

RECENT ADVANCES IN PHYTOTHERAPY OF PYREXIA

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ABSTRACT: Normal body temperature ranges between 37.22°C-40.57°C. A temperature above 40.57 °C is considered pyrexia. The temperature rises due to some disturbances in the body's heat-regulating mechanism. Toxins (pyrogens) act on white blood cells and produce endogenous pyrogens. These endogenous pyrogens directly act on the anterior hypothalamus and in turn lead to an increase in the temperature. There are numerous causes of fever such as infections, injury, inflammation, dehydration, and certain drugs. In this modern era, most medicines made from plants are useful in various ailments. Plants have some active constituents that are involved in treating the disease. People living in developing countries are well known in using these plants for the management of pyrexia and 25% people of the developed world also prefer these plants for their medicinal properties. Management of pyrexia has remained a very concerned issue since early ages and elements derived from the natural medicines have been widely used. Nowadays research in management of pyrexia has enabled us to use natural products in their original form. Purpose of this paper is to review the scientifically proven literature on antipyretic activity of plants.

Keywords: Pyrexia, medicinal plants, efficacy

INTRODUCTION

Pyrexia is a frequent medical symptom that is described as increasing internal body temperature to a level above the normal, characterized by temperature elevation in body's thermoregulatory set and it occurs when there is a disorder in hypothalamic set point. Fever is produced through the generation of pyrogens which provoke prostaglandin E₂. PG E₂ proceed on the hypothalamus, which produce reaction on the entire body and results in a new temperature level (1). Increase in body temperature is the response given by human body due to inflammation, tissue damage, cancer and this term is labeled as pyrexia or more commonly fever (2). Ayurveda best describes the beginning of fever as the combination of indigestion, seasonal changes and alternation of daily routine. Children in developing world are exposed to malnutrition and they suffer

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From fever. This fever also connects with body pain and aches which is the fundamental cause of increase in the disease and death count. There are numerous intermediates which are involved in the pathogenesis of fever. Interleukin-6, tumor necrosis factor and Interleukin-1 β are pyrogenic cytokines which are involved in fever by their direct effect on hypothalamus (3). By the stimulation of pyrogenic cytokines, the exogenous pyrogens cause pyrexia (4). Inflammation is a very complex phenomenon which is triggered by any stimulus which can be mechanical injury, burns, infections or any poison which may affect the welfare of any host. A type of organic intermediate is arachidonic acid that is transformed into a huge number of eicosanoids with effective natural functions. Cyclooxygenase (COX) pathway is one of the major pathways of arachidonic acid, which is involved in the synthesis of thromboxane and prostaglandins (5). There are m

any inflammatory diseases in the world which have caused disruption/disability in human and most common disabling disease is rheumatic disease (6). Researchers are particularly interested in formulating herbal based drugs for treating diabetes, arthritis, hepatitis and incorporating it into national network program. Plants used as medicine are not fully justified as the competition is huge and plenty of other drugs are available which have shown compatible pharmacophores. New pharmacophores need to be developed for targeting drug actions together with that they can be used in combination. One such example is curcumin which is used as target molecules for a large number of combination drug regimens (7). Over 75% of the population in the world depends mostly on medicinal plants for the treatment of different ailments. The modern medicines used to treat inflammation and pain exhibit numerous side effects. This guides to significant attention in exploration of safer medicines for these ailments.

Treatment of pyrexia

There are various anti-pyretic drugs which are available to lower the body temperature (8). NSAIDs have anti-pyretic actions. Their action is due to the reserve of cyclooxygenase (COX), an enzyme accountable for the construction of prostaglandins, which are significant mediators of fever. Therefore, NSAIDs are said to possess anti-pyretic properties which rearrange the hypothalamic thermostat and decrease elevated body temperature in fever. NSAIDs increase heat loss by cutaneous vasodilatation and sweating. Paracetamol is widely used as an anti-pyretic agent. Administration of paracetamol generates an anti-pyretic action by inhibiting the COX pathway. A major tranquillizer chlorpromazine produces fall in body temperature when administered to humans and animals in an impartial environment. Hypothermic action of chlorpromazine has been used as an adjuvant in

production and protection of hypothermia and heat stroke in clinical medicine. Peripheral system for its hypothermic action is adrenoceptor blockade. It is the natural role of body to generate a condition in which microbes cannot survive. COX-2 expression is decreased by antipyretic drug to decrease the temperature by slowing down the formation of PgE₂ (9). Plants account for several important resources in sustaining the planet (10). Plants are known as the primary producers in all food chains, directly supplying human beings with 90% of their total calorific intake, of which 80% is of proteins. A large number of plants are investigated worldwide for management of pyrexia (Table 1). Medicinal plants possessing antipyretic activity are getting sufficient attention in primary well-being of the individuals (Table 2). Herbal products are considered as a safe alternative to modern medicines as they are distinguishing as natural (11-13).

Salix Albalinn (Salicaceae)

1. Europeans scientific cooperative on phytotherapy advocate the use of extracts of *Salix Albalinn* for the symptomatic treatment of pyrexia, arthritis and pain. Although the mode of action is not fully understood but its anti-inflammatory effects cannot be denied (14). The actions are only partly attributable to salicylate (15). A hydro-alcoholic extract of willow bark has shown powerful pain killer, anti-inflammatory and antipyretic activity in animals. Extracts of the bark of *Salix* species had been used for treating fever, mild rheumatic disorders and headache. *Salix alba* contains active constituent salicin, which is the pro-drug of various salicylate derivatives (16). The bark of *Salix* has anti-inflammatory properties (17). The activity of both aqueous and ethanol extracts of *Achillea millefolium* and *Salix alba* as anti-inflammatory, antipyretics and analgesics are proven. The effects of extracts of both plants on sleeping time were also examined. White willow bark (*Salix alba* L.) contains a range of chemical

constituents. The salicin is metabolically transformed in the body to the aspirin metabolite, salicylic acid. Salicylates have anti-inflammatory effects in the body. Ethanolic extracts of both *Achillea millefolium* and *Salix alba* could be used as an anti-inflammatory, antipyretic and analgesic agent.

Trigonella foenum-

***graecum* L. (Leguminosae)**

It contains sucrose, D-3-O-methyl-chiroin, inositol, ethyl- α -D-glucopyranoside, beta-sitosterol, glucopyranoside, stearic acid, glycerol monopalmitate and N,N'-dicarbazyl (18). The leaves were also examined for effective, antipyretic and inflammatory actions in the rats (19). Seeds have

shown dramatic effects against hyperglycemia and are much safer than clinically available medicines. It is also used as an anti-inflammatory and antipyretic agent (19).

***Gongronema latifolium* (Asclepiadaceae)**

Systematic reviews have identified the anti-diabetic and antioxidant activities of aqueous and ethanol extracts of *G. latifolium* leaves (20). Anti-inflammatory, analgesic and antipyretic drugs are a mixture of compounds, chemically not related; however, share certain beneficial actions. *G. latifolium* contains some active constituents that possess anti-pyretic property and has been prescribed in the treatment of pyrexia.

***Asparagus racemosus* (Liliaceae)**

Shatavari, having many branches, spinous, the leaves are small and regular, has minute white flowers, in small barbs and the roots are handle-like and bunch (21). It is a straight, sturdily aromatic herb that is widely cultivated in humid regions in India. Seeds have been documented for its hypoglycemic activity (25). It contains shatavarin IV, tannin, resin, rutin, quercetin, kaempferol, tyrosine, saponins, sarsapogenin, isoflavone, curilloside G, oligofurostanosides, asparagine and racemosol (22). It is very valuable plant and has been used in India for

thousands of years and is a well-known stimulant and can be given to all age groups (23). It is mostly recognized for its many beneficial properties and has several properties like anti-diarrheal, anti-depressant, anti-bacterial, anti-ulcer, anti-oxidant and cardioprotective. *Asparagus racemosus* root is an ideal element of the plant used to treat fever (24).

***Achillea millefolium* (Asteraceae)**

The *Achillea* genus is one of the most important genera in the compound family (26). It contains cosmosiin, cynaroside, flavonoids, alkaloids, fatty acids, amino acid derivatives, achillicin III, proazulene, lignins, terpenoids, p-hydroxyphenethylamide IV, monoterpenes and sesquiterpenes (27). It is an antispasmodic and anti-inflammatory (28-29). This variation can also be found in components of essential oils of *Achillea millefolium*. This plant is used to reduce fever (30-31).

***Mollugopentaphylla* Linn (Molluginaceae)**

It is used in tumors, scabies, inflammation, eye illness, surgery, wounds, gout and rheumatism and malaria (32). It is antipyretic, mild laxative, stomachic, antiseptic, emmenagogue, tonic, diuretic, cholagogue, vesicant, rubefacient and malarial fever (33).

***Moringa oleifera* (Moringaceae)**

The root of *Moringa oleifera* possesses anti-inflammatory action. It contains phytates, oxalates, saponins, tannins, isothiocyanates, glucosinolates, alkaloids, flavonoids, phenolic acids, polyphenols and carotenoids (34). It is used in pyrexia, epilepsy, inflammation, cancer, hypertension and diabetes mellitus (35). It is antifungal, antibacterial, hepatoprotective, hypoglycemic, antioxidant, hypolipidemic, hypotensive, diuretic, spasmolytic, anti-ulcer, anti-inflammatory, anti-epileptic, antipyretic, anticancer and stimulant. *M. oleifera* extracts represented antipyretic and wound healing potential in rats (37).

***Polygonum glabrum* wild (Polygonaceae)**

Polygonum glabrum has been used as folk medicine and as a component in various Ayurvedic preparations. It contains flavonoids, ca

rbohydrates, glycosides and alkaloids (38-39). Traditionally, it is used in pneumonia, gastric ulcer, jaundice, fever and inflammation (40). It is antispasmodic, astringent, diuretic, rubefacient, vermifuge and anthelmintic (41). A mixture has been used as a treatment for irritation and stomach pain. The plant decoction has been prescribed in the management of rheumatic arthritis (42).

***Peperomia pellucida* Linn (Piperaceae).**

Various ingredients present in this plant are reported as anti-neoplastic and antifungal agent (43). It contains methyl ester hexadecanoic acid, 2-naphthalenol and 9,12-octadecadienoic acid (44). It is used in rheumatoid arthritis, renal disorders, headache, gouty arthritis, fatigue, boils, acne, abscesses, abdominal pain, hemorrhage, wounds, hypercholesterolemia, mental disorders, inflammation, depression, pimples, constipation, general weakness, edema, dysuria, hypertension and pyrexia (45).

***Salix babylonica* (Salicaceae)**

Salix babylonica and *Populus nigra* products suggest a possible way to decrease the losses in body development, feed capability and death rate due to heat pressure. It contains terephthalic acid, luteolin-4'-

O-glucoside, apigenin-7-O-galactoside, kaempferol-7-O-glucoside, salicin, trichocarpin, salicin and chrysoeriol (46). It is an anthelmintic (47). A likely mechanism for the antipyretic activity of *Salix babylonica* is due to its substance of natural salicylates which has inhibitory potential on prostaglandin synthesis (48). Salicylate has been shown to present little oral toxicity (LD₅₀ > 1000 mg/kg) and has been usually renowned as safe (49).

CONCLUSION

Above mentioned discussion has proven the efficacy of medicinal plants in pyrexia. Natural products have always become a subject of international significance over the previous years. Most of the World population still relies on herbal medicine for their healthcare in developing countries. Medicinal plants have an extensive record of medicinal uses since ancient times. Popularity of medicinal plants for use in different ailments is due to their low cost and fewer side effects as compared to modern medicine. Economic advantages, identification and development of the natural medicines are on the increase in developing countries.

REFERENCES

1. Wang Y. The Mechanism of Fever and its Clinical Management. *J Pharm Pharm Sci*. 2015;1(2):10-1.
2. Paudel KR, Panth N. Phytochemical profile and biological activity of *Nelumbo nucifera*. Evidence-based Complementary and Alternative Medicine. 2015;2015.
3. Ranjan P, Soneja M, Subramonian NK, Kumar V, Ganguly S, Kumar T, et al. Fever of unknown origin: an unusual presentation of Kikuchi-Fujimoto disease. Case reports in immunology. 2015;2015.
4. Kozak W, Kluger MJ, Kozak A, Wachulec M, Dokladny K. Role of cytochrome P-450 in endogenous antipyresis. *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology*. 2000;279(2):R455-R460.
5. Murakami A, Jiwajinda S, Koshimizu K, Ohigashi H. Screening for in vitro anti-tumor promoting activities of edible plants from Thailand. *Cancer letters*. 1995;95(1-2):139-46.
6. Shah BN, Nayak B, Seth A, Jalalpure S, Patel K, Patel M, et al. Search for medicinal plants as a source of anti-inflammatory and anti-arthritic agents-A review. *Pharmacognosy Magazine*. 2006;2(6):77.
7. Patwardhan B, Vaidya AD, Chorghade M. Ayurveda and natural products drug discovery. *Current science*. 2004:789-99.
8. Duraisankar M, Ravichandran V. Antipyretic potential of polyherbal ayurvedic products. *Asian Journal of Pharmaceutical and Clinical Research*. 2012;5(2):146-50.
9. Luo C, He M-I, Bohlin L. Is COX-

2. a perpetrator or a protector? Selective COX-2 inhibitors remain controversial. *Acta Pharmacologica Sinica*. 2005;26(8):926-33.
10. Mate G, Naikwade N, Magdum C, Chowki A, Patil .
 11. S. Evaluation of anti-nociceptive activity of *Cissus quadrangularis* on albino mice. *International Journal of Green Pharmacy (IJGP)*. 2008;2(2) .
 12. Velavan S, Hazeena Begum V. Lipids regulating activity of *Asparagus racemosus* root in young and aged rats. *Indian Journal of Gerontology*. 2011;25(3):273-85.
 13. Ayyanar M, Ignacimuthu S. Herbal medicines for wound healing among tribal people in Southern India: Ethnobotanical and Scientific evidences. *International Journal of Applied Research in Natural Products*. 2009;2(3):29-42.
 14. Vaidya AD, Devasagayam TP. Recent Advances in Indian Herbal Drug Research Guest Editor: Thomas Paul Asir Devasagayam Current Status of Herbal Drugs in India: An Overview. *Journal of clinical biochemistry and nutrition*. 2007;41(1):1-11.
 15. Chrubasik S, Fiebich B, Black A, Pollak S. Treating low back pain with a *Salix* extract that inhibits COX 2 and the release of cytokines. *European Journal of Anaesthesiology (EJA)*. 2002;19(3):209-10.
 16. Schmid B, Kötter I, Heide L. Pharmacokinetics of salicin after oral administration of a standardised willow bark extract. *European journal of clinical pharmacology*. 2001;57(5):387-91.
 17. Krivoy N, Pavlotzky E, Chrubasik S, Eisenberg E, Brook .
 18. G. Effect of salicin cortex extract on human platelet aggregation. *Planta medica*. 2001;67(03):209-12.
 19. Schilcher H. Efficient phytotherapy. Anti-inflammatory herbal remedies. *Herba Polonica*. 2000;46(2):105-10.
 20. Han Y, Nishibe S, Noguchi Y, Jin Z. Flavonol glycosides from the stem of *Trigonella foenum-graecum*. *Phytochemistry*. 2001;58(4):577-80.
 21. Ahmadiani A, Javan M, Semnani S, Barat E, Kamalinejad M. Anti-inflammatory and antipyretic effects of *Trigonella foenum-graecum* leaves extract in the rat. *Journal of ethnopharmacology*. 2001;75(2):283-6.
 22. Ogundipe O, Moody J, Akinyemi T, Raman A. Hypoglycemic potentials of methanolic extracts of selected plant foods in alloxanized mice. *Plant Foods for Human Nutrition (Formerly Qualitas Plantarum)*. 2003;58(3):1-7.
 23. Thomson M. Herbal Monograph—*Asparagus racemosus*. *Phytomedicine*, NSW, Australia. 2002.
 24. Negi J, Singh P, Joshi G, Rawat M, Bisht V. Chemical constituents of *Asparagus*. *Pharmacognosy reviews*. 2010;4(8):215.
 25. Nikajoo LT. Analgesic activity of aqueous and alcohol root extracts of *Pergularia daemia* (forsk.) Chiov. *Int J Pharm Pharm Sci*. 2009;1(Suppl1):33-7.
 26. Vijayan A, John J, Parthipan B, Renuka C. Traditional remedies of Kani tribes of Kottoor reserve forest, Agasthyavanam, Thiruvananthapuram, Kerala. 2007.
 27. Zia T, Hasnain SN, Hasan S. Evaluation of the oral hypoglycaemic effect of *Trigonella foenum-graecum* L. (methi) in normal mice. *Journal of Ethnopharmacology*. 2001;75(2):191-5.
 28. Farajpour M, Ebrahimi M, Amiri R, Nori SAS, Golzarri R. Investigation of variations of the essential oil content and morphological values in yarrow (*Achillea santolina*) from Iran. *Journal of Medicinal Plants Research*. 2011;5(17):4393-5.
 29. Saeidnia S, Gohari A, Mokhber-Dezfuli N, Kiuchi F. A review on phytochemistry and medicinal properties of the genus *Achillea*. *DARU: Journal of Faculty of Pharmacy, Tehran University*

- of Medical Sciences. 2011;19(3):173.
30. Benedek B, Kopp B. *Achillea millefolium* L. s. rev. cited: recent findings confirm the traditional use. *Wiener Medizinische Wochenschrift*. 2007;157(13-14):312-4.
 31. Farajpour M, Ebrahimi M, Amiri R, Golzari R, Sanjari S. Assessment of genetic diversity in *Achillea millefolium* accessions from Iran using ISSR marker. *Biochemical Systematics and Ecology*. 2012;43:73-9.
 32. Dogan MD, Ataoglu H, Akarsu ES. Effects of different serotypes of *Escherichia coli* lipopolysaccharides on body temperature in rats. *Life Sciences*. 2000;67(19):2319-29.
 33. de Fátima Arrigoni-Blank M, Dmitrieva EG, Franzotti EM, Antonioli AR, Andrade MR, Marchioro M. Anti-inflammatory and analgesic activity of *Peperomia pellucida* (L.) HBK (Piperaceae). *Journal of Ethnopharmacology*. 2004;91(2):215-8.
 34. Valarmathi R, Rajendran A, Akilandeswari S, Senthamarai R. Study on antipyretic activity of a *Mollugo pentaphylla* Linn in albino mice. *Inter J Pharm Tech Res*. 2010;2:2388-90.
 35. Singh S, Pandey S, Srivastava S, Gupta V, Patro B, Ghosh
 36. Chemistry and medicinal properties of *Tinospora cordifolia* (Guduchi). *Indian journal of pharmacology*. 2003;35(2):83-91.
 37. Leone A, Spada A, Battezzati A, Schiraldi A, Aristi J, Bertoli S. Cultivation, genetic, ethnopharmacology, phytochemistry and pharmacology of *Moringa oleifera* leaves: An overview. *International journal of molecular sciences*. 2015;16(6):12791-835.
 38. Gupta R, Mathur M, Bajaj VK, Katariya P, Yadav S, Kamal R, et al. Evaluation of antidiabetic and antioxidant activity of *Moringa oleifera* in experimental diabetes. *Journal of Diabetes*. 2012;4(2):164-71.
 39. Anwar F, Latif S, Ashraf M, Gilani AH. *Moringa oleifera*: a food plant with multiple medicinal uses. *Phytotherapy research*. 2007;21(1):17-25.
 40. Hukkeri V, Nagathan C, Karadi R, Patil B. Antipyretic and wound healing activities of *Moringa oleifera* Lam. in rats. *Indian journal of pharmaceutical sciences*. 2006;68(1):124.
 41. Jacobsson U, Muddathir AK. Four biologically active sesquiterpenes of the drimane type isolated from *Polygonum glabrum*. *Phytochemistry*. 1992;31(12):4207-11.
 42. Ezhilan B, Neelamegam R. GC-MS Determination of Bioactive Compounds of *Polygonum glabrum* (Wild). *Journal of Phytology*. 2011;3(9).
 43. Singh B, Pandey V, Joshi V, Gambhir S. Anti-inflammatory studies on *Polygonum glabrum*. *Journal of Ethnopharmacology*. 1987;19(3):255-67.
 44. Muddathir A, Balansard G, Timon – David P, Babadjamian A, Yagoub A, Julien M. Anthelmintic properties of *Polygonum glabrum*. *Journal of pharmacy and pharmacology*. 1987;39(4):296-300.
 45. Meera R, Raphael J, Devi P, Venkataraman S, Aruna A, Parameswari S, et al. Analgesic and Antimicrobial Activity of Aerial Parts of *Polygonum Glabrum*. *International Journal of Pharmaceutical Research & Allied Sciences*. 2013;2(4).
 46. Xu S, Li N, Ning M-M, Zhou C-H, Yang Q-R, Wang M-W. Bioactive Compounds from *Peperomia pellucida*. *Journal of natural products*. 2006;69(2):247-50.
 47. Wei L S, Wee W, Siong J Y F, Syamsumir D F. Characterization of anticancer, antimicrobial, antioxidant properties and chemical compositions of *Peperomia pellucida* leaf extract. *Acta Medica Iranica*. 2011;49(10):670.
 48. Majumder P, Kumar KA. Establishment of quality parameters and pharmacognostic evaluation of leaves of *Peperomia pellucida* (L.) HBK. *Int J Pharm Sci*. 2011;3(5):3-6.

49. Salem A, Olivares M, Lopez S, Gonzalez-Ronquillo M, Rojo R, Camacho L, et al. Effect of natural extracts of *Salix babylonica* and *Leucaena leucocephala* on nutrient digestibility and growth performance of lambs. *Animal Feed Science and Technology*. 2011;170(1):27-34.
50. Hernandez PM, Salem AZ, Elghandour MM, Cipriano-Salazar M, Cruz-Lagunas B, Camacho LM. Anthelmintic effect of *Salix babylonica* L. and *Leucaena leucocephala* Lam. extracts in growing lambs. *Tropical animal health and production*. 2014;46(1):173-8.
51. Sneader W. The discovery of aspirin: a reappraisal. *Bmj*. 2000;321(7276):1591-4.
52. Almeida E, Almeida R, Navarro D, Bhattacharyya J, Silva B, Birnbaum J. Central antinociceptive effect of a hydroalcoholic extract of *Dioclea grandiflora* seeds in rodents. *Journal of ethnopharmacology*. 2003;88(1):1-4.
53. Nisar M, Khan I, Simjee SU, Gilani AH, Perveen H. Anticonvulsant, analgesic and antipyretic activities of *Taxus wallichiana* Zucc. *Journal of Ethnopharmacology*. 2008;116(3):490-4.
54. Padhan AR, Agrahari AK, Meher A. A study on antipyretic activity of *Capparis zeylanica* Linn. plant methanolic extract. *International Journal of Pharma Sciences and Research*. 2010;1(3):169-71.
55. Asha V, Pushpangadan P. Antipyretic activity of *Cardiospermum halicacabum*. 1999.
56. Saini NK, Singha M. Anti-inflammatory, analgesic and antipyretic activity of methanolic *Tecomaria capensis* leaves extract. *Asian Pacific journal of tropical biomedicine*. 2012;2(11):870-4.
57. Jaiswal A, Sutar N, Garai R, Pati MK, Kumar A. Antipyretic activity of platycladus orientalis leaves extract. 2011.
58. Niazi J, Gupta V, Chakraborty P, Kumar P. Anti-inflammatory and antipyretic activity of *Aleuritis moluccana* leaves. *Asian Journal of Pharmaceutical and Clinical Research*. 2010;3(1):35-7.
59. Saptarini NM, Deswati DA. The Antipyretic Activity of Leaves Extract of *Ceiba pentandra* Better than *Gossypium arboreum*. 2015.
60. Ukwuani A, Abubakar M, Warra S. Antipyretic activity of some Nigerian medicinal plants in rats. *Int J Pharm Res*. 2012;4:48-51.
61. Akindele A, Ibel, Adeyemi O. Analgesic and antipyretic activities of *Drymaria cordata* (Linn.) Willd (Caryophyllaceae) extract. *African Journal of Traditional, Complementary and Alternative Medicines*. 2012;9(1):25-35.
62. Igbe I, Ozolua RI, Okpo SO, Obasuyi O. Antipyretic and analgesic effects of the aqueous extract of the fruit pulp of *Hunteria umbellata* K Schum (Apocynaceae). *Tropical Journal of Pharmaceutical Research*. 2009;8(4).
63. Akapa TC, Kehinde AO, Beatrice OO, Olajide O. Antipyretic activity of *Abutilon mauritianum* (Jacq.) roots in Wistar Rats. *International Journal of Pharmaceutical Sciences and Research*. 2014;5:44-6.
64. Safari V, Ngugi M, Orinda G, Njagi E. Antipyretic, anti-inflammatory and analgesic activities of aqueous leaf extract of *Urtica dioica* L. in albino mice. *Medicinal and Aromatic Plants*. 2016;5(2):1-7.
65. QU A. Investigation of In Vivo Antipyretic Activity of *Thottea dependens* leaves. *International Medical Journal Malaysia*. 2015;14(2). Mothana R, Alsaied M, Khaled JM, Alharbi NS, Alatar A, Raish M, et al. Assessment of antinociceptive, antipyretic and antimicrobial activity of *Piper cubeba* L. essential oil in animal models. *Pakistan journal of pharmaceutical sciences*. 2016.
66. Tanira M, Shah A, Mohsin A, Ageel A, Qureshi S. Pharmacological and toxicological investigation on *Foeniculum vulgare* dried fruit extract in experimental animals. *Phytotherapy Research*. 1996;10(1):33-6.
67. Farag M, El Gamal A, Kalil A, Al-Rehaily A, El Mirghany O, El Tahir K. Evaluation

- of some biological activities of *Albizia lebbek* flowers. *Pharmacology & Pharmacy*. 2013 Sep 1;4(6):473.
68. Khan MD. Evaluation of Analgesic and Antipyretic activity of *Marsilea trifolia* Blanco. *International Journal of Scientific & Engineering Research*. 2011;2(8):1-3.
69. Haque A, Kumer DA, Mahmudul A, Bashir SS, Al-Mahmud R, Rahmatullah M. Analgesic and antihyperglycemic activity evaluation of *Bambusa vulgaris* aerial parts. 2015.
70. Zhou Y-X, Wang S-J, Li Y, Xia W, Meng X-Y, Peng C, et al. EVALUATION OF ANALGESIC, ANTI-INFLAMMATORY AND ANTI-PYRETIC ACTIVITIES OF THE ETHANOL EXTRACT FROM *Speranskia tuberculata*. *African Journal of Traditional, Complementary and Alternative Medicines (AJTCAM)*. 2015;12(3):49-54.
71. Ratnasooriya W, Fernando T, Senevirathna C. Antipyretic activity of Sri Lankan black tea (*Camellia sinensis* L.). *Sri Lanka J Tea Sci*. 2007;72:54-60.
72. Pendota S, Yakubu M, Grierson D, Afolayan A. Anti-inflammatory, analgesic and antipyretic activities of the aqueous extract of *Hippobromus pauciflorus* (L.) Radlk leaves in male Wistar rats. *African Journal of Biotechnology*. 2009;8(10).
73. Loonat F, Amabeoku GJ. Antinociceptive, anti-inflammatory and antipyretic activities of the leaf methanol extract of *Rutagraceolens* L. (Rutaceae) in mice and rats. *African Journal of Traditional, Complementary and Alternative Medicines*. 2014;11(3):173-81.
74. Shukla S, Mehta A. In vivo anti-inflammatory, analgesic and antipyretic activities of a medicinal plant, *Caesalpinia bonducella* F. *Pakistan journal of pharmaceutical sciences*. 2015.
75. Gupta R, Kaur J. Evaluation of analgesic, antipyretic and anti-inflammatory activity on *Cordia dichotoma* G. Forst. Leaf. *Pharmacognosy research*. 2015;7(1):126.
76. Okokon JE, Nwafor PA. Anti-inflammatory, analgesic and antipyretic activities of ethanolic root extract of *Croton zambesicus*. *Pak J Pharm Sci*. 2010 Oct 1;23(4):385-92.
77. Patel R, Mahobia N, Upwar N, Waseem N, Talaviya H, Patel Z. Analgesic and antipyretic activities of *Momordica charantia* Linn. fruits. *Journal of advanced pharmaceutical technology & research*. 2010;1(4):415.
78. Bhattacharya S, Roy B. Preliminary investigation on antipyretic activity of *Cuscuta reflexa* in rats. *Journal of advanced pharmaceutical technology & research*. 2010;1(1):83.
79. Sivakumar T, Perumal P, Sambath Kumar R, Vamsi M, Gomathi P, Mazumder U, et al. Evaluation of analgesic, antipyretic activity and toxicity study of *Bryonia laciniata* in mice and rats. *The American journal of Chinese medicine*. 2004;32(04):531-9.
80. Subedi NK, Rahman S, Akbar MA. Analgesic and Antipyretic Activities of Methanol Extract and Its Fraction from the Root of *Schoenoplectus grossus*. *Evidence-Based Complementary and Alternative Medicine*. 2016;2016.
81. Usmanhani K, Azhar I, Akram M, Saeed Ahmad, Syed Muhammad Ali Shah 2, Muhammad Khurshid Alam. *Pak J Pharm Sci*. 2014;27(4):931-4.
82. Rauf A, Uddin G, Siddiqui BS, Muhammad N, Khan H. Antipyretic and antinociceptive activity of *Diospyros lotus* L. in animals. *Asian Pacific journal of tropical biomedicine*. 2014;4:S382-S6.
83. Alam MK, Ahmed S, Anjum S, Akram M, Shah S MA, Wariss HM, et al. Evaluation of antipyretic activity of some medicinal plants from Cholistan desert Pakistan. *Pak J Pharm Sci*. 2016;29(2):529-33.
84. Sundararajan P, Dey A, Smith A, Doss AG, Rajappan M, Natarajan S. Studies of

- anticancer and antipyretic activity of *Bidens pilosa* whole plant. African health sciences. 2006;6(1):27-30.
85. Tag H, Namsa ND, Mandal M, Kalita P, Das A, Mandal
86. Garg V, Dutt R. Antipyretic Plants: An Updated Review. Current Bioactive Compounds. 2020 Feb 1;16(1):4-12. Indian journal of pharmacology. 2010;42(5):273.
87. Borikar V, Jangde C, Philip P, Rekhe D, Atole S. Study of Antipyretic Activity of *Bauhinia racemosa* Lam in Rats. Veterinary world. 2009;2(6):217-8.
88. Manjula RR, Anand TJ, Sudhir M, Ali SL, Kishore CN. Evaluation of antiPyretic activity of *Tephrosia purpurea* LINN in albino rats. American Journal of Phytomedicine and Clinical Therapeutics. 2013 Sep 30;1(6):467-70.
89. Hossain E, Mandal SC, Gupta JK. Phytochemical screening and in-vivo antipyretic activity of the methanol leaf-extract of *Bombax malabaricum* DC (Bombacaceae). Tropical journal of Pharmaceutical research. 2011;10(1).
90. Nardev S, Gupta AK, Vijay J, Renu C. Study on antipyretic activity of extracts of *Bergenia ligulata* Wall. International Journal of Pharma and Bio Sciences. 2010;1(3).
91. Sini K, Karpakavalli M, Sangeetha P. Analgesic and antipyretic activity of *Cassia occidentalis* Linn. World Applied Sciences Journal. 2010;11(10):1216-9.
92. Ashfaq K, Choudhary BA, Uzair M, Hussain SN, Ghaffari MA, Sarwar W, et al. Antipyretic, analgesic and anti-inflammatory activities of methanol extract of root bark of *Acacia jacquemontii* Benth (Fabaceae) in experimental animals. Tropical Journal of Pharmaceutical Research. 2016;15(9):1859-63.
93. Mutalik S, Paridhavi K, Rao CM, Udupa N. Antipyretic and analgesic effect of leaves of *Solanum melongena* Linn. in rodents. Indian journal of pharmacology. 2003 Sep 1;35(5):312-5.
94. Khan A, Haque E, Mukhlesur Rahman M, Mosaddik A, Abdul Alim Al-Bari M, Rahman M. Antipyretic activity of rhizome of *Drynaria quercifolia* in rabbit. Pharmaceutical biology. 2007;45(4):312-5.
97. Maina GS, Kelvin JK, Maina MB, Muriithi NJ, Kiambi MJ, Umar A, John MK, Ann NW, David MN, Piero NM. Antinociceptive properties of dichloromethane: methanolic leaf and root bark extracts of *Carissa edulis* in rats. J Phytopharmacol. 2015;4(2):106-12.
98. Gege-Adebayo GI, Bassi AS, Igbokwe VU, Shafe MO. Antipyretic effect of *Ocimum gratissimum* on brewer's yeast induced fever in wistar rats. J Med Med Sci. 2013 Jun;4(6):247-51.
99. Sc. 2013;4(6):247-51.
100. Yousuf PMH, Noba NY, Shohel M, Bhattacharjee R, Das BK. Analgesic, Anti-Inflammatory and Antipyretic Effect of *Mentha spicata* (Spearmint). 2013.

Table1: Ethnobotanical distribution of plants for which data from animal experiments exist

Country	Plant name
Pakistan	<i>Alhagimaurorum</i> , <i>Cymbopogonjwarancusa</i> , <i>Echinopsechinatus</i> , <i>Fagoniacretica</i> , <i>Panicumturgidum</i> , <i>Taxuswallichiana</i> (50).
India	<i>Capparis zeylanica</i> (51). <i>Melia azedarach</i> , <i>Cardiospermum halicacabum</i> (52). <i>Alstoniamacrophylla</i> , <i>Moringa oleifera</i> (37). <i>Tecomaria capensis</i> (53). <i>Platycladus orientalis</i> (54). <i>Aleuritismoluccana</i> (55)
Indonesia	<i>Ceibapentandra</i> , <i>Gossypiumarborescens</i> (56).
Nigeria	<i>Gongronema latifolium</i> , <i>Grewia crenata</i> , <i>Striga hermontheca</i> (57). <i>Drymariacordata</i> (58). <i>Hunteriaumbellata</i> (59). <i>Abutilonmauritianum</i> (60).
Kenya	<i>Aloevolkensii</i> (61).
Malaysia	<i>Thottea dependens</i> (62).
Saudi Arabia	<i>Pipercubeba</i> (63). <i>Foeniculum vulgare</i> (64). <i>Albizia lebbek</i> (65).
Bangladesh	<i>Marsilea trifolia</i> Blanco(66). <i>Bambusa vulgaris</i> (67). <i>Morinda angustifolia</i>
China	<i>Speranskia tuberculata</i> (68).
Sri Lanka	<i>Camellia sinensis</i> (69)
South Africa	<i>Hippobromus pauciflorus</i> (70). <i>Rutagraveolens</i> (71).
Korea	<i>Caesalpinia bonducella</i> (72)

104.

Table2: Medicinal plants having antipyretic activities							
Plant Name	Family	Part used	Chemical constituents	Extraction/ dosage form design	Dosage	Model	References
<i>Cordia dichotoma</i>	Boraginaceae	Leaves	Phenolic contents, flavonoids, alkaloids, saponins, carbohydrates, glycosides	Methanol extract	400mg/kg	Rats	(73)
<i>Croton zambesicus</i>	Euphorbiaceae	Roots	Isovitexin, apigenin-6-C-glucoside, kaempferol, quercetin, diterpenes	Ethanol extract	27-81mg/kg	Mice	(74)
<i>Momordica charantia</i>	Cucurbitaceae	Fruit	Alkaloids, carbohydrate, tannins, glycosides, proteins, steroids	Ethanol extracts	250 and 500 mg/kg	Rats	(75)
<i>Cuscuta reflexa</i>	Cuscutaceae	Whole plant	Flavonoids, Saponins, organic acids	Aqueous and ethanol extracts	200 and 400 mg/kg	Rats	(76)
<i>Bryonia laciniosa</i>	Cucurbitaceae	Leaves	Bryonin, glucomannan, saponin, goniothalamine, punicic acid	Methanol extract	125 and 250 mg/kg	Mice and rats	(77)
<i>Schoenoplectus grossus</i>	Cyperaceae	Roots	Tannins, alkaloids, flavonoids	Methanol extract	400	Mice and rats	(78)

<i>Moringa oleifera</i>	Moringaceae	Bark	Phenolic acid, flavonoids, glucosinolates, thiocyanates, flavonol, kaempferol, quercetin, rutinoids, caffeic acid	Hydro-alcoholic extract	50 and 100 mg/kg	Rats	(79)
<i>Diospyros lotus</i> L.	Ebenaceae	Roots	Lupin, triterpenes, dimeric naphthoquinones, naphthalene, sugar, fatty acids, phenolic compounds	Chloroform, ethyl acetate, hexane and butanol fractions	50 and 100 mg/kg	Mice	(80)
<i>Fagonia cretica</i>	Zygophyllaceae	Roots	Glycosides, steroids, sterols, coumarins, tannins, saponins, terpenoids, flavonoids, alkaloids	Ethanol extract	500 mg/kg	Rabbits	(81)
<i>Bidens pilosa</i>	Asteraceae	Whole plant	Flavonoids, polyacetylene, terpenoids, sterols, phenyl propanoids	Methanolic extract	500 mg/kg	Rabbits	(82)
<i>Cardiospermum halicacabum</i>	Sapindaceae	Whole plant	Xanthoprotein, Tannins, Saponins, Triterpenoids, Steroids, Flavonoids	Ethanol as well as hexane	400 mg/kg	Rats	(52)

105.

<i>Chloranthus serectus</i>	Chloranthaceae	Leaves	Flavonoids, alkaloids, saponins, glycosides	Methanol extract	100 and 200 mg/kg	Rats	(83)
<i>Tecomaria capensis</i>	Bignoniaceae	Leaves	Alkaloid, phenolic compounds, flavonoids, saponins, glycosides, terpenoids, steroids, coumarins, quinines	Methanol extract	100, 200 and 500 mg/kg	Rats	(53)
<i>Drymaria cordata</i>	Caryophyllaceae	Whole plant	Tannins, phenols, flavonoids, alkaloids, saponins, glycosides	Aqueous extract	100, 200, and 400 mg/kg	Mice and rats	(58)
<i>Bauhinia racemosa</i>	Caesalpiniaceae	Stem bark	Flavonoids, tannins, methyl gallate, kaempferol, quercetin	Alcoholic extract	100, 200 mg/kg	Rats	(84)
<i>Tephrosia purpurea</i>	Fabaceae	Whole plant	flavones, flavanones, prenylated flavonoids, chalcone and rotenoids	Methanolic extract	250 and 500 mg/kg	Rats	(85)
<i>Bombax malabaricum</i>	Bombacaceae	Leaves	Steroids, carbohydrates, tannins, flavonoids, triterpenoids, deoxy-sugars and coumarin glycosides	Methanolic extract	200 and 400 mg/kg	Rats	(86)
<i>Bergenia ligulata</i>	Saxifragaceae	Roots, rhizomes & leaves	Steroids, alkaloids, Flavonoids and terpenoids	Ethanol extract	300 & 500 mg/kg	Rats	(87)

<i>Cynanchum Viminale</i>	Asclepiadaceae	Stem	Flavonoids, saponins, tannins, glycosides, alkaloids and steroids	Aqueous extract	150mg/kg	Mice	(61)
<i>Cassia occidentalis</i>	Caesalpinaceae	Leaves	Sennoside, anthraquinone, fatty oils, tannins, glycoside, flavonoid glycosides, galactomannan and polysaccharides	Ethanol and water extract	150 and 300 mg/kg	Rats	(88)
<i>Stachytarpheta indica</i>	Verbenaceae	Stem bark	Saponins, carbohydrates, steroid s, terpenoids and alkaloids	Methanolic extract	50, 100 and 150 mg/kg	Mice	(58)
<i>Acacia jacquemontii</i>	Fabaceae	Root bark	Tannins, cardioactive glycosides, saponins and flavonoids	Methanolic extract	50 and 100 mg/kg	Mice	(89)
<i>Solanum melongena</i>	Solanaceae	Leaves	Flavonoids, alkaloids, tannins and steroids	Dry residues	100, 250 and 500 mg/kg	Rats	(90)

106.

<i>Drynaria Quercifolia</i>	Polypodiaceae	Rhizome	Steroids, tannins, and flavonoids	Petroleum ether and ethyl acetate soluble fraction of ethanol extract	80 mg/kg	Rabbits	(91)
<i>Carissae dulis</i>	Apocynaceae	Leaves	Alkaloids, flavonoids, steroids, phenolics and terpenoids	Methanolic extract	50, 100 and 150 mg/kg	Rats	(92)
<i>Ocimum gratissimum</i>	Labiatae	Leaves	Tannins, flavonoids, saponins, steroid, alkaloids, cardiac glycosides, terpenoids and phenols	Methanolic extract	100, 200 and 300 mg/kg	Rats	(93)
<i>Azima tetraacantha</i>	Salvadoraceae	Leaves	Alkaloids, flavonoids, glycosides, β -sitosterol, tannins, terpenes, protein and coumarin	Ethanol extract	100 and 200 mg/kg	Rats	(94)
<i>Mentha spicata</i>	Labiatae	Whole plant	Carvone and limonene	Methanolic extract	250 and 500 mg/kg	Mice	(95)