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Review on Anti-Pyretics & Analgesic Herbs in Siddha Medicine

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Abstract

In Siddha system of medicine, there are many polyherbal formulations used as antipyretics. This review article looks into the details of few commonly used herbs and elucidates scientifically as anti-pyretics, analgesic, anti-microbial & anti-inflammatory potential. Also Siddha compound herbal and herbo-mineral preparations in treating fever are included.anti-malarial activity of Andrographis paniculata, Cedrus deodara are also of great significance.

Keywords: Anti-pyretic herbs, phytochemicals,pharmacological activity,Siddha medicine.

INTRODUCTION

Fever is also known as pyrexia & febrile response. It is defined as having a temperature above the normal range due to an increase in the body's temperature setpoint.A fever can be a only symptom in variety of medical conditions ranging from simple to potentially serious. It can be due to viral, bacterial & parasitic infections, systemic conditions, side effects of medication and even cancer. Fever is one of the most common medical signs. About 30% in children and 75% in adults who visit healthcare centres.In the eventof antibiotic resistance to infections,epidemic and endemic outbreak threat of infections particularly of viral like ebola,dengue,chikungunya, and unknown cause, effective,alternative, safer,newer moiety of antipyretics are in dire need. Microbes such as bacteria,viral,fungi & parasites adapt to their environment and change their ways that ensure their survival.These microbes antibiotics and thrives by means of mutation and carrying resistance genes,and remain dominant throughout their span. The emergence of drug-resistant microbes has become a great cause of concern for healthcare community as they are not affordable & difficult to treat.In Siddha system of medicine,plethora of herbs are used to treat fever and its related illnesses.Here,review of commonly used antipyretic herbs are putforth for assured management of infectious fever.

1. Andrographis paniculata

Antimicrobial [1]

Crude powder suspended in water was reported to be devoid of invitro antibacterial activity against Salmonella,Shigella,E.coli,Gram A streptococci & Staphylococcus aureus even at a concentration of 25mg/ml.crude powder.Singh et al. reported significant antibacterial activity of an aqueous extract & attributed it to the combined effect of Andrographoloides & arabinogalactan proteins.The crude aqueous extract of leaves (Zaidan et al) exhibit significant anti-microbial activity against Gram positive S.aureus,methicillin-resistant S.aureus (MRSA),& Gram negative Pseudomonas aeruginosa,but had no activity against E.coli or KlebsiellaPneumoniae.The ethanol extract was devoid of significant activity against enterohemmorhagic strains of E.coli.

Anti-viricidal [2]

Andrographolide,Neoandrographolide & 14,deoxy-11,12,-didehydroandrographolide are reported to be viricidal against herpes simplex virus1 (HSV-1) without having any significant cytotoxicity at viricidal concentrations.A.paniculata has been reported to inhibit viral replication in HIV infected cells.

Antimalarial [3]

The methanol extract of Andrographis paniculata (Mishra et el) significantly inhibited Pl.Falciparum at a 50% inhibitory concentration (IC 50) OF 7.2 µg/Ml. The four xanthones- 1,8-dihydroxy-3,7- dimethoxy xanthone,4,8-dihydroxy-2,7-dimethoxy xanthone,1,2- dihydroxy 6,8-dimethoxy xanthone,1,3,7,8-trimethoxy-1-hydroxy-xanthone isolated from the roots of the plant,also showed invitro anti-malarial activity against plasmodium falciparum & in vivo activity in Swiss albino mice infected with P.berghei.The same xanthones also exhibited anti-protozoal activity against Trypanosoma brucei,T.Cruzi and Leishmania infantum.Water decoction of the leaves exhibited filaricidal activity, both in vitro and dogs.

In URTI: [4]

In a randomized,double-blinded ,controlled study,Thamlikitkul et al gave A.paniculata a dose of 6g/day for seven days to 152 Thai adults suffering for pharygotonsillitis.Efficacy was comparable to acetaminophen in relieving of symptoms of fever and sorethroat.

In an another study, (Kligler B et al 2006) of 158 patients suffering from common cold used a standardized A.paniculata extract SHA-10 (1200 mg/day) for five

days.The extract significantly reduced the symptoms of tiredness,sleeplessness,sorethroat & nasal secretions starting from the second day of treatment.The existing evidence suggests that best results may be obtained if taken within first 24 hrs of URTI symptoms.

Melchoir et al. in 2000 conducted 2 randomised double-blind,placebo-controlled parallel group clinical trials of a fixed dose combination of standardised extracts of the leaves of Andrographis paniculata (60 mg andrographolide/day) in uncomplicated ac.URTI, which was statistically significant P=0.0006.

Antipyretic activity & Anti-inflammatory activity [5]
The ability of Andrographis paniculata has been demonstrated independently in several studies.It has shown that andrographolide lowered the fever produced by different fever- inducing agents such as bacterial endotoxins,Pneumococcus, haemolytic streptococcus,typhoid, paratyhoid.The analgesic activity of andrographolide was weaker than aspirin while anti-pyretic activity was comparable to that of aspirin (Vedavathy et al & Madhav.H.C.et al)

Immunological potential [6]
The extract of A.paniculata may have the potential for interfering with the viability of HIV (Stephen et al., 2000 & Nanduri et al., 2003). Andrographolide interrupted or modified the cellular signal transduction pathway of the virus,resulting in interfering the key enzymes & viral reproduction Consequently.

2. Cyonodon dactylon

Antipyretic activity [7]
The antipyretic activity of the aqueous extract of Cyonodon dactylon showed significant activity at 400mg/kg & 600mg/kg dose levels.At 400mg/kg dose the rectal temperature found to be 37.88 after 1 hour & 38.05 after 4 hours while compared to the standard drug paracetamol which is 37.68 & 37.80 after 1 hour & 4 hours respectively.

Analgesic activity [8]
The aqueous extract of Cyonodon dactylon has shown dose dependent activity.After administration of the aqueous extracts at 200mg/kg, 400mg/kg, and 600mg/kg. dose levels,there is statistically significant increase in the hot plate reaction time.At 600mg/kg dose level,after 3 hours reaction time is 28.48 compared to the standard drug pentazocine 31.15 respectively.

The aqueous extract at dose levels of 200mg/kg, 400mg/kg, 600mg/kg exhibited 30.55%, 68.55 %& 82.10% respectively the inhibition of writhing as compared to that of 82.96% inhibition shown by aspirin.The extract at 600mg/kg showed comparable activity to that of the aspirin.

3. Evolvulus alsinoides

Antipyretic activity [9]
The ethanolic plant extract produced a reduction in hyperpyrexia induced by yeast infection in rats,with activity being pronounced within 90 minutes.Also,within 2 hours of the administration of the plant extract was as effective as paracetamol in reducing hyperthermia with p (≤0.05).

Anti-inflammatory activity [10]
Carrageenan-induced rat paw edema was markedly inhibited on treatment with ethanol extract (250mg/kg & 500m9] g/kg body weight dose) 7 Indomethacin (20 mg/kg body weight dose).In the acute inflammation model,a dose of 250mg/kg body weight of the extract showed significant inhibition (p≤0.05) at 3 &4 hour whereas indomethacin & evolvulus alsinoide plant extract at 500mg/kg body weight exerted significant inhibition at 2,3 &4 hours.

4. Tinospora cordifolia

Anti-inflammatory activity [11]
The aqueous extract of Tinospora cordifolia exerted a significant anti-inflammatory effect on cotton pellet granuloma & formalin induced arthritis models.Its effect was comparable with Indomethacin and its mode of action resembled that of a non-steroidal anti-inflammatory agent.The dried stem of Tinospora cordifolia produced significant anti-inflammatory effect in both acute & subacute models of inflammation.This herb is found to be more effective than acetyl salicylic acid in acute inflammation.In subacute inflammation, the drug was inferior to phenylbutazone(JanaU,Chattopadhyay RN etal 1993)

5. Clerodendron serratum

Anti-bacterial [12]
The ethanolic root extract (7.5 mg/disc) showed broadspectrum anti-bacterial activity against gram +ve & gram-ve bacteria.The results were compared with the standard drug streptomycin (10µg/disc). The zone of inhibition was found to be increased with the increase in concentration of the extract & thus exhibiting concentration of the extract & thus exhibiting concentration dependent activity (Mackei & Mc.Caitney, 1996).

Anti-inflammatory activity [12]
The ethanolic extract of Clerodendron serratum showed significant anti-inflammatory activity in Carrageenan-induced edema in rats, & also in the cotton pellet model in experimental mice,rats & rabbits at concentrations of50,100 & 200 mg/kg(Narayanan et al,1999).

6. Costus speciosus

Antipyretic activity [13]
There was a mild reduction in rectal temperature of rats treated with 800mg/kg etanolic extract.The effect happened after 180 min. of drug was administered & it persisted even after 270 mins.

Anti-inflammatory activity [14]
The anti-inflammatory effect of ethanolic extract of Costus speciosus was studied by Carrageenan induced paw edema. The ethanolic extract of Costus speciosus inhibited the development of edema after 3 hours & the effect was dose dependent & was statistically significant ($p \leq 0.05$).The effect was most prominent with 800mg/kg dose which was measured as 37.78% inhibition of granulation tissue formation when compared to the standard drug hydrocortisone as 51.2%.The effect produced by 800mg/kg dose was about 63% of the effect produced by acetyl salicylic acid,the standard drug.

In cotton pellet induced granuloma formation study,regarded as an animal model for subacute inflammation, there was a statistically significant ($p \leq 0.05$) reduction in granuloma formation at all doses in comparison to the control group.The effect produced by the extract at 400mg/kg & 800mg/kg doses was almost similar.

7. Piper nigrum

Antimicrobial [15]
Aqueous & methanolic extract were analysed for antimicrobial activity by agar cup plate method.The aqueous extract of P.nigrum at 10mg/ml. showed significant zone 19mm,24mm, 18mm,19mm,18mm. and whie 10mg/ml methanolic extract showed 23mm,19mm,23mm,19mm,21mm and 19mm respectively , compared to the standard drug 100µg/ml as 24 & 23mm against S.aureus & E.coli respectively.

8. Zingiber officinale

Anti-inflammatory [16]
The ethanol extract of ginger showed marked anti-inflammatory activity against acute inflammation, suppressing the rat paw edema both at the early & late phases,though not in dose dependent manner .The 100mg/kg etanol extract of ginger on egg albumin induced rat paw edema showed inhibition of edema as15.79%,41.18%,46.43 & 63.04% at 1hr,2hr,3hr & 4hr. respectively inhibition of edema relative to control Indomethacin as 26.47%,35.71% & 41.3% in same duration as above.

Shen et al (2005) also reported the anti-inflammatory effect of ginger roots showing its strong inhibition of cox-2 enzyme,pro-inflammatory cytokines & prostaglandins which are all components of the inflammatory response.Phytochemical study of ginger showed that it is abundantly rich in flavonoids which may be one of the main ingredients of anti-inflammatory activity.

Anti-microbial activity [17]
Ingenol & [6] - Shogaol, isolated from ginger rhizome demonstrated anti-viral activity.32 [10] gingerol has been reported as active inhibitor of M.avium & M.tuberculosis in vivo.[6]- gingerol & [12]-gingerol, isolated from rhizome, demonstratd anti-bacterial activity against peri-odontal bacteria.

9. Piper longum

Anti-microbial activity [18]
The aqueous extract of Piper longum at 10mg/ml showed powerful zone of inhibition against S.aureus,Bacillis subtilis,E.coli,Pseudomonas aeruginosa, & Aspergillus niger ,Candidaq albicans as 24mm,20mm,24mm,19mm,18mm,21mm compared to the standard as24mm,23mm,23mm,21mm respectively.The methanolic extract 10mg/mi showed zone of inhibition as 24mm,20mm,24mm,19mm,18mm,21mm compared to the standard drug as 24mm,22mm,23mm & 21mm respectively.While against griseofulvin as 23mm & 23mm as zone of inhibition against A.niger and Candida albicans.

10. Alstonia scholaris

Anti-microbial activity [19]
Invitro anti-bactericidal activity of methanolic extract,aqueous & total alkaloid extracts from the trunk bark against two gram positive bacteria including Bacillus subtilis & Streptococcus pyrogens & four gram negative bacteria,E.coli,Pneumoniae,Pseudomonas aeruginosa & Proteus mirabilis using disc diffusion method.All extract showed varying degrees of inhibitory activity against all bacteria.Aqueous extract was found to be active against both gram positive & gram negative bacteria.

Analgesic & Anti-inflammatory activity [20]
The invitro anti-inflammatory effect of alkaloids from Alstonia scholaris showed the percentage of inhibition of stophanine & tubotainine to cox-2 & 5-Lox was 54.3%,63.3% and 57.3% respectively.

In acetic acid induced writhing test,the alkaloids fraction picrinine,vallesamine,scholaricine demonstrated significant analgesic effects.In the formalin test, the experimental results shows thatalkaloids produced a significant inhibitory effect,during the second phase.

Alkaloids fraction at 3 doses (10,20,80 mg/kg),picrinine (10mg/kg), vallesamine (8mg/kg), & Scholaricine (5mg/kg) treated by intragastrical increased SOD activity significantly, & decreased levels of NO,PGE2 & MDA significantly,in mice air pouch model,rougly comparable to aspirin at 200mg/kg.

11. Hemidesmus indicus [21]

The methanolic extract of Hemidesmus indicus found that extract at a dose of 100mg/kg caused significant lowering of body temperature at 4 hr. folloeing its administration. This effect was maximal at doses of 200 & 400 mg/kg in dose dependent manner & it caused significant lowering of T 4 hr after its administration.The anti-pyretic activity started as early as 1 hr & the effect was maintained for 4hr after its administration.Both the standard drug & paracetamol 100mg/kg and Hemidesmus indicus extract significantly reduced the yeast elevated rectal temperature compared to the control drug.

12. Picrorrhiza kurroa [22]

It is evident from the studies,methanol extract possess anti-microbial activity in cup plate method & MIC study.The cup plate method result showed response as 18mm,20mm & 16mm diameter of methanol extract against S.aureus,B.subtilis & E.coli. The aqueous extract showed diameter of 10mm, 12mm in diameter against A.niger & Candida albicans when compared with the standard drug ciprofloxacin showing activity at 26mm, 28mm & 24mm against the strain S.aureus.B.subtilis & E.coli.

13. Withania somnifera

Analgesic & Anti-inflammatory effect [23]

Withaferin A & 3-b-OH-2,3,dihydro withanolide 7 isolated from Withania somnifera shows promising anti-bacterial effect,anti-inflammatory properties (Buddhiraga & Sudhir,1987).This herb is an analgesic that soothes nervous system from pain response (Twajj et al,1989).Withania (1000mg/kg) produced significant analgesic activity for a rat by hotplate method.The peak analgesic effect of Withania was recorded as 78.03% at 2^{nd} hr. of administration.The analgesic activity of Withania somnifera was potentiated significantly by cyprohepatidine.However,paracetamol failed to exhibit any significant change in its activity,suggesting the involvement of serotonin,but not prostaglandin in the analgesic activity of the root .(Mazen et al., 1990).

14. Phyllanthus emlica

Anti-pyretic & Analgesic activity [24]

A single dose of ethanolic extract & aqueous extract (500mg/kg,i.p) showed significant reduction in hyperthermia in rats induced by brewer's yeast. Both of these extracts elicited pronounced inhibitory effect on acetic acid induced writhing response in mice in analgesic test.This may be due to the presence of tannins,alkaloids,phenolic compounds,aminoacids and carbohydrates.

15. Ocimum sanctum

Anti-pyretic activity [25]

The antipyretic activity of fixed oil was evaluated by testing it against typhoid-paratyphoid A/B vaccine induced pyrexia in rats.The oil on ip administration considerably reduced the febrile response indicating its antipyretic activity.At a dose of 3ml/kg,the anti-pyretic activity of the oil was comparable to aspirin.Also the fixed oil possessed prostaglandin inhibitory activity.

The Ocimum sanctum oil was effective against acetic acid induced writhing method in a doe dependent manner. This is suggested to be peripherally mediated due to combined inhibitory effect of prostaglandins, histamine & acetylcholine.

Methanolic extract (500mg/kg) & aqueous extract of Ocimum showed analgesic antipyretic activity in acute carrageenan induced pedal edema & chronic inflammation in rats.

16. Smilax chinensis

Anti-inflammatory & Analgesic activity [26]

The methanolic extract of Smilax chinensis. 250mg/kg i.p showed decreased edema volume at 56% at 5 hr.,ethyl acetate extract showed decrease in edema volume at 68.23% at 5 hr,while standard drug Indomethacin showed decrease in edema volume as 82.35% at 5 hr.respectively.The methanolic extract of Smilax chinensis 400mg/kg i.p. on hot plate reaction time showed 8.02 at 1 hr while ethylacetate extract is 9.35 at 1 hr, compared to the standard drug pentazocine as 14 at 1 hr.

17. Cedrus deodara

Anti-malarial activity [27]

Essential oil from Cedrus deodara was evaluated for bioactivity against the adults of C.quinuefasciatus & A.aegypti. Adults of A.aegypti were insensitive towards the oil of Cedrus deodara under the concentration range & 1 hr. of exposure whereas agaist C.quinuefasciatus reported LC 50 was 2.48% respectively,indicating low effectivity. Plant shows moderate activity against these two mosquitoes.

Anti-inflammatory activity

An aqueous extract of an dried stem bark of plant was screened for anti-inflammatory & anti- arthritic activity by Carragenan induced inflammation (Winter et al., 1962) & compared with standard drug, betamethasone & phenylbutazone. Cedrus deodara was found to be less effective than standard drug.

18. Pavonia odorata

Anti-microbial activity [28]

Pavonia odorata has good anti-microbial activity against S.aureus,Diplococcus pneumonia,Chrysoporium indicum & Botrydiplodia sps.

19. Glycyrrhiza glabra

Anti-pyretic activity [30]

Glycyrrhetic acid showed anti-pyretic activity similar to that of Na salicylate on rectal temperature of normal & pyretic rats.In a clinical trial for traumatic inflammation,it was noted that Glycyrrhiza glabra possess more potent antipyretic effect than oxyphenylbutazone.

20. Aconitum ferox

Anti-pyretic activity [31]

Aconitum sps.possesses wide range of alkaloids,flavonoids and other active constituents which is responsible for their medicinal properties.Aconitum ferox & Aconitum chasmanthum roots are potent antipyretic and analgesic & high therapeutic index (Jabeen et al 2006).

S.No	Botanical Name	Tamil name	Family	Parts used
1	Andrographis paniculata	Nilavembu	Acanthaceae	Whole plant
2	Cyonodon dactylon	Arugampul	Poaceae	aerial parts
3	Evolvulus alsinoides	Vishnugrandhi	Convolvulaceae	Whole plant
4	Tinospora cordifolia	Seenthil	Menispermaceae	wood
5	Clerodendron serratum	Siruthekku	Lamiaceae	Root
6	Costus speciosus	Koshtam	Costaceae	Rhizome
7	Piper nigrum	Milagu	Piperaceae	Fruit
8	Zingiber officinale	Chukku	Zingiberaceae	Rhizome
9	Piper longum	Thippili	Piperaceae	Fruit
10	Alstonia scholaris	Ezhilaipalai	Apocyanaceae	Bark
11	Hemidesmus indicus	Nannari	Solanaceae	Root
12	Picrorrhiza kurroa	Kadugurokini	Scrophulariaceae	Root
13	Withania somnifera	Amukkra	Solanaceae	Root
14	Phyllanthus emblica	Nelli	Euphorbiaceae	Fruit
15	Ocimum sanctum	Thulasi	Lamiaceae	Leaf
16	Smilax chinensis	Parangipattai	Liliaceae	Root
17	Cedrus deodara	Devadaru	Pinaceae	wood
18	Pavonia odorata	Peramutti	Malvaceae	Rhizome
19	Glycyrrhiza glabra	Adhimathuram	Fabaceae	Root
20	Aconitum ferox	Naabhi	Ranunculaceae	Root

Commonly used Siddha medicines in fever

1. Nilavembu kudineer [31]
2. Nochi Kudineer [31]
3. Adathoda Kudineer [31]
4. Vatha sura Kudineer [32]
5. Pitha sura Kudineer [32]
6. Kapha sura Kudineer [32]
7. Panchamooli Kudineer [32]
8. Muppini sura Kudineer [32]
9. Chandamarutha Kudineer [32]
10. Brahmananda vayiravam mathirai [31]
11. Kasthuri mathirai [31]
12. Korosanai mathirai [31]
13. Vasanthakusumakaram mathirai [31]
14. Vishnuchakra mathirai [31]
15. Thalisathi choornam [31]
16. Sivanar amirtham [31]
17. Kasthuri karuppu [31]
18. Annabedhi chenduram [31]
19. Linga chenduram [31]
20. Sangu parpam [31]
21. Thirikadugu choornam [31]
22. Arumuga chenduram [31]
23. Chandamarutha chenduram [31]

CONCLUSION

All these herbs are most promising in coming up with new generation of anti-pyretics.These pharmacological studies only emphasises the magnificience of Siddha medicine and its richness in sources of medicine which are being proven to the world by scientific validation.

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