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Original Research Article

EVALUATION OF ANTIPYRETIC ACTIVITY OF VARIOUS EXTRACTS OF LEAVES OF *MENTHA ARVENSIS* IN RAT

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Abstract: *Mentha arvensis Linn*. is described as a antipyretic in Ayurveda, the Indian system of Medicine. There is no reaserch reports in themodern literature regarding its usefulness as a antipyretic agent. The present studywas carried out to evaluate the antipyretic activity of extracts of leaves of *Mentha arvensis Linn*. Brewer'syeastinduced pyrexia in male Albino rats. **Materials and Methods**: Different leaf extracts of *Mentha arvensis Linn* were subjected to preliminary phytochemical analysis and evaluated for their antipyretic potential employing yeast induced pyrexia in Albino rats. **Results:** The ethanolic, chloroform and petroleum ether leaf extract exhibited maximum antipyretic activity ($P<0.001$) at doses of 250 and 500 mg/kg-1b.w. p.o. in a dose dependent manner and the antipyretic activity was comparable to that of reference standard paracetamol and aqueous extract did not showed any significant antipyretic activity. Phytochemical analysis revealed presence of flavonoid, triterpenoids, sterols and alkaloids, which have been known for their antipyretic activities. **Conclusion:** The Ethanolic extract of *Mentha arvensis Linn* of leaves. Possessed antipyretic activity and this may be due to the presence of flavonoids and triterpenoids, because as per literature they showed good antipyretic activity. However, further molecular level word is required to determine the exact mechanism involved in antipyretic activity of *Mentha arvensis Linn*. leaves.

Key words: *Mentha arvensis Linn*, Brewer'syeast, antipyretic, phytochemical analysis, paracetamol.

Introduction: Plants have been used by man from prehistoric times for relieving suffering and curing ailments. The therapeutic use of plants is as old as4000–5000 B.C. and Chinese used first the natural herbals preparations as medicines.

In India, however, earliest references of use of plants as medicine appear in Rig-Veda which is said to be written between 3500–1600 B.C. Later the properties and therapeutic uses of medicinal plants were studied in detail and recorded empirically by the ancient physicians

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in Ayurveda which is a basic foundation of ancient medical science in India[1].

The knowledge about the use of medicinal plants has been accrued through centuries and such plants are still valued even today, although synthetics, antibiotic, etc. have attained greater prominence in modern medicine.[1.]

Today, investigations in the field of pharmacognosy and pharmacology have supplied valuable information on medicinal plants with regards to their availability, botanical properties, and methods of cultivation, collection, store, and therapeutic use

The indigenous systems of medicine practiced in India are based mainly on the use of plants. Charaka Samhita (1000 BC-100 AD) records the use of2000 vegetable remedies. Ancient medicine was not solely based on empiricism and this is evident from the fact that some medicinal plants which were used in ancient times still have their place in modern therapy.

Thus, for example 'Ephedra' a plant used in China 4000 years ago is still mentioned in modern pharmacopoeias as the source of an important drug, 'ephedrine'.

The plant Sarpagandha (Rauvolfia serpentine) which was well known in India as a remedy for insanity has now shown that one of its constituents, reserpine, is a wonder drug today for curing mental ailments. Quinine, another important antimalarial drug of modern medicine, was obtained from the cinchona tree. Synthetics and antibiotics although they often show miraculous and often instantaneous results, prove harmful in the long run and that is why many synthetics and antibiotics have become outdated or have been specified to be prescribed strictly under medical supervision.[2]

Pellet size and shape were determined using an image analysis system. Photomicrographs

The medicinal plants are rich in secondary metabolites which are potential sources of drugs and essential oils of therapeutic importance. The important advantages claimed for therapeutic uses of medicinal plants in various ailments are their safety besides being economical, effective and their easy availability[3, 4.]

Because of these advantages the medicinal plants have been widely used by the traditional medical practitioners in their day to day practice.

According to a survey (1993) of World Health Organization (WHO), the practitioners of traditional system of medicine treat about 80% of patients in India, 85% in Burma and 90% in Bangladesh[4, 5.]

In traditional systems of medicine the Indian medicinal plants have been used in successful management of various disease conditions like bronchial asthma, chronic fever, cold, cough, malaria, dysentery, convulsions, diabetes, diarrhea, arthritis, emetic syndrome, skin diseases, insect bite etc. and in treatment of gastric, hepatic, cardiovascular & immunological disorders [6,7].

In Asia, the practice of herbal medicine is extremely well established and documented. As a result, most of the medicinal plants that have international recognition come from this region, particularly from China and India. In Europe and North America, the use of herbal medicine is increasing fast, especially for correcting imbalances caused by modern diets and lifestyles. Many people now take medicinal plant products on a daily basis, to maintain good health as much as to treat illness8.

Herbal medicine is still the mainstay of about 75–80% of the world's population, mainly in developing countries, for primary health care because of better cultural acceptability, better compatibility with the human body and lesser side effects. It is estimated that approximately one quarter of prescribed drugs contain plant extracts or active ingredients obtained from or modeled on plant substances.

Atropine, artimesinin, colchicine, digoxin, ephedrine, morphine, physostigmine, pilocarpine, quinine, quinidine, reserpine, taxol, tubocurarine, vincristine and vinblastine are a few important examples of what medicinal plants have given us in the past. Most of these

plant-derived drugs were originally discovered through the study of traditional cures and folk knowledge of indigenous people and some of these could not be substituted despite the enormous advancement in synthetic chemistry.

The resurgence of herbal drug usage in recent years may be attributed to the associated hazardous side effects that many of the synthetic drugs appear to cause. Hence, this is the opportune time to be involved in herbal medicine research andeducation[8, 9]. Indigenous people have shown evidences of historical continuity of resource use and possess a broad base knowledge of the complex ecological system existing in the vicinity of their habitat. Over the past decade, herbal medicine has become a topic of increasing global importance, having repercussion on both world health and international trade. Recognition of the medicine and economic benefits of the plants based medicines is growing in both developing and industrialized countries, although it varies greatly from country to country.

Herbal medicine is a major component in all indigenous peoples' traditional medicine and a common element in ayurvedic, homeopathic, naturopathic, traditional oriental, and Native American Indian medicine.

WHO notes that of 119 plant-derived pharmaceutical medicines, about 74 percent aroused in modern medicine in ways that correlated directly with their traditional uses aslant medicines by native cultures[10].

The age-old Indian system of medicine, have been neglected mainly because of the rapid expansion of the allopathic system of medical treatment. This is despite the fact that our country has a long history of local health tradition, which is backed by thousands of scriptures left behind by practitioners of these systems of medicine. A vast majority of the world population today is finding them unable to afford the products of the western pharmaceutical industry, and they have to depend mainly upon the use of traditional medicine. This reality has been recognized, documented and compiled by the WHO in an inventory of medicinal plants numbering over 20000species2. More than 50,000 plants have been used for medicinal purposes. India is represented by rich culture, traditions, and natural biodiversity, and offer unique opportunity for the drug discovery researchers. India is one of diverse countries in the

World, rich in medicinal herbs and plants. In Indian traditional system of medicine, herbal medicines have been used primordially[11].

The annual production of medicinal and aromatic plant's raw material is worth about Rs.200 cores. This is likely to US $5 trillion by 2050. It has been estimated that in developed countries such as United States, plant drugs constitute as much as 25% of the total drugs, while in fast developing countries such as China and India, the contribution is as much as 80%. India is one of the world's 12 biodiversity centers with the presence of over 45000 different plant species. In India, drugs of herbal origin have been used in traditional systems of medicines such as Unani and Ayurveda since ancient times. The Ayurveda system of medicine uses about 700species, Unani 700, Siddha 600, Amchi 600 and modern medicine around 30 species.

In many of the developing countries the use of plant drugs is increasing because modern life saving drugs are beyond the reach of three quarters of the third world's population although many such countries spend 40-50% of their total wealth on drugs and health care. The forest in India is the principal repository of large number of medicinal and aromatic plants. Among the various systems of medicine, Ayurveda is most developed and widely practiced in India. Ayurveda dating back to 1500-800 BC has been an integral part of Indian culture. Ayurveda, a system of herbal medicine in India, Sri Lanka and South-East Asia has more than 8000 plant remedies and using around 35,000-70,000 plant species. Many secondary metabolites of plant are

commercially important and find use in a number of pharmaceutical compounds.

Pyrexia: Ayurveda, an ancient healing system refers fever as jwara, a condition in which the body condition goes beyond the normal temperature and is characterized by disturbance in normal functioning of the system. It believes that it is due to disruption of any one or all the doshas or energy fields within the body system and if not attended immediately might damage other parts of the body.

It classifies fever into eight types which ranges from internal to external to parasitic to seasonal and mental and that if the fever chapter is completed then half of treatment is over. The main symptoms of fever are a raise in body temperature, chills, sore throat, body stiffness, muscle aches, headache, disturbed digestion, lack of appetite etc. Fever according to ayurveda occurs when the digestive fire (Agni) and digestive toxins (ama) which are normally found within the gastrointestinal tract are thrown out of their place by disrupted doshas and then they overflow into the blood and lymphatic system. Its circulation in the body causes the typical symptoms like high temperature, heaviness etc. Because of this the tridoshas are further irritated and it spreads throughout the blood stream. When supplemented with its own heat plus the heat of the misplaced agni, the temperature of the body raises can causes the symptoms of fever.

Ayurveda, a holistic medical system, emphasis that fever is due to toxicity in the rasa dhatu (the body's basic vital tissue) and manages fever by: Fasting (langana), Sudation (swedana), Time-Waiting/Patience (kala), Light diet (yavagu), bitter drugs Department of Pharmacognosy, NCP, Shimoga. (tikta bheshajam) and Detoxification (ama pachana). Bitter Ayurvedic medicines such as Dasamoola kaduthryam qwath, Amruthothram qwath, Indukantham qwath, Dhanwantharam qwath, Amrutharishta, Sudarsanasava, Dasmoolarishta, Vettumarantablet, Gorochanadi tablet, gopichandanadi tablet, sooryprabha tablet, sirasooladi vajra rasam, laxmi vilas rasam, ananda bhairava ras, etc. burns ama, increases the white blood cell count which help the body to fight infections[14,15.]

The scientific investigations on pathogenesis of fever revealed that various exogenous and endogenous factors are involved in pyrexia. The febrile response, of which fever is but one component, is a complex physiologic reaction to disease involving a cytokine-mediated rise in body temperature, generation of acute-phase reactants, and activation of numerous physiologic, endocrinologic, and immunologic systems[16.] The temperature of the body is dependent on maintaining a balance between the production and dissipation of heat.

Under normal circumstances, heat is generated internally during metabolic processes or when external environmental temperatures exceed those of the body. Heat can also be produced by increased skeletal muscle activity, such as that which occurs with shivering. Heat loss occurs predominantly from the skin via evaporative losses and also, to some extent, via the lungs. Much like other fundamental aspects of human biology, core body temperature is regulated closely by intricate control mechanisms, involving a complex interplay of autonomic, endocrine, and behavioral responses.

The hypothalamus is central to this process, functioning as a thermostat, controlling thermoregulatory mechanisms that balance heat production with heat loss. Integral to the process are the heat-sensitive receptors located in the pre optic area of the anterior hypothalamus. These receptors, which are sensitive to elevations in blood temperature, increase signal output as the temperature rises above a fixed thermal set point (37.1°C average) and decrease output when the temperature drops below the set point. Similar receptors are in the skin, spinal cord, and abdomen, sending impulses to the hypothalamus via the spinal cord. With core body temperature elevations, the sympathetic system is inhibited, leading to vasodilation of skin vessels and stimulation of

the sweat glands to facilitate evaporative loss. This process prevails until the body temperature matches the thermal set point, when heat production matches heat loss. Similarly, when body temperature is below the thermal set point, a variety of responses are initiated to conserve and increase production of heat. They include activation of the sympathetic nervous system to induce vasoconstriction of skin blood vessels; inhibition of sweating; activation of the shivering center in the posterior hypothalamus, thereby increasing muscle heat production; and secretion of neurotransmitters, which increase cell metabolism and, consequently, heat production. The hypothalamus also affects behavioral influences in humans, with individuals changing clothes and/or seeking appropriate shelter to maintain body temperature.

In-vivo experiments with rabbits revealed that thermoregulation requires an intact sympathetic nervous system and can be modulated by various adrenoreceptor antagonists[17, 18]

Material and Methods:

Pharmacognostic Investigation:

- ❖ Collection and Authentication of *Mentha arvensis Linn.* leaves
- ❖ Preliminary Pharmacognostic Characterstics
- ❖ Determination of Physical Constants

I. Loss on Drying

II. Extractive Values

a. Alcohol soluble extractive

b. Aqueous soluble extractive

c. Chloroform soluble extractive

Extraction of powdred leaves of *Mentha arvensis linn.*

Preliminary phytochemical investigation:

- ❖ Qualitative Chemical Tests

Pharmacological activity: Albino rats of either sex (Wistar strain) weighing between 150-200 gm were selected for present study. They were maintained under uniform laboratory conditions in standard steel cages and provided with food and water ad libitum. All the animalswere kept for 15 days under standard laboratory conditions in a 12h: 12h light anddark cycles and maintained under controlled temperature 27± 20C for acclimatization. The experiment was conducted in accordance with the direction of Institutional Animal Ethical Committee (IAEC) CPCSEA, Government of India.

Acute Toxicity Study: Various extracts of Mentha arvensis leaves were subjected for acute toxicity study according to the recommendedmethods120 as follows:

Healthy Swiss Albino mice of either sex weighing 25 to 30gms were used to determine the safer dose. The animals were fasted overnight prior to the acute toxicity study. The extracts were suspended in Tween 80 (1% w/v) and administered at a dose of 100-5000mg/kg b.w orally via a gastric catheter. The groups were almost continuously observed for mortality and behavioral changes during first 24hr and then daily for fortnight. The dose which caused no mortality and was well tolerated was determined in a step wise manner and the effective dose was calculated.

Since all three extracts were found to be safe and no mortality observed up to 5000 mg, the maximum tolerated dose (MTD) was considered as 5000 mg/kg body weight. Hence 1/10th of the MTD ie, 500mg was selected for further study.

Animals for antipyretic activity: The complete course of the experiment was carried out using healthy adult WistarAlbino rats of either sex weighing 150–200gm were maintained at standard housing conditions and fed with commercial laboratory animal feed and tap water. The rats were housed in the laboratory for about 2 weeks for acclimatization with natural 12:12hr light–dark cycle. The animals were starved overnight, but tap watered lib prior to the day of experimentation.

Drug Formulation: The test doses of the extracts were prepared in Teen 80 (1% w/v). Paracetamol was used as a standard drug (200 mg/kg b.w).

Procedure: Preliminary screening of ethanolic and petroleum ether extracts of Mentha arvensis

for antipyretic activity extracts were screened independently to evaluate their antipyretic potential.

The assessment of antipyretic activity was carried out using Brewer's yeast induced pyrexia in Wistar Albino rats. Pyrexia was induced by injecting subcutaneously.

10.0 ml / kg, b.w. of 15% aqueous suspension of Brewer's yeast in normal saline (0.9%).The experimental animals were fasted overnight with water ad libitum before the experiments. The normal body temperature of each animal was measured by inserting a flexible telethermometer probe coated with the lubricant 3-4 cm deep into rectum. After18 hrs of yeast injection the rectal temperature was again recorded and the animals that showed an increase in temperature of at least by 0.5-10C were selected for further study.

For the preliminary screening of various extracts for antipyretic activity, the animals were grouped as follows:

Group I - (Negative control, n=1): Animals treated with 0.9% saline solution at a dose of 10 ml /kg b.w, p.o.

Group II - (Positive control, n=1) – Animals treated with standard drug Paracetamol at dose of 200 mg/kg b.w, p.o.

Group III (n=2): 1animals treated with 250mg and the other 1 with 500 mg/kgb.w, p.o of ethanolic extract of leaf of Mentha arvensis.

Group IV (n=2): 1animals treated with 250mg and the other 1 with 500 mg/kg b.w,p.o. of petroleum ether extract of leaf of Mentha arvensis.

Group V (n=2) 1 animals treated with 250mg and the other 1 with 500 mg/kg b.w,p.o. of chloroform extract of leaf of Mentha arvensis.

Group VI (n=2) 1 animals treated with 250mg and the other 1 with 500 mg/kg b.w,p.o. of aqueous extract of leaf of Mentha arvensis.

The rectal body temperature of all the animals in the above groups were recorded at the interval of 1h, 2h, 3h and 5h by as described above.

Statistical Analysis

The data obtained from each experiment was subjected to one way ANOVA followed by Turkey's multiple comparison tests. The P values were analyzed and recorded in respective tables.

Result:

Table 1: Pharmacognostic Investigation:

S.No.	Physical constants	Result
1	Ash values (%w/w) Total ash value Water soluble ash value Water insoluble ash value	 20.23% 2.07% 0.74%
2	Loss on Drying	6.20%
3	**Extractive Values** Alcohol Soluble Aqueous Soluble Extractive Value Petroleum Ether Soluble Extractive Value	 19.16% 28.64% 5.21%

Table No.2 Nature, Colour and % Yield of Extracts

S.No.	Name of extract	Nature of extract	Colour	Weight w/w	%yield
1	Pt. Ether	Semi-solid and sticky	Green	5.23	4.3%
2	Chloroform	Semi-solid and sticky	Greenish-black	6.64	2.5%
3	Ethanol	Semi-solid	Dark green	13.92	3.5%
4	Aqueous	Solid	Dark brown	17.49	4.5%

Table 3: Phytochemical Investigation

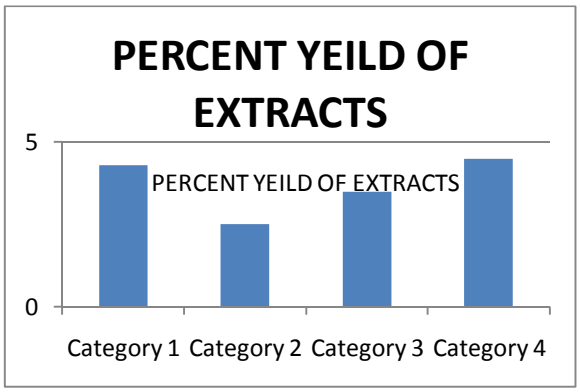
	Name of the Test	Petroleum Ether	Ethanol Extract
1.	Test for Carbohydrates: Molisch's Test Reducing Sugar	+	+
	Fehling's Test	+	+
	Benedict's Test	+	+
	Monosaccharide's		
	Barfoed's Test	+	+
2.	Test for Proteins: Millon's Test	-	-
	Xanthoproteic Test	-	-
	Biurette's Test	-	-
	Ninhydrin's Test	-	-
3.	Test for Sterols: Salkowaski Test	+	-
	Liebermann-Burchard	-	-
	Test Sulphur Test	+	-
4.	Test for Triterpenoids: Salkowaski Test	+	+
	Liebermann-Burchard Test	+	+
5.	Test for Glycosides: Baljet's Test	+	+
	Keller Killani Test	-	-
	Raymond's Test	+	+
	Bromine Water Test	+	+
	Legal's Test	+	+
6.	Test for Saponins: Foam Test	-	-
	Haemolysis Test	-	-
	Raymond's Test	-	-
	Bromine Water Test	-	-
	Legal's Test	-	-
7.	Test for Alkaloids: Mayer's Test	-	-
	Wagner's Test	-	-
	Hager's Test	-	-
	Dragendroff's Test	-	-
8.	Test for Flavonoids: Ferric chloride Test	-	+
	Shinoda Test	-	-
	Zn-HCl Reduction Test	-	+
	Alkaline Reagent Test	-	+
	Lead acetate Solution Test	-	+
9.	Test for Tannins: Ferric chloride test	-	-
	Gelatin Test	-	-
10.	Test for Lipids	-	-

Table No. 4: Effect of different fraction of ethanolic leaf extract of **Mentha arvensis Linn** and Paracetamol on Brewer's yeast induced pyrexia in Albino rats

GROUP	DOSE Mg/Kg b.wt. p.o	Normal rectal tempt. before yeast administration	Normal rectal tempt after yeast administration	Rectal tempt after 1hr	Rectal tempt after 2hr	Rectal tempt after 3hr	Rectal tempt after 5hr
Group I	10 ml/kg	36.50±0.03	37.15±0.04	37.17±0.04	37.23±0.05	37.27±0.04	37.35±0.04
Group II	200mg/kg	36.65±0.08	37.40±0.10	37.23±0.05***	37.00±0.10***	36.85±0.08***	36.65±0.08***
Group III	250mg/kg	36.95±0.16	37.60±0.14	37.60±0.14	37.60±0.14	37.70±0.14	37.70±0.14
	500mg/kg	37.05±0.11	37.75±0.08	37.75±0.08	37.75±0.08	37.80±0.06	37.85±0.08
Group IV	250mg/kg	37.15±0.09	37.75±0.06	37.58±0.07***	37.48±0.07***	37.35±0.09***	37.15±0.09***
	500mg/kg	36.55±0.04	37.13±0.08	37.03±0.08***	36.92±0.07***	36.77±0.05***	36.52±0.05***
GROUP V	250mg/kg	36.75±0.04	37.63±0.04	37.47±0.18*	37.45±0.18*	37.43±0.18*	37.40±0.19*
	500mg/kg	36.75±0.04	37.62±0.05	37.45±0.18*	37.43±0.24*	37.40±0.18*	37.35±0.24*
GROUP VI	250mg/kg	36.72±0.05	37.35±0.04	37.08±0.04***	36.97±0.07***	36.63±0.14***	36.57±0.07***
	500mg/kg	36.95±0.16	37.65±0.12	36.91±0.21***	36.83±0.08***	36.67±0.06***	36.43±0.07***

Values represent Mean ± S.E.M, (n=6), Control (0.9% Normal saline solution) *P<0.05, **P<0.01, ***P<0.001. Significant compared to corresponding data of the control.

Percent Yield of Extracts: The plant materials were extracted with 95% v/v ethanol, petroleum ether, chloroform and water in Soxhlet extractor (hot extraction) and the extracts were evaporated using Rota flash evaporator. The percent yield of ethanolic, petroleum ether, chloroform and aqueous extracts were 4.3 %, 2.5 %, 3.5% and 4.5 % respectively



Category 1. Ethanolic extract - 4.3%
Category2. Petroleum ether -2.5%
Category3. Chloroform extract -3.5%
Category4. Aqueous extract -4.5%

Observation: The animals of Group –IV treated with pet. ether , Group-III treated with ethenol and The animals of Group –V treated with chloroform showed to exhibit maximum antipyretic activity at 250 mg and 500 mg/kg b.w in a dose dependent manner (P<0.001). Group VI treated with aqueous leaf extract of Mentha arvensis showed the significant effect on lowering the body temperature of the rat. The initial and final rectal temperatures (0C) in the group treated with pet ether fraction (250mg/kg bow. and 500mg/kg bow.) were found to be 37.75±0.06 and 37.15±0.09, 37.13±0.08 and 36.52±0.05respectively, while that of group treated with aqueous fraction were 37.18±0.06 and36.57±0.07, 37.07±0.07 and 36.43±0.07 respectively, compared to 37.40±0.10 and36.65±0.08 in group II animals treated with standard drug Paracetamol. Thus the results were comparable with that of standard. The group I animals treated with normal saline shown gradually increase in rectal temperature (initial 37.15±0.04 and final 37.35±0.04.

Discussion: In the present work, four different leaf extracts of Mentha arvensis were selected for evaluation of their antipyretic activity. This plant is also used in traditional medicine for treatment of various disorders including fever.

A bibliographic survey revealed that there are no scientific reports on the antipyretic activity of these plants.

Acute toxicity study All four extracts were found to be safe and no mortality observed up to 5000 mg, the acute toxicity results revealed that these plants may be considered as broad nontoxic ones.

Preliminary screening of the extracts for antipyretic activity At both 250 and 500 mg/kg b.w. the aqueous and petroleum ether leaf extract exhibited significant antipyretic activity (P<0.001) by decreasing rectal temperature of the rats in a dose dependent manner. The antipyretic effect started as early as 1h and maintained for 5h after its administration and the result was comparable to that of standard drug paracetamol. The standard drug paracetamol (200mg kg-1b.w.) reduced the yeast provoked elevation of body temperature significantly.

Fever may be due to infection or one of the sequels of tissue damage, graft rejection and/or other disease states. Yeast-induced pyrexia is called pathogenic fever and its etiology involves production of prostaglandins (PGE2)132, which set the thermoregulatory centre of hypothalamus at a higher. Pyrogens either activate the enzymecyclooxygenase COX), which converts arachidonic acid to prostaglandin (PG), or make available the substrate for the enzyme. In these activities, synthesis of prostaglandin, especially PGE1 is thought to be increased in the hypothalamus. Antipyretics prevent rise in body temperature generally in response to microbial or endogenous pyrogens, as excessive rise in body temperature may cause irreversible tissue damage and possibly death. Antipyretics

compete with arachidonic acid at site of cyclo oxygenase. During fever, arachidonic acids synthesis the active may be inhibited by antipyretics. Most of the currently available antipyretics inhibit bothcyclooxygenase1 and cyclo oxygenase 2 (COX1 and COX-2, respectively), inhibiting the synthesis of prostaglandins and thromboxanes in the central nervous system[84, 133, 134].

Paracetamol acts by blocking the effect of pyrogens on temperature sensitive neurons in the preoptic region of the hypothalamus121.The antipyretic action of extract may thus be dependent on its inhibition ofPGE1 synthesis that was similar to that of paracetamol. Previous papers on similar activity reported that the mechanism of antipyretic action of plant extract could be attributed to the presence of flavonoids in plantextracts[135-139]. The presence of tannins, phytosterols, alkaloids, triterpenoidsmay is responsible for the antipyretic activity[140-144]Herbal medicine frequently a part of larger therapeutic system such as traditional and folklore medicine. It is necessary to evaluate, in a scientific base, the potential use of folk medicine for the treatment of infectious disease produced by common pathogens. Medicinal plant might represent an alternative treatment in non-severe cases of infectious diseases. It can also be possible source for new potent antipyretics, analgesics, anticonvulsants, antibiotics etc. the search and use of drugs and dietarysupplementsderivedfromplantshavebeenaccelerated inrecentyears.

References

1. Sirkar NN. Pharmacological basis of Ayurvedic therapeutics. In: Cultivation and utilization of medicinal plants. Editors: Atal CK and Kapoor BM (Published by PIDCSIR) 1989.

2. Azhar Ali Farooqi, Sreeramu BS. Cultivation of Medicinal and Aromatic Crops. Universities Press (India) Ltd. 2001; 5-10.

3. Atal CK, Kapoor BM. Cultivation and utilization of medicinal plants (Eds. PID CSIR), 1989.

4.Siddiqui HH. Safety of herbal drugs-an overview. Drugs: News & Views. 1993; 1(2): 7–10.

5. WHO survey. In medicinal plants (Eds. Haq. I.) Hamdard Foundation Press, Karachi, 13, 1993.

6. Sen P. Therapeutic potentials of Tulsi: from experience to facts. Drugs News & Views1993; 1(2):15–21.

7. Nadkararni AK, Nadkarni KM. Indian Materia Medica (Published by Popular Prakashan Pvt. Ltd., Bombay) 1976.

8. Jacob GA, Benard K, Daniel W, Goretti NN. Market Survey of Mondia Whytei (Mulondo) Roots in Kampala City, Uganda. Afr J Tradit Complement Altern Med. 2008;5(4): 399–408.

9. A report on the International Conference on 'Medicinal Plants and Herbal Drugs: Challenges and Opportunities in Cultivation, Sustainable Utilization and Conservation (ICMPHD 2010)' held at the Department of Botany, Pachaiyappa's College, Chennai.2010; 98(12): 1558-59.

10. World Health Organization – Traditional Medicine Regulatory Situation of Herbal Medicine. A World wide Review. 1998; 2 WHO Geneva, Switzerland.

11. Sankaranarayanan S, Bama P, Ramachandran J, Kalaichelvan PT, Deccaraman M, Vijayalakshmi M et al. Ethnobotanical study of medicinal plants used by traditionally users in Villupuram district of Tamil Nadu, India. Journal of Medicinal Plants Research.2010; 4(12): 1089 – 1101.

12. Joy PP, Thomas J, Samuel M, Baby PS. Aromatic and medicinal Plants Research Station– Kerala Agricultural University. 1998; 1-211.

13. De Smut PAGM. Should herbal medicine like products be licensed as medicines? BMJ. 1995; 310: 1023-24.

14. Ayurpatra, your monthly health e-newsletter Vol.1. Diseases of above shoulder region. Series Urdhwajatrugata; XXXI: May 2007.

15. http://en.wikipedia.org/lili/List_of_herbs_&_minerals_in_Ayurveda
16. Mackowiak PA, Bartlett JG, Borden EC, et al. Concepts of fever: recent advances andlingering dogma. Clin Infect Dis. 1997; 25: 119–138.
17. Bencsics A, Elenkov IJ, Vizi EJ. Alpha 2-, alpha 2A-, alpha 2B/2C-adrenoceptor subtype antagonists prevent lip polysaccharide-induced fever response in rabbits. Brain Res.1995; 705: 302–6.
18. Ohashi K, Saigusa T. Sympathetic nervous responses during cytokine-induced fever unconscious rabbits. Plungers Arch. 1997; 433: 691–98.
19. Chattopadhyay D, Arunachalam G, Ghosh L et al. Antipyretic activity of Alstoniamacrophylla Wall ex A. DC: An ethnomedicine of Andaman Islands. J PharmPharmaceutical Sci. 2005; 8: 558-564.
20. Spacer CB, Breder CD. The neurologic basis of fever. N Engl J Med. 1994: 330: 1880-86.
21. Sternberg EM. Neural-immune interactions in health and disease. J Clin Invest.1997; 100: 2641–47.
22. Watkins LR, Maier SF, Goehler LE. Cytokine-to-brain communication: a review and analysis of alter-native mechanisms. Life Sci. 1995; 57: 1011–1026.
23. Elmquist JK, Scammell TE, Saper CB. Mechanisms of CNS response to systemic immune challenge: the febrile response. Trends Neurosci. 1997; 20:565–70.
24. Breder CD, Dinarello CA, Saper CB. Interleukin-1 immunoreactive innervation of the human hypo-thalamus. Science. 1988; 240: 321–24.
25.Woiciechowsky C, Asadullah K, Nestler D, *et al*. Sympathetic activation triggers systemic interleukin-10 release in immunodepression induced by brain injury. Nat Med.1998; 4: 808–813.
26.Luheshi GN, Stefferl A, Turnbull A, *et al*. Febrile response to tissue inflammationinvolves both pe-ripheral and brain IL-1 and TNF-alpha in the rat. Am J Physiol. 1997;272: 862–68.
27. Roth J, Conn CA, Kluger MJ, *et al*. Kinetics of systemic and intrahypothalamic IL-6 and tumor necrosis factor during end toxin fever in the guinea pig. Am J Physiol. 1993; 265:653–58.
28. Kozak, W, Kluger MJ, Soszynski D, *et al*. IL6 and IL1 in fever: studies using cytokine-Decent (knock-out) mice. Ann N Y Acad Sci. 1998; 856: 33–47.
29.Leon LR, Kozak W, Rudolph K, Kluger MJ. An antipyretic role for interleukin-10 in LPSfever in mice. Am J Physiol. 1999; 276: 81–89.
30. Li S, Ballou LR, Morham SG, *et al*. Cyclooxygenase-2 mediates the febrile response of mice to interleukin-1 beta. Brain Res. 2001; 910: 163–173.
31.Rivest S, Lacroix S, Vallieres L, *et al*. How the blood talks to the brain parenchyma and the paraven-tricular nucleus of the hypothalamus during systemic inflammatory and infectious stimuli. Proc Soc Exp Biol Med. 2000; 223: 22–38.
32. Li S, Sehic E, Wang Y. Relationship between complement and the febrile response of guinea pigs to systemic end toxin. Am J Physiol. 1999; 277: 1635–1645.
33. Vizi ES. Receptor-mediated local one-tuning by noradrenergic innervations of neuroendocrine and immune systems. Ann N Y Acad Sci. 1998; 851: 388–396.
34. Types And Stages Of Fever: http;//hubpages.com/hub/Types-And-Stages-of-fever.
35. Shalini D, Donna SZ. Path physiology and Management of fever. J Support Oncol.2006; 4(1): 1-8.
36. Prakash P, Neelu Gupta. Therapeutic uses of Ocimum sanctum Linn (Tulsi) with a noteon Eugenol and its pharmacological action. A short Review. Indian J Physiol Pharmacol.2005; 349(2): 125-131.
37.David SY. Wang. Secondary metabolites from plants. Department of forestry. NCHU.

38. Antal AB, Eyong EU, Eteng MU, Itam EH, Eko ME, Ita SO. Serum protein and enzyme levels in rats following administration of ethanolic leaf extract of Ageratum conyzoides (Goat Weed). Nigerian Journal of Physiological Science. 2009; 24(2):117-20.
39. Michael A, Francine G, Matthias H. Plant traditionally used in age related brain disorders–A survey of ethnobotanical literature. Journal of Ethnopharmacology. 2007; 113(3):363-381.
40.Jigna P, Darshana J, Samitra C. Efficacy of Aqueous and Methanol extract of some Medicinal plants for potential antibacterial activity, Turk Biol. 2005; 29: 203-10.
41.Md. Abdul Halim, Mohammad SHC, Nur M, Masao K, Shampa B. Indigenous knowledge in nature resource utilization by the hill people. A case of the Mro tribe in Bangladesh. Proceedings of the National Workshop held in Rangamati. 15-16 February2006.
42.Lawal IO, Uzokwe NE, Igboanugo ABI, Adio AF, Awosam EA, Nwogwugwu JO *et al*.Ethno Medicinal information on collation and identification of some medicinal plants in Research Institute of South-West Nigeria. African Journal of Pharmacy and Pharmacology. 2010; 4(1): 01-07.
43.Vishwanatham AS, Basavaraju R. A review on vitex negundo L. A medicinally important plant. EJBS. 2010; 3(1): 30-42.
44.Petr B. Vojtech A, Ladislav H, Rene K. Noteworthy Secondary Metabolites Naphthoquinones – their occurrence, Pharmacological properties and Analysis, current Pharmaceutical analysis. 2009; 5: 47-58.
45.Nadine BC, Carla LD, Rosa EN, Silvia E, Alexandra Z, Alvaro P *et al*. Active constituents isolated from Psoralea glandulosa L. with anti-inflammatory and antipyretic activities. Journal of Ethnopharmacology. 2001; 78: 27-31
46. Pallab M, Dhananjay H, Vday B, Dipak kumar M. Biological activities of crude extract and chemical constituents of Bael, Eagle mammals (L). Corr. Indian Journal of Experimental Biology. 2009; 47: 849-861.
47.Sajeli B, Bhagawati S, Madhur G, Rakesh R, Vijaya BJ, Ch.Rao. V *et al*. Study of anti-inflamory, analgesic and antipyretic activities of seeds of Hyoscyamus Niger and isolation of a new Coumarinolignan. Fitoterapia. 2010; 81:178-184.
48. Evanprince Sabina, Sonal C, Mahaboob KR. Evaluation of analgesic, antipyretic andulcergenic effect of Withaferin A. International Journal of Integrative Biology. ISSN-0973-8363; 2009; 6(2): 52-56.
49.Moran A, Martin ML, Montero MJ, Ortiz de urbina AV, Sevilla MA, San Roman L.Analgesic, antipyretic and anti-inflammatory activities of the essential oil of Artemisiacaeralescens subsp. Gallica Journal Ethnopharmacology. 1989; 27: 307-317.
50. Keriman G, Sezer S. Phytochemical studies on Ruta chalepensis (Lam). Lamarck. Natural product Research. 2005; 19(3): 203-10.
51. Srinivasam GV, Unnikrishanan KP, Rema Shree AB, Indira B. HPLC estimation of berberine in Tinospora cordifolia and Tinospora sinensis. Indian Journal of Pharmaceutical Sciences. 2008; 70(1): 96-99.
52.Neha S, Ranvir GD, Jangade CR. Analgesic and antipyretic activities of Curcuma long rhizome extracts in Wister rats. Veterinary World. 2009; 2(8): 304-6.
53. Bhattacharya, S. Chrinjib Banoushadi. 3rd ed., Vol. 2, and Publishing Ltd., Calcutta-9. 1990; 236-37.
54. Cheng, L., Mingliang H, Lars B. Is COX-2 a perpetrator or a protector? Selective COX-2inhibitors remain controversial. Acta Pharmacological Sinica. 2005; 26: 926-933
55.
Planttaxonomy:http://zipcodezoo.com/plants/Mussaenda_frondoasa/Eclipta_prostrata
56. Prajapti N, Dr. Kumar U. Text book of Agro's Dictionary of Medicinal Plants. 2005; Pub- Agrobios (India). Pp-220.
57. Siju EN, Rajalakshmi GR, Kavitha VP, Anju J. In vitro Antioxidant Activity ofMussaenda frondosa. International Journal of Pharma Tech Research. 2010; 2(2): 1236-40.

58. Joshi VG, Patil SA, Sutar PS, Karigar AA, Joshi NH. Aqueous extract of Mussaenda frondosa leaf has Wound-healing and antibacterial activities in Albino rats. Journal of Pharmacy Research. 2010; 3(8): 2020-22.
59. Kirtikar.K.R, Basu. BD. Indian Medicinal Plants. 2nd edition Vol II. International book distributors, Dehradun.1987.
60. Huxley AM Griffiths, M Levy. The new Royal Horticulture Society dictionary of gardening. Groves Dictionary, Inc. New York.1999; 3: 271-72.
61.Jayasinghe,U.L.B,C.P.Jayasooriya,B.M.R Bandara, *et al*. Antimicrobial activity of some Sri Lankan Rubiaceae and Meliaceae. Fitoterapia. 2002; 73(5): 424-27.
62. Ranarivelo YAL Skaltsounis M, Andriantsiferana F.Tillequin. Glycosides from Mussaenda arcuata Lam. ex Poiret leaves. Ann Pharm Fr. 1990; 48(5): 273-77.
63. Biswanath Dinda, Sudhan Debnath, Santanu Majumder. Chemical constituents of Mussaenda incana. Ind J Chem.2005; 44B (11): 2362-65.
64. WHO. Medicinal plants in the south Pacific. Ed Michael Doyle. WHO regional publications. Western packs serious. 1998: 125.
65. Dilip C, Ameena K, Saraswathi R, Krishnan PN, Simi SP, Sanker C. Evaluation of a new tablet excipient from the leaves of Mussaenda frondosa Linn. Research Journal of Pharmaceutical Biological and Chemical Science. 2010; 1(3): 401-411.
66. John Wesley J. Hypolipidemic effect of Methanolic extract of Mussaenda frondosa linn. Leaves in high fat diet fed rats. J. of Pharmacol Research. 2009; 2(4): 579-581.
67. Sambrekar SN, Patil PA, Kangralkar VA. Protective activity of Mussaenda frondosa leaf extracts against paracetamol induced hepatic damage in wistar rats. Journal of Pharmacy Research. 2010; 3(4): 711-13.
68. Roshan P, Komal S, Priyanka P, Nidhi L. Anti-inflammatory effect of ethanolic &aqueous extracts of Mussaenda frondosa Linn. in rat. 61st Indian Pharmaceutical Congress, Ahmedabad, India. 2009.
69. Prajapti N, Dr. Kumar U. Text book of Agro's Dictionary of Medicinal Plants. 2005; Pub- Agro bios (India). pp-119.
70. Arunachalam G, Subramanian N, Pazhani GP, Ravichandran V. Anti-inflammatory activity of methanolic extract of Eclipta prostrata L (Astearaceae). African Journal of Pharmacy and Pharmacology. 2009; 3(3): 97-100.
71. Kirtikar.K.R, Basu. BD. Indian Medicinal Plants. 2nd edition Vol II. International book distributors, Dehradun.1998.
72. Mors WB, Do Nascimento MC, Parente JP, Da Silva MH, Melo PA, Suarez-KurtzG. Neutralization of lethal and myotoxic activities of South American rattlesnake venom by extracts and constituents of the plant Eclipta prostrata (Asteraceae). Toxicon. 1989; 27: 1003-9.
73. Melo PA, Do Nascimento MC, Mors WB, Suarez-Kurtz G. Inhibition of the myotoxi can dhemorrhagic activities of crotalid venoms by Eclipta prostrate (Asteraceae) extracts and constituents. Toxicon. 1994; 32: 595-603.
74. Kim, D.I., S.H., Lee, J.H., Choi, H.S., Lillehoj, M.H., Yu, G.S., Lee. "The butanolfraction of Eclipta prostrata (Linn) effectively reduces serum lipid levels and improves antioxidant activities in CD rats." Nutrition Researches 2008; 28: 550–54.
75. Asolkar AV, Kakkar KK, Chakre OJ. Glossary of Indian Medicinal lants with active principles. Publication and information directorate (CSIR), New Delhi. 1992; 1: 287.
76. Wagner H, Fessler B. In vitro 5-lipoxygenase hemmung durch Eclipta alba extract and das coumestan derivative wedelolactone. Planta Medica. 1986; 52: 374-77.
77. Khanna, V.G., and K., Kannabiran. "Antimicrobial activity of saponin fractions of the leaves of Gymnema sylvestre and Eclipta prostrata." World Journal of Microbiology and Biotechnology. 2008; 24: 2737-40.
78. Ogunbinu A.O., G., Flamini, P.L., Cioni, I.A., Ogunwande, S.O., Okeniyi. "Essential oil

constituents of Eclipta prostrata (L.) and Vernonia amygdalina Delile." Natural ProductCommunications. 2009; 4: 421-24.
79.Supaluk P, Orapin W, Thummaruk S, Somsak R, Virapong P. Bioactivity Evaluation ofEclipta prostrata Linn. A potential Vasorelaxant. European Journal of ScientificResearch. 2010; 44(2):167-176.
80. Xiong-Hao Lin, Yan-Bin Wu, Shan L, Jian-Wei Z, Pei-Yuan Z, Jin-Zhong Wu. Effect of Volatile components and Ethanolic extract from Eclipta prostrata on Proliferation and Differentiation of Primary Osteoblasts. Molecules. 2010; 15: 241-50.
81. Dhandapani R. Hypolipidemic activity of Eclipta prostrata (L.) L. leaf extract inatherogenic diet induced hyperlipidemic rats. Indian Journal of Experimental Biology.2007; 45: 617-19.
82. Karthikumar S, Vigneswari K, Jegatheesan K. Screening of antibacterial and antioxidant activities of leaves of Eclipta prostrata (L). Scientific Research and Essay. 2007; 2(4):101-4.
83. Kyung-Mi Chang, Gun-Hee Kim. Constituents of the Essential Oil from Ecliptaprostrata L. Journal of Food Science and Nutrition. 2009; 14(.2): 95-171.
84.Morimoto A, Nakamori T, Watanabe T, Ono T, Murakami N. Pattern differences inexperimental fevers induced by endotoxin, endogenous pyrogen, and prostaglandins AmJ Physiol. 1988;254(4): 633-40.
85.Kumari CS, Govindasamy S, Sukumar E. Lipid lowering activity of Eclipta prostrata inexperimental hyperlipidemia. J Ethnopharmacol. 2006; 105(3): 332-35.
86. Liu X, Jiang Y, Zhao Y, Tang H. Effect of ethyl acetate extract of Eclipta prostrata onmice of normal and immunosupression. Zhong Yao Cai. 2000; 23(7):407-9.
87.Mors WB, do Nascimento MC, Parente JP, da Silva MH, Melo PA, Suarez-Kurtz G.Neutralization of lethal and myotoxic activities of South American rattlesnake venom byextracts and constituents of the plant Eclipta prostrata (Asteraceae). Toxicon. 1989; 27(9): 1003-9.
88. Pithayanukul P, Laovachirasuwan S, Bavovada R, Pakmanee N, Suttisri R. Anti-venom potential of butanolic extract of Eclipta prostrata against Malayan pit viper venom. JEthnopharmacol. 2004; 90(2-3): 347-352
89. Zhang JS, Guo QM. Studies on the chemical constituents of Eclipta prostrata (L). YaoXue Xue Bao. 2001; 36(1): 34-37.
90.Zhao YP, Tang HF, Jiang YP, Wang ZZ, Yi YH, Lei QY. Triterpenoid saponins from Eclipta prostrata L. Yao Xue Xue Bao. 2001; 36(9): 660-63.
91. Venkatesan GK, Krishnan K. Antimicrobial activity of saponin fractions of the leaves of Gymnema sylvestre and Eclipta prostrata. World Journal of Microbiology and Biotechnology. 24(11); 2737-40.
92.Tewtrakul S, Subhadhirasakul S, Cheenpracha S, Karalai C. HIV-1 protease and HIV-1integrase inhibitory substances from Eclipta prostrata. Phytother Res. 2007; 21(11):1092-95.
93. Plant taxonomy: http://zipcodezoo.com/plants/A/Aporosa_lindleyana/.
94. Kirtikar, K.R., Basu, B.D. Indian Medicinal Plants. International Book Publisher, Dehradun. 1993; 225-26.
95. Jayakar B, Suresh B. Antihyperglycemic and hypoglycemic effect of Aporosa lindleyanain normal and alloxan induced diabetic rats. Journal of Ethnopharmacology. 2003; 84:247-49.
96. Bhakuni, D.S., Goel, A.K., Jain, S., Mehrotra, D.N., Patnaik, G.K., Prakash, V. Screening of Indian plants for biological activity. Indian Journal of Experimental Biology. 1988; 26(11): 883-904.
97. Venkataraman R, Gopalkrishnan S, Thyagarajan SP. Antiviral activities of Aporosalindleyana Baill. Annals of Biological Research. 2010; 1(2): 68-70.
98.Lingadahalli PS, Hosadu MV, Basavanakote MB, Vijayavittala PV. Evaluations of

antimicrobial and analgesic activities of Aporosa lindleyana (Euphorbiaceae) barkextract. International Journal of Green Pharmacy. 2008; 155-57.
99. Shrishailappa B, Sujay RR, Suresh B. Antioxidant activity of Aporosa lindleyana root. Journal of Ethnopharmacology. 2005; 101: 180-84.
100 Nardev S, Atul KG, Vijay J, Renu C. Study on Antipyretic activity of extracts of Bergenia ligulata Wall. International Journal of Pharma and Bio Sciences. 2010; 1(3):1-5.
101. Karunakar H, Arun BJ. Preliminary phytochemical screening and antipyretic activity of Carissa spinarum root extract. Der Pharmacia Lettre. 2010; 2(3): 255-60.
102. Amiya RD, Anuj KA, Ashutosh M. A study on Antipyretic activity of Capparis zeylanicaLinn. plant methanolic extract. International Journal of Pharma Science and Research.2010; 1(3): 169-171.
103. Sanjib B, Bodhisattva R. Preliminary investigation on antipyretic activity of Cuscutareflexa in Rats. Journal of Advanced Pharmaceutical Technology and Research. 2010; 1(1): 83-87.
104. Alam K, Moizur R, Shariful I. Antipyretic activity of Peperomia pellucid Leaves inrabbit. Turk J Biol. 2008; 32: 37-41.
105. Varsha T, Abhishek T, Madhavan V. Preliminary phytochemical analysis, HPTLC studies and antipyretic activity of alcohol and aqueous extract of Helieteres isora. L Root. International Journal of Pharmacy and Pharmaceutical Sciences. 2010; 2(21): 74-79.
106. Deepa PK, Usha PTA, Chandrasekharan NAM, Prasannakumari KT. Antipyretic activity of seeds from red and white type of lotus (Nelumbo nucifera) in Albino rats. Veterinary World. 2009; 2(6): 213-14.
107. Sushil B, Prakash R, Paridhi B, Shivshankar S. Antipyretic potential of Swertia chirataBuch Hum. Root extract. Sci Pharm. 2009; 77: 617-623.
108. Alam K, Md. Abdullahil B, Abdul AM, Al-Bari, Sohl H, Ashik MM *et al*. Antipyretic activity of roots of Laportea crenulata Gaud in Rabbit. Research Journal of Medicine and Medical Science. 2007; 2(2): 58-61.
109. Satya PV, Anindya B, Mahasin ASM, Soma S, Tarun J. Evaluation of the antipyretic potential of methanolic extract of the leaves of Abies spectabilis (D.Don) Spach. Natural Product Radiance. 2007; 6(5): 369-371.
110. Debprasad C, Ganeshan A, Lopamudra G, Rajendran K, Asit B.M, Bhattacharya S.K.Antipyretic activity of Alstonia marcrophylla Wall ex A. DC: An Ethnomedicine of Andaman Islands. J Pharm Pharmaceut Sci. 2005; 8(3): 558-564.
111. Priyanka V, Rekha V. Analgesic, anti-inflammatory and antipyretic activity of Cissus quadrangularis. Journal of Pharmaceutical Science and Technology. 2010; 2(1): 111-18.
112. Junaid N, Vikas G, Prithviraj C, Pawan K. Anti-inflammatory and antipyretic activity of Aleuritis moluccana leaves. Asian Journal of Pharmaceutical and Clinical Research.2010; 3(1): 35-37.
113. Sajeli B, Bhagawati S, Madhur G, Rakesh R, Vijaya BJ, Ch Rao V. Study of anti-inflammatory, analgesic and antipyretic activities of seeds of Hyoscyamus niger and isolation of a new coumarinolignan. Fitoterapia. 2010; 81: 178-184.
114. Nanda BK, Jena J, Rath B, Behera BR. Analgesic and antipyretic activity of whole parts of Sphaeranthus indicus Linn. Journal of Chemical and Pharmaceutical Research. 2009; 1(1): 207-212.
115. Arjun P, Shivesh J, Narasimha MP, Aherr VD, Pronobesh C, Ghanshyam P. Anti-inflammatory and Antipyretic activities of Hygrophila spinosa T. Anders Leaves(Acanthaceae). Tropical Journal of Pharmaceutical Reseach. 2009; 8(2): 133-37.
116. Mahesh SP, Swati P, Sachin RP, Ravi K, Patil MB. Evaluation of analgesic and antipyretic activities of ethanolic extract of male flowers (Inflorescences) of Borassus flabellifer L. (Arecaceae). International Journal of

Pharmacy and Pharmaceutical Science.2009; 1(2): 98-106.
117. Neha S, Ranvir GD, Jangade CR. Analgesic and antipyretic activities of Curcuma long rhizome extract in Wister Rats. Veterinary World. 2009; 2(8): 304-6.
118. BamideleVO, Stephen OO, Kemi D, Bolatito AO, Elizabeth AA, Ayodele OS. Analgesic, anti-inflammatory and antipyretic activities from flavonoids fraction of Chromolaenaodorata. Journal of Medicinal Plants Research. 2008; 2(9): 219-225.
119. Khandelwal KR. Text book of Practical Pharmacognosy Techniques and Experiments. Nirali Prakashan. 149-156.
120. Ghosh MN. Fundamentals of experimental Pharmacology. 2nd Edition, Scientific Book Agency, Culcutta. 1986: 156.
121. Rajeswara Rai P, Rajendra BM, Krishna Rao RV. Studies on antipyretic, analgesic and hypoglycaemic activites of root of Gynandropsis dynandra linn. Indian Drugs, 1997; 34(12): 690-93.
122. Paul C, Arnold JV, Berghe DV, Macs L. Anti-infective potential of natural products: How to develop a stonger in vitro 'proof-of-concept'. Journal of Ethnopharmacology.2006; 106: 290-302.
123. Cunningham AB. African medicinal plants. Setting priorities at the interface between conservation and primary health care. Paris: UNESCO; 1993. People and Plants Working Paper No. 1.
124. Cunningham AB. Medicinal plants for forest conservation and heath care. Rome, Italy: FAO; 1997. An Africa-wide overview of medicinal plant harvesting, conservation and health care, Non-Wood Forest Products 11.
125. Joshi H, Joshi AB, Sati Hemlata, Gururaja MP, subrahmanya EVS, Satyanarayana D.evaluation of antipyretic potential of Memecylone umbellatum root extract. Indian J. Nat. Prod. 2009; 25(1): 13-15.
126. Mukherjee, P.K., Das, J., Saha, K., Giri, S.N., Pal, M, Saha, B.P. Antipyretic activity of Nelumbo nucifera rhizome extract. Indian J. Exp. Biol. 1996; 34: 275-76.
127. Jeon HJ, Kang HJ, Jung HJ, Kang YS, Lim CJ, Kim YM, *et al*. Antiinflammatory activity of Taraxacum officinale. J Ethnopharmacol 2008; 115: 82-88.
128. Ji W, Gong BQ. Hypolipidemic effects and mechanisms of Panax notoginseng on lipid profile in hyperlipidemic rats. J Ethnopharmacol 2007; 113: 318-324.
129. Puri A, Khaliq T, Rajendran SM, Bhatia G, Chandra R, Narender T. Antidyslipidemic activity of Indigofera tinctoria. J Herb Pharmacother 2007; 7: 59-64.
130. Ganesan P, Kumar CS, Bhaskar N. Antioxidant properties of methanol extract and its solvent fractions obtained from selected Indian red seaweeds. Bioresour Technol 2008;
99: 2717-2723.131. Aderogba MA, McGaw LJ, Ogundaini AO, Eloff JN. Antioxidant activity and cytotoxicity study of the flavonol glycosides from Bauhinia galpinii. Nat Prod Res. 2007; 21: 591-99.
132. Deepa PK, Usha PTA, Chandrasekharan Nair AM, Prasannakumari KT. Antipyretic activity of seeds from Red and White type of lotus (Nelumbo nucifera) in Albino rat. Veterinary World. 2009; 2(6): 213-14.
133. Howard M. Fever: causes and consequences. Neurosci Biobehav Rev. 1993; 17(3): 237–269.
134. Chandrashekaran NV, Dai H, Roos KL *et al*. COX-3, a cyclooxygenase-1 variantinhibited by acetaminophen and other analgesic/antipyretic drugs: cloning structure and expression. Proc Natal Accad Sic 2002; 99(21): 13926-931.
135. Metallic S, Paridhavi K, Rao CM, Udupa N. Antipyretic and analgesic effect of leaves of solanum melongena linn. in rodents. Indian J. Pharmacol. 2003; 35: 312-15.
136. Hajare SW, Chandra S, Tandan SK, Sharma J, Lal J, Telang AG. Analgesic and antipyretic activities of Dalbergia sissoo leaves. Indian J. Pharmacol. 2000; 32: 357-60.

137. Brasseur T. Anti-inflammatory properties of flavonoids. Journal de pharmacie deBelgique. 1989; 44: 235-241.
138. Vimala RS, Nagarajan M, Alam T, Susan, Joy S. Anti-inflammatory and antipyretic activity of Michelia champaca Linn. (White variety), Ixora brachiata Roxb. And Rhynchosia cana (wild.) D. C. flower extract. Indian Journal of experimental Biology.1997; 35: 1310-1314.
139. Rajnarayan K, Reddy MS, Chaluvadi MR. Bioflavonoids classification, pharmacological, biochemical effect and therapeutically potential. Indian J. of Pharmaceutical Sciences.2006; 68(3): 380-84.
140. Ahmadini A, Javana M, Semnanianb S, Barata E, Kamalinaja M. Anti-inflamatory and antipyretic effect of Trigonella foenum-graecum leaves extract in the rat. J.Ethnopharmacol. 2001; 75(2-3): 283-86.
141. Taesotikul T, Panthong A, Kanjanapothia D, Verpoorteb R, schhefferb JJC. Anti-inflamatory, antipyretic and antinociceptive activities of Tabernaemontana pandacaquiPoir. J. Ethnopharmacol. 2003; 84(1): 31-35.
142. Cho CH, Chunng CY, Chen CF. Study of the antipyretic activity of Matrine. A Lupinalkaloids isolated from Sophora subprostrata. Planta Med. 1986; 5: 343-45.
143. Reanmongkol, Wantana, Matsumoto K, Watanabe H, Subhadhirasakul S, Sakai SI.Antinociceptive and antipyretic effect of alkaloids extracted from the stem bark of Hunteria zeylancia. Biological pharmaceu Bull. 1994; 17(10): 1345-50.
144. Reanmongkol W, subhadhirasakul S, Kongsang J, Tanchong M, Kitti J. Analgesic and antipyretic activities of n-butanol alkaloids extracted from the stem bark of Hunteriazeylancia and its major constituents, strictosidinic acid, in mice. Pharm Biol. 2000; 38:68-73.