVA followed by Dunnett's multiple comparison tests. The experimental results are represented as ± SEM (standard error mean).

Boiled Milk Induced Pyrexia in Rabbits:[15]

The above experiment was carried out on 13-15 months old rabbits of both sexes about 1.5-1.6 kg. Food and water will be withdrawn 6 hours prior to the experiment. Animals will be divided into 5 groups each having 6 animals.

Group I - Received Saline (i.p. - 2 ml/kg)
Group II - Boiled milk (i.p.) + Saline (i.p. - 2 ml/kg)
Group III - Boiled milk (i.p.) + Ethanolic extract of C. *crista* (100 mg/kg)
Group IV - Boiled milk (i.p.) + Aqueous extract of C. *crista* (100 mg/kg)
Group V - Boiled milk (i.p.) + Standard drug Paracetamol (150 mg/kg)

Before experimentation rectal temperature of rabbits were recorded by inserting a well lubricated bulb of a thermometer in the rectum. Milk was collected from local cow and boiled. When temperature of the boiled milk equilibrates to room temperature then rabbits were injected with boiled milk at the dose of 0.5 ml/kg body weight, to induce pyrexia. After administration of extracts rectal temperatures were recorded in every 1 h intervals up to 6 hour.

Statistical Analysis

The significance of difference among the various treated groups and control group was analyzed by means of one-way ANNOVA followed by Dunnett's multiple comparison tests. The experimental results are represented as ± SEM (standard error mean).

RESULTS

Brewer's Yeast Induced Pyrexia in Rats

As shown in Table 1 and Figure 1, the ethanolic and the aqueous extracts of *Caesalpinia crista*at a dose of 100 mg/kg caused a significant lowering in rectal temperature of hyperthermic rats. This decrease persisted when an assessment was made 6 h after test drug administration and the efficacy was comparable to that of Paracetamol at a dose of 150 mg/kg (Table 1 and Figure. 1).

Table 1. Effect of seed extracts of *Caesalpinia crista* linn. On Brewer's Yeast Induced Pyrexia in Rats

S. No	Group	RECTAL TEMPERATURE IN °C AT HOURLY INTERVEL							
		-18hr	0hr	1hr	2hr	3hr	4hr	5hr	6hr
I	NORMAL CONTROL	36.7± 0.218	36.7±0.230	36.7 ± 0.243	36.8±0.22	36.7±0.202	36.7±0.233	36.7±0.218	36.7±0.234
II	PYRETIC CONTROL (SALINE)	37.0±0.220	38.6±0.425	38.6±0.412	38.7±0.290	38.7±0.282	38.7±0.252	38.8±0.252	38.8±0.232
III	CCED (100mg/kg)	36.6± 0.141	38.9± 0.131	38.2± 0.299	37.7± 0.232**	37.4± 0.189***	37.2± 0.223***	37.0± 0.200***	36.8± 0.161***
IV	CCAD (100mg/kg)	36.5±0.085	38.5±0.042	38.1±0.142	37.8±0.221*	37.5±0.167**	37.2±0.201***	37.1±0.226***	37.0±0.220***
V	PARACETAMOL-150mg/kg)	36.9±0.117	38.6±0.266	38.2±0.223**	37.9±0.163**	37.7±0.128***	37.6±0.147***	37.6±0.124***	37.5±0.131***

Values are expressed as mean ± S.E. N=6. ***P<0.001, **P<0.01,*P<0.05compared with 0 hr. of the same group, CCE-*Caesalpinia crista* Ethanolic extract, CCA- *Caesalpinia crista* Aqueous extract.

Table 2. Effect of seed extracts of *Caesalpinia crista* linn. On Tab Vaccine Induced Pyrexia in rabbits

S. No.	TREATMENT	RECTAL TEMPERATURE IN °C AT HOURLY INTERVEL							
		Initial temp.	0 hr	1hr	2hr	3hr	4hr	5hr	6hr
I	NORMAL CONTROL	38.3± 0.071	38.3± 0.071	38.3± 0.069	38.3± 0.069	38.3± 0.072	38.3± 0.071	38.3± 0.073	38.3±0.069
II	PYRETIC CONTROL (SALINE)	38.2 ± 0.047	39.4±0.016	39.4± 0.017	39.4±0.018	39.4±0.019	39.4±0.012	39.5±0.006	39.5±0.047
III	CCED (100mg/kg)	38.2±0.063	39.4±0.040	39.0±0.038*	38.8±0.024**	38.7±0.038**	38.7±0.049***	38.6±0.031***	38.5±0.046***
IV	CCAD (100mg/kg)	38.0±0.022	39.2±0.046	39.0±0.013	38.8±0.013**	38.7±0.012**	38.6±0.013**	38.6±0.013***	38.5±0.011***
V	PARACETAMOL-150mg/kg)	38.1±0.004	39.5±0.078	39.2±0.035**	39.0±0.038***	38.8±0.022***	38.6±0.006***	38.4±0.013***	38.2±0.004***

Values are expressed as mean ± S.E.M. (n = 6);***-P≤0.001,**P≤0.01,*P≤0.05 Compared in the same group with 1 hr. of the tab Vaccine, CCEE- *Caesalpinia crista* Ethanolic extract, CCAE- *Caesalpinia crista* Aqueous extract.

Table 3. Effect of seed extracts of *Caesalpinia crista* linn. On Boiled Milk Induced Pyrexia In Rabbits

S. No	TREATMENT	RECTAL TEMPERATURE IN °C AT HOURLY INTERVEL							
		Initial temp.	0 hr.	1hr	2hr	3hr	4hr	5hr	6hr
I	NORMAL CONTROL	38.3±0.064	38.3±0.066	38.3±0.064	38.3±0.064	38.3±0.068	38.3±0.064	38.3±0.060	38.3±0.064
II	PYRETIC CONTROL (SALINE)	38.1±0.028	39.4±0.022	39.5±0.021	39.5±0.022	39.5±0.019	39.5±0.021	39.5±0.016	39.5±0.017
III	CCED (100mg/kg)	38.3±0.016	39.5±0.019	39.1±0.091	38.9±0.058**	38.7±0.038***	38.6±0.039***	38.5±0.027***	38.4±0.030***
IV	CCAD (100mg/kg)	38.3±0.018	39.5±0.016	39.2±0.027	39.0±0.025**	38.8±0.028**	38.7±0.034***	38.6±0.041***	38.5±0.034***
V	PARACETAMOL-150mg/kg)	38.3±0.027	39.6±0.037	39.3±0.035**	39.1±0.029**	38.9±0.023***	38.8±0.030***	38.6±0.037***	38.5±0.036***

Values are expressed as mean ± S.E.M. (n = 6); *** P≤ 0.001, ** P≤0.01 compared with 0 h of the same group, CCEE- *Caesalpinia crista* Ethanolic extract, CCAE- *Caesalpinia crista* aqueous extract.

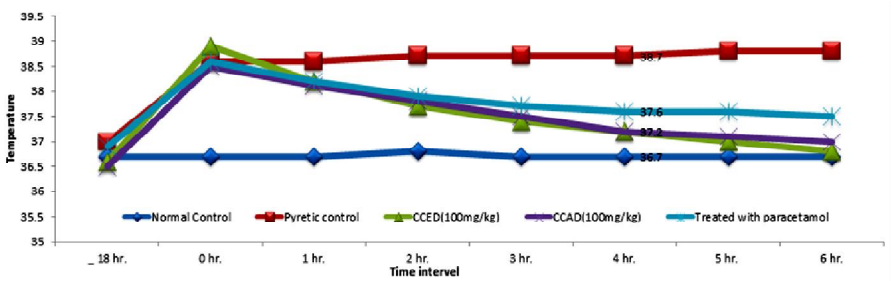

Figure 1: Effect of Seed extracts of *Caesalpinia crista linn.* on Brewer's Yeast Induced Pyrexia

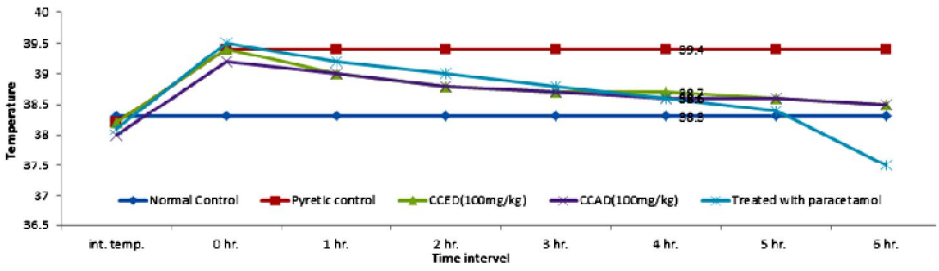

Figure 2: Effect of Seed extracts of *Caesalpinia crista linn.* on TAB Vaccine Induced Pyrexia

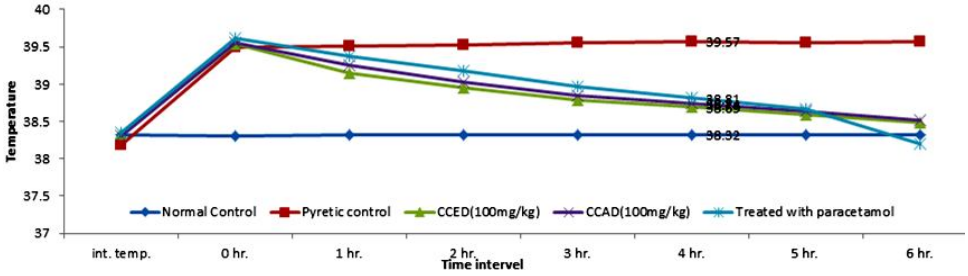

Figure 3: Effect of Seed extracts of *Caesalpinia crista linn.* on Boiled milk Induced Pyrexia

TAB vaccine-induced pyrexia in Rabbits

When the ethanolic and aqueous extracts were administered to rats with established TAB vaccine-induced fever, the fever was significantly reduced and the body temperature was normalized by administration of 100 mg/kg dose of extracts orally. However, 100 mg/kg dose of aqueous extract had less significant effect then ethanolic extract on the rectal temperature of rabbits. The effect was observed upto 6 hours (Table 2 and Figure 2).

Boiled milk induced pyrexia Rabbits

As shown in Table 3 and Figure 3, when ethanolic and aqueous extracts of *Caesalpinia crista* linn. at the dose of 100 mg/kg was administered to the hyperthermic rabbits the rectal temperature decreased significantly. The efficacy was comparable to Paracetamol at a dose of 150 mg/kg. The efficacy of aqueous extract of *Caesalpinia crista* linn was less significant then ethanolic extract of *Caesalpinia crista* linn. (Table 3 and Figure 3)

DISCUSSION

Fever may be a result of infection or one of the sequels of tissue damage, inflammation, graft infection or other diseases states. Antipyretics are drugs which reduce elevated body temperature. Regulation of body temperature requires a delicate balance between the production and loss of heat and the hypothalamus regulates the set point at which body temperature is maintained. In fever this set point is elevated and drugs like paracetamol don't influence body temperature when it is elevated by factors such as exercise or increase in ambient temperature.[(16)] Search for safe herbal remedies with potent antipyretic activity received momentum recently as the available antipyretic, such as Paracetamol, Aspirin, Nimusulide etc. have toxic effect to the various organs of the body.[(2)] The preliminary phytochemical screening of the ethanolic and aqueous extracts of the plant *Caesalpinia crista* linn. showed the presence of phytoconstituents such as Flavonoids, Tannins, Proteins, Alkaloids, Carbohydrates Reducing Sugars, Phytosterols, Saponins and Triterpenoids. In many earlier studies like Brasseur in 1989 worked on anti-inflammatory properties of flavonoids[17], Vimala R et al. in 1997 worked on anti-inflammatory and anti-pyretic activity of Micheliachampaca Linn., Ixora brachiata Roxb. and Rhynchosia cana etc. and the results revealed that flavonoids compounds exhibit antipyretic effect[18] as some flavonoids are predominant inhibitors of cyclooxygenase or lipooxygenase.[19, 20]Flavonoids are known to target prostoglandins which are involved in the late phase of acute inflammation, pyrexia and pain perception. Flavonoids reduce lipid peroxidation by preventing or slowing the onset of cell necrosis and by increasing the vascularity.[21, 22] In general non-steroidal anti-inflammatory drugs produce their antipyretic action, through inhibition of prostaglandin synthesis within the hypothalamus.[23,24]The anti-pyretic action of *Caesalpinia crista* linn. may be due to the inhibition of prostaglandin synthesis.

Conclusion

Ethanolic and aqueous seed extracts of *Caesalpinia crista* linn. showed antipyretic activity but the maximum anti-pyretic activity was given by the standard drug paracetamol and the ethanolic extract of *Caesalpinia crista* showed antipyretic activity nearly equal to that of the standard drug. However further investigations are required to isolate active constituents responsible for this activity and to elucidate the exact mechanisms of action.

REFERENCES

1. Fauci AS, Braunwald E, Kasper DL, Hauser Sl, Longo DL, Jameson JL., Loscalz J, "Harrison's -Principles of internal medicine", McGraw Hill publication, 2008, Vol. I; 17:117-121.
2. Guyton AC, Hall JE, "TEXT BOOK of Medical Physiology", Elsevier Saunders Publication, 2006, 11:889-895.
3. Boon NA, Colledge NR, Walker BR, "Davidson's Principles and practice of Medicine", Churchill Livingstone publication, 2006, 20; 286-287.
4. Das B., Y. Srinivas, C. Sudhakar, I. Mahender and K. Laxminarayan, "New diterpenoids from *Caesalpinia crista* species and their cytotoxic activity" Bioorg. Med. Chem. Lett. 2010;20:2847-2850
5. Kirtikar and Basu, "Indian Medicinal Plants" II: 842-845.
6. Handa S.S. and Kaul M.K., "Supplement to cultivation and utilization of medicinal plants" 727-739.
7. Abdul Jabbar, Muhammad Arfan Zamana, Zafar Iqbala, Muhammad Yaseenb, and Asim Shamima "Anthelmintic activity of *Chenopodium album (L.)* and *Caesalpinia crista (L.)* against trichostrongylid nematodes of sheep" Journal of Ethnopharmacology 8 October 2007;114(1):86-91.
8. Kshirsagar SN. "Nootropic Activity of dried Seed Kernels of *Caesalpinia crista Linn* against Scopolamine induced Amnesia in Mice" International Journal of Pharm. Tech Research, Jan-Mar 2011; 3(1):104-109
9. Mandal Sourav, Bibhabasu Hazra, Rhitajit Sarkar, Santanu Biswasand Nripendranath Mandal "Assessment of the Antioxidant and Reactive Oxygen Species Scavenging Activity of Methanolic Extract of *Caesalpinia crista* Leaf" Hindawi Publishing Corporation, 2011;114-118.
10. Kokate C.K., Gokhale S.B., Purohit A.P. "Pharmacognosy" Nirali Prakashan, 39:106-109.
11. Gill NS, Kaur R, Arora R, Bali M, "Phytochemical investigation of *Caesalpinia crista* seed extract for their therapeutic potential" Research journal of medicinal plants.2012;6(1):100-107
12. "CPCSEA Guidelines for laboratory animal facility" Indian journal of pharmacology, 2003 vol.-35(4) Pg. No.-257-274
13. Gupta N, Subhramanyam EVS, Jha S, Bhatia V and Narang E, "A comparative antipyretic activity of the crude extracts of the plant Leucas aspera and Glycosmispenta phylla" J. Chem. Pharm. Res., 2011;3(1):320-323.
14. Chidambaram K, Albert J, Karpagam K, Noohu S, "Antipyretic Activity of Crateva Magna Bark On Tab-vaccine Induced Pyrexia" IJPSR, 2011; 2(4): 856-859.
15. Khan A, Md. Baki A , Abdul M, Al-Bari A, Hasan S, Mosaddik MA, Rahman MM, Haque ME, " Antipyretic Activity of Roots of Laportecrenulata Gaud in Rabbit" Research Journal of Medicine and Medical Sciences,2007;2(2):58-61.
16. Goodman and Gillman. The Pharmacological basisof therapeutics, Joel G. Hardman, Lee. Limbrideds. 9th ed, 1996;620.
17. Brasseur T. Antiinflammatory properties of flavonoids.J Pharm Belg 1989:44;235-41
18. Vimala R, Nagarajan S, Alam M, Susan T, Joy S.Anti-inflammatoryand antipyreticactivity of Micheliachampaca Linn., (white variety), Ixora brachiata Roxb. and Rhynchosia cana (Willd.) D.C. flower extract. Indian J Exp Biol 1997; 35:1310-4
19. Trease GE, Evans WC. Flavone and related flavonoid glycoside. Pharmacognosy. 4th ed. London: Bailliere Tindall; 1972
20. Mathew AG, Parpia HAB. Food browning as a polyphenol reaction. In: Chichester CO, Mrak EM, Stewart GF,editors. Advances in food research. New York: Academic Press; 1971. p. 75-145
21. Rajnarayana K, Reddy MS, Chaluvadi MR. Bioflavonoids clarification, Pharmacological andbiopharmacol.2001;33:2-16.
22. Manjunatha BK, Vidhya SM, Krishna V,Mankani KL. Wound healing activity of Leucas hirta,Ind.J.PHARM.Sci. 2006; 60(3),380-384.
23. Clark WO, Cumby HR. The antipyretic effect ofindomethacian J.Physiol.1975;248: 625-38.
24. Zell R, Krupp P.Schorbaum E, Lomax P, Jacob J. eds: Temperature regulation and drug action,Basel, S.Karger. 1975; 233-241.

****