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Original Article

Comparison of antipyretic effectiveness between standard drugs with different doses of Ocimum *sanctum linn (Tulsi*)

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ABSTRACT

Background: *Tulsi*, also known as holy basil, is indigenous to the Indian continent and highly revered for its medicinal uses within the Ayurvedic and Siddha medical systems. Many in vitro, animal and human studies attest to *tulsi* having multiple therapeutic actions including adaptogenic, antimicrobial, anti-inflammatory, cardioprotective, and immunomodulatory effects. Yet to date there are very few studies pertaining to the antipyretic activity. ***Objective***: To compare the anti-pyretic property of aqueous form of *Ocimum Sanctum Linn (tulsi) fresh leaves*, in different doses with that of standard drug, in experimentally induced acute fever in animal models. ***Methodology:*** Adult *Wistar Albino Rats* of both sex weighing 125-150 grams were randomly divided into 3 groups (n=6); First group were the standard drug (control) subjects (Paracetamol 100 mg/kg), the second and the third groups were the test group (*Tulsi* 400mg/kg & 800mg/kg). After recording the initial temperature, fever was induced by injecting 15% of brewer's yeast. 18 hrs post challenge, each rat was fed orally with standard and test drugs respectively. Temperature were recorded at basal level, and at 30, 60, 120 and 180 minutes respectively. ***Results:*** There was a statistically significant reduction of temperature in the *tulsi* treated group. ***Conclusion:*** Fever control was comparable with that of standard drug.

Key words: *Ocimum Sanctum Linn (tulsi)*, Effectiveness, Paracetamol, Pyrexia

INTRODUCTION

In the recent past there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and less side effects. In the Indian system of medicine, herbal medicines play a major role, because of their easy procurability together with effectiveness and safety are the prime reasons for the choice of plants in therapeutic applications, and from centuries herbs have been the original source for most of the drugs [1]. Various medicinal plants like Neem, Arjuna, Aswagandha, *Tulsi-The Indian Holy Plant, etc*. are traditionally used for treating fever [1]. Herbal drugs as antipyretics herbal care or traditional system of medicine are used throughout the world. Medicinal plants contain so many chemical compounds which, are the major source of therapeutic agents to cure human diseases. Recent discovery and advancement in medicinal and aromatic plants have lead to the enhancement of health care of mankind. The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world. Among these 2500 species are in India, out of which 150 species are used commercially on a fairly large scale. India is the largest producer of medicinal herbs and is called as botanical garden of the world [2]. *Ocimum sanctum* natively known as *tulsi* and the word " *Tulsi*" gives the connotation of the incomparable one, mentioned in the Charaka Sanhita, an ancient aurvedic text by Charaka for its medicinal importance. Ayuervedic remedies used extracts of *tulsi* for relieving common colds, headaches, heart disease, inflammatory, allergic disorders, as a cough alleviator, a sweat-inducer and as a mitigator of stomach disorders like indigestion and anorexia. Several medicinal properties have been attributed to *tulsi* in ancient Indian and other systems of medicine like Ayurveda, Siddha, Greek, Roman and Unani[3,4,5]. The leaves have been used as expectorant, diaphoretic, antiemetic, antirheumatic,

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anticancer, anti-cataract, against typhoid fever, anthelmintic, antiseptic, analgesic, antipyretic and in relieving various gastric disorders[6,7,8,9]. The juice from the leaves possess anabolic, hypotensive, cardiac depressant, smooth muscle relaxant, hypoglycemic, sedative, antimicrobial, antispermatogenic and antifertility actions *etc*[10,11]. The main pharmacological actions of tulsi are, brought about by the main chemical constituents:oleanolicacid, ursolicacid, rosmarinica cid, eugenol, carvacrol, linalool, β-caryophyllene β-elemene(c.11.0%), β-caryophyllene (about 8%), and germacrene D (about 2%). β-Elemene has been studied for its potential anticancer properties, but human clinical trials have yet to confirm its effectiveness[12]. The effect of some indigenous drugs on pain by some studies stated that the effect of *Tulsi* on nociception, has produced differential degrees of both opioid and non-opioid mechanisms which may be responsible for the analgesic effect of these indigenous drugs and recent studies suggested that *tulsi* may be a COX-2 inhibitor, like many modern pain killers, due to its high concentration of eugenol (1-hydroxy-2-methoxy-4-allylbenzene)[13,14].

Tulsi apart from religious belief, it is an easily available *household remedy* for many health problems.***To list few***: due to its kapha removing properties, it is an excellent medicine for common cold. Tea made from leaves of *tulsi* controls nasal catarrh, cures body-ache and gives a refreshing feeling. Similarly, taking a few leaves mixed with a teaspoonful of ginger juice and honey immediately controls bouts of ***dry cough*** and removes any ***bronchial spasm***. In chronic dysentery when a patient passes stool mixed with mucous, *tulsi* leaves twice a day after mixing with a pinch of rock salt offer great help, and half a teaspoon of roasted jeera powder in a bowl of curd acts as a good digestive. This treatment if continued for a week or 10 days also helps to dispel persistent flatulance and abdominal distension. *Tusli* seeds are well known for their anthelmintic action. Children suffering from roundworm infection can be safely given a quarter of a teaspoon of crushed tulsi seeds at bedtime for at least three consecutive days. However, a healthy person can take up to 10 leaves of *Tulsi* in a day.

Skin diseases and headache: Applied locally, *Tulsi* juice is beneficial in the treatment of ringworm and other minor skin diseases. Its pounded leaves, mixed with sandalwood paste, is a famous home remedy for headache. *Tulsi* seeds are used in anti-leucoderma preparations.

Other diseases: Its seeds are given in chronic urinary infections and by their mucilagenous action they are also helpful in treating diarrhoea, habitual constipation and piles. The dose of Tulsi juice is 10 to 20 ml whereas the powdered seed can be taken 1-3 gm twice a day. *Tulsi* strengthens the immune response by enhancing both cellular and humoral immunity. Regular use of its leaves during the season of viral fever acts as a good preventive medicine, five to ten leaves as described by Vatsyayan [15.16].

Stress management: Taking the lead from the recent studies that *Tulsi* has stress-busting and antioxidant properties, more and more pharmaceutical companies are coming up with its preparations [17].

Because of *tulsi's* various pharmacological actions, wide range of therapeutic applications, numerous scientific studies are on progress and are the subject of focus in the field of scientific research. All the previous studies were done for its analgesic and anti-inflammatory, antidiabetic and other pharmacological actions *etc.*[18,19,20]. Hence the present study was undertaken on animals models with an effort to find out the antipyretic property of this medicinal plant *Tulsi* with the following objective:1.To evaluate the antipyretic efficacy of different doses of *Tulsi,* when compared with that of standard drug and 2. The safety of *Tulsi*

METHODOLOGY

Our study was a randomized control trial, conducted after getting approval from the Institutional Animal Ethics Committee. Both female and male *Wistar Albino Rats* weighing 125-150 grams were selected. They were randomly divided into 3 groups (n=6). The first one was standard drug (Paracetamol 100 mg/kg body weight) group, and the second and third were the test drug (*Tulsi* 400mg/kg and 800mg/kg) groups. The initial rectal temperature was recorded by using digital clinical thermometer, 2 cm depth in the rectum. Those animals with 38 degree centigrade of temperature were included. Fever was induced by injecting 15% of brewer's yeast suspension, given subcutaneously behind the nape of the neck and the injection site was massaged to spread the medicine. 18 hrs after giving injection basal temperature was recorded. The standard and test drugs were given by oral route. The test drug *tulsi* was prepared by grinding in mortar and suspended in distilled water. The 1st group was fed with the standard drug Paracetamol 100 mg/kg, the 2nd and 3rd groups were treated with two different doses of *tulsi* 400mg/kg, 800mg/kg body weight respectively. The temperature recordings were done at 30, 60,120 and 180 minutes to all the study

subjects. The findings were analyzed for statistical significance.

***Statistical analysis and interpretations*:** The weights of the three groups were compared for homogeneity by 'ANOVA'. The improvements by means of reduction in temperature, in the three groups were compared from basal to 30 minutes, 30-60, 60-120 and 120-180 minutes by student paired "t" test. The differences of improvements between the groups were interpreted by Anova. The improvements within and in between the groups were confirmed by repeated measures of Anova. The P values less than or equal to 0.05 ($P \leq 0.05$) were considered for statistical significance.

RESULTS

The homogeneity of the three groups in respect of their weights was compared. The homogeneity of the three groups was shown in the above table-1. The mean weights of three groups were 125.0±1.9 gm, 125.8±3.8 gm and 125 ±2.9 gm respectively. The difference of means between the three groups were not statistically significant (P>0.05) as shown in table 1.

DISCUSSION

The findings in this study demonstrated a promising effect in reduction of febrile response in the 3rd group, as indicated by the mean reduction 2.8±0.2, which differed with statistical significance with that of the other two groups stating that, 800mg/kg was very effective than the first and second groups (P<0.001). All the 3 groups showed reduction of temperature from basal to first half an hour, of medication which was comparable with that of standard drug Paracetamol, and it was highly significant statistically (P<0.001). In respect of the second group there was significant reduction of fever in the first hour of therapy than the other groups (P<0.05). Similarly there was no difference in reduction of temperature between the two groups at 60-120 minutes which was statistically significant (P>0.05) and there was an increase of temperatures in all three groups at 120-180 minutes, which was also not significant statistically (P>0.05). The findings made in this research is well correlating with one study, wherein they have used (i.p) intra-peritonial injection of *ocimum sanctum* preparation for treating typhoid and paratyphoid A/B Vaccine induced fever. Results of that study showed, that *ocimum sanctum* has considerably reduced the temperature in rats and the antipyretic activity was comparable to aspirin[21,22].

In our trial we have used, two different doses of *tulsi*. Observations regarding the safety of *ocimum sanctum* has depicted, no alterations in the cage side observations like grooming, scratcing, biting, and hyperactivity *etc*. and there was no mortality, no change in body weight, food and water intake which is very similar to another acute toxicity study done in mice with *ocimum sanctum*. In that study, they had administered *tulsi* in doses ranging from 3gm/kg and increased up to 7gm/kg of body weight and they had followed the study subjects for a period 15 days. Even though the doses were heavy, there was no/any significant toxic effects identified, and also other morphological, physiological parameters were not affected meaning, that tusli was well tolerated by the study subjects and the same was proved in our study too, as there was no abnormalities noticed among the trial groups [23].

CONCLUSION

This trial has proved that *tulsi* is very effective in the therapy of pyrexia comparable with of standard drug Paracetamol. Further large scale studies are required to explore exact mechanisms of action, clearly clarify the dose and dosage formulations, and to determine the specific populations that are going to be most likely to be benefitted. To date, however, there are no systematic human clinical trials conducted on *Tulsi,* regarding the clinical efficacy and safety as a single herbal medication, for the future therapeutic interventions in general population. Various studies have evidenced the effectiveness of *tulsi,* in the management of life style-related chronic diseases including diabetes, metabolic syndrome, and psychological stress. Therefore to conclude, human clinical trials are requested to critically appraise the current evidences on clinical efficacy and safety of *tulsi.*

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TABLE-1: COMPARISON OF THREE GROUPS IN RESPECT OF THEIR WEIGHT.

Sl. No	Groups	N	Mean	SD	"F"	Df	Significance
1	Paracetamol	6	125.0	1.9	0.159	2.15	P>0.05
2	400 gm Tulsi	6	125.8	3.8			
3	800 gm Tulsi	6	125.0	2.9			

The homogeneity of the three groups was shown in the above table-1. The mean weights of three groups were 125.0±1.9 gm, 125.8±3.8 gm and 125 ±2.9 gm respectively. The difference of means between the three groups were not statistically significant (P>0.05).

TABLE-2: comparison of temperature reductions within the groups at different intervals.

Group	Intervals (n=6)		I		II		Reductions		"t"	df	Sig
	I	II	Mean	SD	Mean	SD	Mean	SD			
1	**Base**	30	102.3	1.1	100.8	0.7	1.5	0.5	7.273	5	P<0.01
	30	60	100.8	0.7	99.3	0.4	1.5	0.3	10.799	5	P<0.001
	60	120	99.3	0.4	98.5	0.4	0.8	0.6	3.232	5	P<0.05
	120	180	98.5	0.4	99.6	0.6	-1.1	0.6	4.987	5	P<0.01
2	**base**	30	102.4	0.8	101.4	0.6	1.0	0.4	6.644	5	P<0.01
	30	60	101.4	0.6	98.9	0.5	2.4	0.9	6.546	5	P<0.01
	60	120	98.9	0.5	98.4	0.3	0.5	0.3	4.099	5	P<0.01
	120	180	98.4	0.3	100.0	0.9	-1.6	0.9	4.217	5	P<0.01
3	**Base**	30	102.3	0.5	99.6	0.5	2.7	0.2	28.723	5	P<0.001
	30	60	99.6	0.5	98.9	0.6	0.7	0.8	2.326	5	P>0.05
	60	120	98.9	0.6	98.2	0.2	0.6	0.5	2.960	5	P<0.05
	120	180	98.2	0.2	100.3	0.5	-2.1	0.4	10.851	5	P<0.001

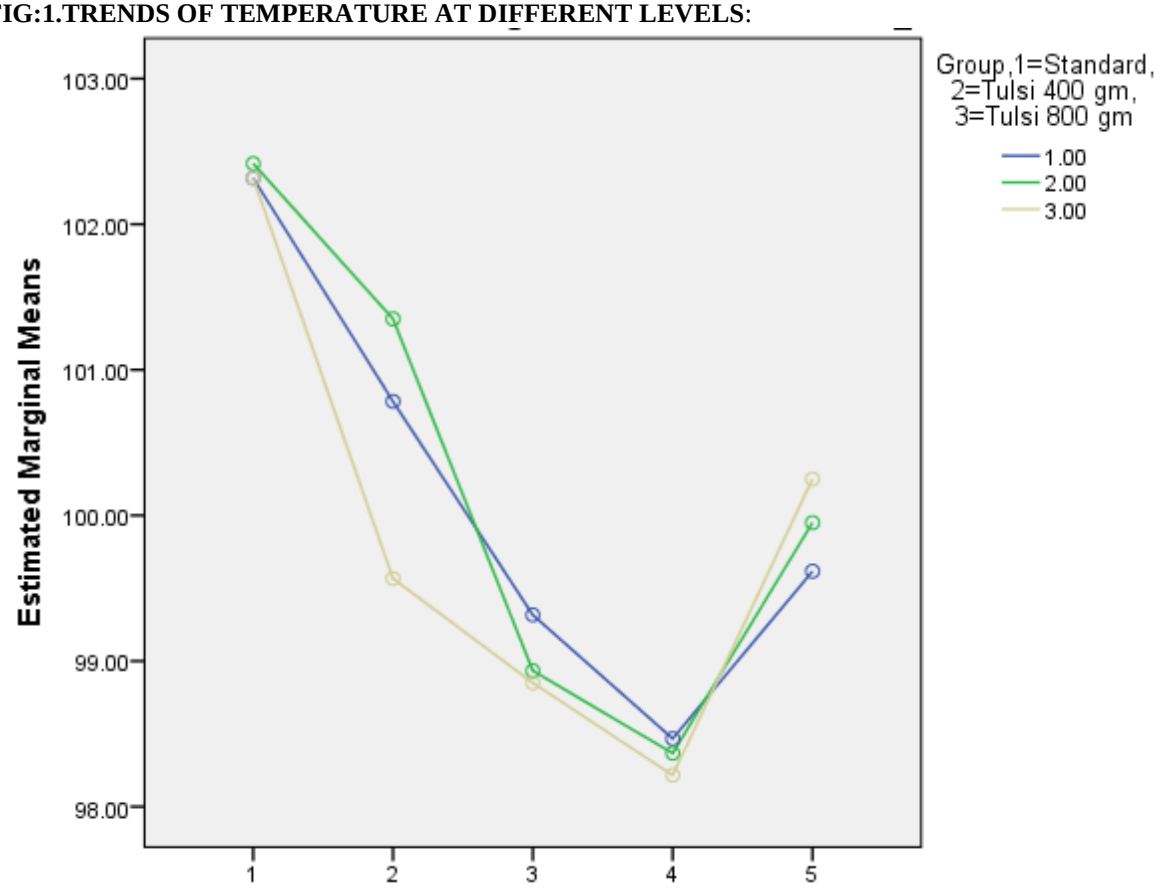
The above table-2 states the temperature reductions at different levels of intervals. The reduction of temperature in group one, up to the 3rd level was highly significant (P<.0.01), very highly significant (P<0.001) and significant (P<0.05). Whereas at level 4, the temperature was increased with a highly significant statistical value (P<0.01). In respect of the group 2, temperature decrease was uniform up to 3rd level, with high statistical significance (P<0.01). At 4th level, the temperature was increased statistically (P<0.01). The temperatures reduction in group 3, at first level were very highly significant (P<.0.001), but not statistically significant at second level (P>0.05), and was significant statistically at 3rd level (P<0.05). At 4th level, the temperature was increased with very high statistical value (P<0.001).

TABLE-3: COMPARISON OF TEMPERATURE IMPROVEMENTS BETWEEN THE GROUPS AT DIFFERENT INTERVALS

Improvements	Groups	Mean	SD	"F"	Sig	Interpretations
Basal to 30	1	1.5	0.5	28.541 (2,15)	P<0.001	The means of 1&2 were not significant. 3 was significant with 1&2
	2	1.1	0.4			
	3	2.8	0.2			
30-60	1	1.5	0.3	8.722 (2,15)	P<0.01	The mean of 2 was significant with 1&3.
	2	2.4	0.9			
	3	0.7	0.8			
60-120	1	0.8	0.6	0.491 (2,15)	P>0.05	The means of three groups were not statistically significant
	2	0.6	0.3			
	3	0.6	0.5			
120-180	1	1.2	0.6	2.553 (2,15)	P>0.05	The means of three groups were not statistically significant
	2	1.6	0.9			
	3	2.0	0.4			

The above table-3 states the comparison of improvements between the three groups. The temperature from basal to 30 minutes, in all the three groups were statistically significant (P<0.001). Among the three, the mean reduction in the 3rd Group was 2.8±0.2, which differed with statistical significance with that of the other two groups. There was no statistically significant reduction of the mean, in the first and second groups 1.5±0.5, 1.1±0.4 (P>0.05). In the 2nd group, the mean reduction was statistically significant at 30-60 minutes than the other two groups (P<0.05). The difference in reduction of temperature between the two groups at 60-120 minutes, were not statistically significant (P>0.05). Similarly, the increase of temperatures between the three groups at 120-180 minutes, were not statistically significant (P>0.05).

FIG:1.TRENDS OF TEMPERATURE AT DIFFERENT LEVELS:



Times base 30 Minutes 60 120 180 Minutes.

The figure-1 clearly illustrates the reduction of temperatures from base to 120 minutes and increase of temperature from 120 to 180 minutes of three groups.

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