WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.074
Volume 7, Issue 11, 811-821. Research Article ISSN 2277– 7105

PHARMACOLOGICAL EVALUATION OF *OXALIS DEHRADUNENSIS RAIZADA* (LEAF EXTRACT) FOR ANALGESIC AND ANTIPYRETIC ACTIVITY ON WISTAR RATS

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Article Received on
07 April 2018,

Revised on 27 April 2018,
Accepted on 17 May 2018,

DOI: 10.20959/wjpr201811-12401

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ABSTRACT

Oxalis dehradunensis Raizada (oxalidaceae) is one of the important medicinal plants used traditionally for the treatment of fever, pain, inflammation and wound healing. The present study was aimed to validate folk use of *oxalis dehradunensis* Raizada as analgesic and antipyretic remedy. The analgesic activity of methanolic extract of *oxalis dehradunensis* Raizada was performed by hot plate, tail flick and tail immersion methods, while antipyretic activity was performed by Brewer's yeast induced pyrexia method. The extract was screened at the dose of 200mg/kg and 400mg/kg by P.O. route. The drugs diclofinac sodium (10mg/kg P.O.) and paracetamol (150mg/kg P.O.) were taken as standard. Pyrexia was induced by 10ml/kg of 15% suspension of brewer's yeast in 0.9% saline S.C. route. The study therefore, supports its use in folk medicine both as analgesic and antipyretic agent and calls for further investigations to elucidate its mechanism of action.

KEYWORDS: *Oxalis dehradunesis* Raizada analgesia, pyrexia, diclofenac, PCM.

INTRODUCTION

Many plants conveniently available in india are used in traditional folk medicine for the treatment of fever, pain, wound healing and inflammation. The plant selected for present studies is *oxalis dehradunensis* Raizada (*oxalidaceae*). Very common weed found throughout warmer parts of india and other country.[1] *Oxalis dehradunensis* Raizada is a species of flowering plant in the woodsorrel family known by the common names garden pink-sorrel and brosdleaf woodsorrel. *Oxalis dehradunensis* Raizada is a herbaceous perennial herb in the *oxalidaceae or geraniaceae* family that is native to maxico, south and central America

and widespread throughout the southeastern united states, central America, the Caribbean, and northern south America (Colombia, Peru, and Brazil).[2] It is also used as complimentary medicine in antiseptic, refrigerant, wound healing. Other alternative used are anthelminthic, anti-inflammatory, astringent, diuretic, urinary tract infections, fever.[3] Chemical characterization showed the presence of oxalic acid, fatty acids, vitexin and isovitexin, neutral lipid, glycolipids. Phytochemical investigation of *oxalis dehradunensis* Raizada have revealed the presence of tannins, palmitic acid, lenoleic, linolenic and stearic acids.[4] methanolic extract of this plant show the presence of carbohydrate, glycosides, phytosterols, phenolic compounds, flavonoids, proteins, amino acids, volatile oil. It also show the presence of calcium fiber and tannins. Leaves contain tartaric acid, citric acids and calcium oxalate, flavones (apigenin), flavonols (quercetin), glycoflavones (vitexin, orientin). This herb is well known to have an acid taste due to the high content of oxalate in its leaves.[5] Herbal medicine is a major component in all traditional medicine system and a common element in Ayurvedic, Unani, Homeopathic, Naturopathic, Traditional Chines medicine and native Amercan medicine. As per literature herbal medicines are assuming greater importance in the primary health care of individuals and communities in rural areas. Plants and their derivatives are invaluable source of therapeutic agents to treat various disorders. Herbal products are safe because they are natural and having less side effect. Considerable efforts have been directed towards the development of natural products from various plant source.[6] Substanial number of drugs are developed from plants which are active against various diseases and disorders.[7] Present study was designed to evaluate analgesic and antipyretic potential of methanolic leaf extract of *oxalis dehradunensis* Raizada.

MATERIALS AND METHODS

Plant material

Leaves of *oxalis dehradunensis* Raizada were collected in the month of October 2016 from Bhimtal in the Nainital district of uttrakhand. It was authenticated by Dr. Ambrish Kumar (Scientist-D) Botanical Survey of India, Dehradoon. Voucher specimenn No. is (117452). The leaves (5.6 kg) were air dried and pulverized using a mechanical grinder.

Extraction and isolation

Dried and powdered leaves (50g) of the plant were Defating with 100ml Petrolium ether and extracted with 100ml Methanol for 24 h. using soxhlet apparatus. The extracts were dried using a rotary vacuum evaporator and stored in a refrigerator until further use.

Animals

Wistar rats (150-200g) weighing 150-200g were housed under laboratory condition, in groups of six each and used for analgesic and antipyretic activity. The animal had free access to water and food *ad libitum*. The ethical committee of the institute approved the protocol of the study having Protocol no. KUDOPS/60.

Analgesic activity by hot plate method

Central nociceptive activity was evaluated using the hot plate method.[8] wistar rats were divided into 4 groups of six animal each. The first group served as control and received only vehicle (distilled water) and the second group was administered standard drug diclofinac sodium 10mg/kg (p.o.). The animal of third and forth group T_1 and T_2 were treated with extract of *oxalis dehradunensis* Raizada dose 200mg/kg and 400mg/kg respectively. The extracts, standard drugs were dissolved into the vehicle. The rats were placed individually on the hot plate maintained at 55^0c and latency of nociceptive response such as licking, flicking, of the hind limbs or jumping was noted. The reading were taken at 0,30,60,90,120,180 min after treatment. The cut off time was taken as 15 second on the hot plate to avoid damage to the paws.[9]

Analgesic activity by tail flick method

Central nociceptive activity was evaluated using the Tail flick method.[10] wistar rats were divided into 4 groups of six animal each. The first group served as control and received only vehicle (distilled water) and the second group was administered standard drug diclofinac sodium 10mg/kg (p.o.). The animal of third and forth group T_1 and T_2 were treated with extract of *oxalis dehradunensis* Raizada dose 200mg/kg and 400mg/kg respectively. The tail of rats were placed individually on the analgesiometer maintained at 55^0c and latency of nociceptive response time flicking of tail was noted. The reading were taken at 0,30,60,90,120,180 min after treatment. The cut off time was taken as 12 second to avoid damage to the tail.[11]

Analgesic activity by Tail immersion method

Central nociceptive activity was evaluated using the Tail immersion method. wistar rats were divided into 4 groups of six animal each. The first group served as control and received only vehicle (distilled water) and the second group was administered standard drug diclofinac sodium 10mg/kg (p.o.). The animal of third and forth group T_1 and T_2 were treated with extract of *oxalis dehradunensis* Raizada dose 200mg/kg and 400mg/kg respectively. The tail

of rats use at mark 5cm and dip individually in water beaker temperature maintained at 55± 0.2^0c and latency of nociceptive response, such as withdrawal time of tail was noted. The reading were taken at 0,30,60,90,120,180 min after treatment. The cut off time was taken as 15 second in the hot water beaker to avoid damage to the tail.[12]

Antipyretic activity by Brewer's yeast induced pyrexia method

Wistar rats (male) of constant rectal temperature for a week were selected for the experiment. Rectal temperature (T_R) were recorded by inserting a lubricated digital thermometer (external diameter: 3mm, 0.1^0c precision) 2.8 cm into the rectum of rats. Animal presenting initial rectal temperature between 36 and 37^0c were selected for the antipyretic tests. The antipyretic activity of the extracts was evaluated based on Brewer's yeast induced pyrexia in rats. Pyrexia was induced by subcutaneous injection of 10ml/kg of 15% w/v brewer's yeast suspension below the nape of neck. The rectal temperature of each rat was measured at time, 0 hour, using a lubricated thermometer and before injection of the yeast. At 18 h following yeast injection, the different groups were treated with the vehicle, extracts (200and 400mg/kg p.o.) and standard drug, Paracetamol (150mg/kg p.o.). The rectal temperatures were recorded at 1, 3 and 5 hour after treatment.[13]

$$\textbf{Percentage reduction in rectal temperature} = \frac{Y-X_X}{Y-Z} 100$$

Where Z = Initial rectal temperature ^{0}C, Y = Rectal temperature 18 hour after yeast administration, X =Rectal temperature after extract administration.

RESULTS

The results from the present study show that the crude extract of *oxalis dehradunensis* Raizada exhibit activities in varying degrees against pain and fever.

Effect of the extracts on hot plate test

ODRME were found to cause time- dependently prolongation of the hot plate latency. The longest latency was obtained at 180 min post administration of the extract or the reference drug. The standard drug diclofenac (10mg/kg) was more potent than the extracts. The leaves extract showed significant result at 60, 90,120 and 180 min in compare to control and standard drugs.

Table 1: Effect of *oxalis dehradunensis* Raizada leaves extracts on analgesia by hot plate method.

Groups	Dose (mg/kg)	Reaction time in sec					
		0 min	30 min	60min	90min	120min	180min
Control	10 ml/kg	3.716± 0.2088	4.2± 0.2633	4.816± 0.1887	4.316± 0.16	4.516± 0.1302	5.6± 0.0966
Standard Diclofenac sod.	10 mg/kg	4.95± 0.1147*	5.766± 0.2231*	6.833± 0.1874*	7.516± 0.212*	8.05± 0.2405*	9.066± 0.1783*
Test drug (T1)	200mg/kg	3.983± 0.2136	4.416± 0.174	4.8± 0.1892	6.566± 0.0918	7.316± 0.0872	7.4± 0.093
Test drug (T2)	400 mg/kg	4.466± 0.2155*	5.883± 0.1537*	6.866± 0.021*	7.216± 0.1493*	7.666± 0.182*	8.8± 0.1438*

Values are expressed as mean ±SEM (N=6), In standard $p<0.05$ significant with respect to the control, and in test 2 $p<0.05$ significant with respect to the control group by one way ANOVA test.

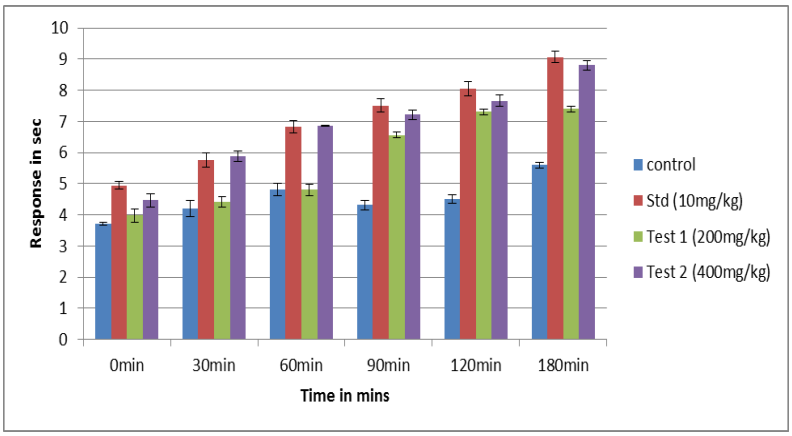

Fig 1: Effect of *oxalis dehradunensis* Raizada leaves extracts on analgesia by hot plate method.

Effect of the extracts on tail immersion test

The treatment of rats with the plant extract at dose of 200 mg/kg and 400mg/kg exhibit a significant increase in reaction time while compared with control. Diclofenac and ODRME showed highly significant increase in reaction time at 90 min after drug administration. Standard drug was more potent than both of the extracts.

Table 2: Effect of leaves extracts and Diclofenac sodium on analgesia by tail immersion test.

Groups	Dose	Reaction time in min					
		0 min	30 min	60min	90min	120min	180min
Control	10 ml/kg	3.11± 0.153	3.133± 0.133	3.15± 0.067	3.883± 0.1815	4.066± 0.1783	3.805± 0.2121
Standard Diclofenac sod.	10 mg/kg	4.466± 0.042**	5.6± 0.073**	6.333± 0.066**	7.966± 0.323**	8.786± 0.498**	8.825± 0.507**
Test drug (T1)	200 mg/kg	3.616± 0.1537*	4.683± 0.2301*	5.933± 0.1145*	6.733± 0.224*	7.433± 0.095*	7.695± 0.320*
Test drug (T2)	400 mg/kg	4.2± 0.233**	4.683± 0.330**	6.216± 0.238**	7.3± 0.188**	8.383± 0.279**	8.566± 0.236**

Values are expressed as mean ±SEM (N=6), In standard $p<0.01$ significant with respect to the control, and in test 1 $p<0.05$ with respect to the control and test 2 $p<0.01$ significant with respect to the control group by one way ANOVA test.

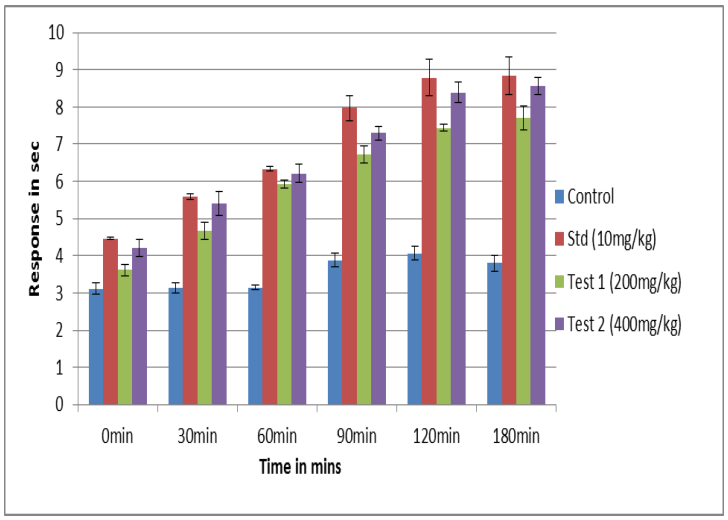

Fig 2. Effect of leaves extracts and Diclofenac sodium on analgesia by tail immersion test.

Effect of the extracts on analgesia by Tail flick method

ODRME were found to cause time- dependently prolongation of the tail flick latency. The longest latency was obtained at 180 min post administration of the extract or the reference drug. The standard drug diclofenac was more potent than the extracts at all time levels. The leaves extract showed significant result at 60, 90,120 and 180 min in compare to control and standard drugs.

Table 3: Effect of the extracts and diclofenac sodium on analgesia by Tail flick method.

Groups	Dose	Reaction time in sec					
		0 min	30 min	60min	90min	120min	180min
Control	10 ml/kg	3.613± 0.200	4.14± 0.149	4.105± 0.184	4.303± 0.065	4.376± 0.054	4.421± 0.052
Standard Diclofenac sod.	10 mg/kg	4.573± 0.170*	5.238± 0.2087*	5.898± 0.0190*	6.556± 0.2284*	7.245± 0.3428*	8.711± 0.2955*
Test drug (T1)	200 mg/kg	3.73± 0.202	4.536± 0.108	5.341± 0.046	5.76± 0.138	6.77± 0.216	7.765± 0.166
Test drug (T2)	400 mg/kg	4.538± 0.1684*	5.426± 0.0553*	5.933± 0.0998*	6.298± 0.4888*	6.998± 0.1486*	8± 0.176*

Values are expressed as mean ±SEM (N=6), $p<0.05$ significant with respect to the control group by one way ANOVA test.

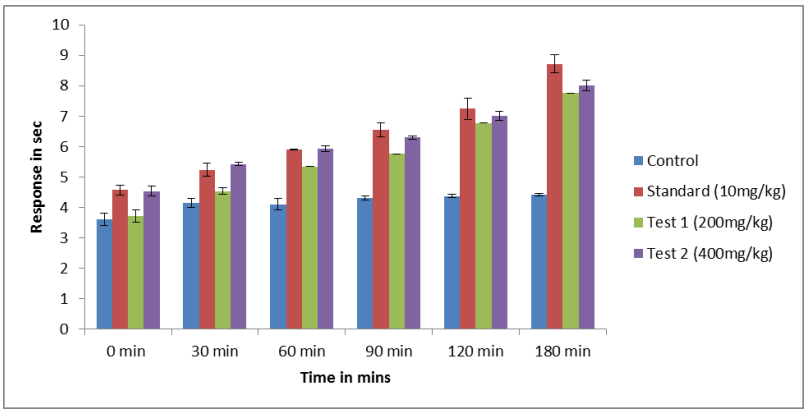

Fig 3: Effect of the extracts and diclofenac sodium on analgesia by Tail flick method.

Effect of the extracts on brewer's yeast suspension induce pyrexia

Standard drug Paracetamol 150 mg/kg and test drugs (t2) 400 mg /kg orally showed statistically significant ($P<0.05$) difference in 1hr, 2hr, 3hr, and 4hr respectively.

Table 4: Effect of *oxalis dehradunensis* Raizada leaves extracts and paracetamol on pyrexia.

Groups	Dose	Reaction in hours				
		0 hr	1hr	2hr	3hr	4 hr
Control	10 ml/kg	38.666± 0.305	38.6± 0.255	38.68± 0.250	38.6± 0.272	38.483± 0.0872
Std PCM	150mg/kg	37.616± 0.246*	37.066± 0.206*	37.56± 0.229*	36.65± 0.240*	36.116± 0.320*
Test drug (T1)	200mg/kg	39.366± 0.231	38.833± 0.260	37.883± 0.237	37.316± 0.177	36.98± 0.177
Test drug (T2)	400mg/kg	39.6± 0.3724*	38.1± 0.227*	37.51± 0.168*	36.866± 0.235*	36.483± 0.204*

Values are expressed as mean ±SEM (N=6), $p<0.05$ significant with respect to the control group by one way ANOVA test.

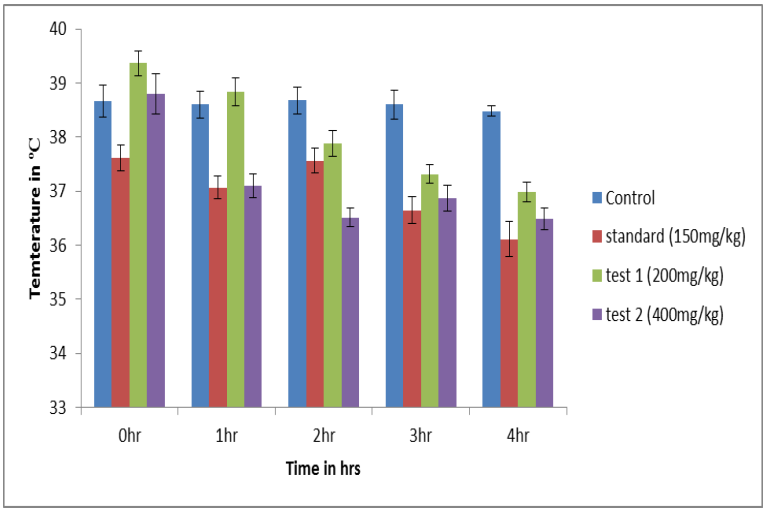

Fig 4: Effect of the extracts and standard (Paracetamol) on brewer's yeast suspension induce pyrexia.

DISCUSSIONS

Currently available drug regimens for management of Analgesic and antipyretic activity have certain drawbacks and therefore there is a need for safer and more effective drugs. The use of traditional medicine and medicinal plants in most developing countries, as a normative basis for the maintenance of good health has been widely observed.

The study indicated that *oxalis dehradunensis* Raizada leaves extract has both analgesic as well as antipyretic property. The analgesic effect of the extract was determined from hot plate, Tail flick and Tail immersion method.[14] The antipyretic activity of the extract was determined from brewer's yeast induce pyrexia method.

The analgesic activities were also studied using thermal tests. The thermal test (hot plate, Tail flick and tail immersion test) was selected because the test is sensitive to strong analgesics and limited tissue damage because of a cutoff point that is usually applied to limit the amount of time the animal spends on the hot plate.[15] The extracts produced a prolongation of time latency in all the three tests. These tests are supraspinally mediated and therefore a test of central activity. The groups treated with test extracts did not show any toxicity. Thus the test extracts are safe and may be used as an analgesic agent.

It is an established fact that any agent that causes a prolongation of the latency using this test may be acting centrally.[16] This is however, subject to its not having any effect on motor activity and not causing any sedative action. From the present work, the mechanism (s) of the

analgesic effects of the *oxalis dehradunensis* Raizada tested is not readily apparent. It can, however, be spectulated that it may be linked to processes involved in the prevention of sensitization of the nociceptor, down regulation of the sensitized nociceptors and/or blockade of the nocieptor at peripheral and/or central levels. One of the well characterized signaling systems believed to participate in this mechanism (s) is the arachidonic acid metabolic pathway.[17] In this regard, it inhibits the production of prostaglandins and thromboxanes similar to acetylsalicylic acid and thus reduces pain libration.

It is well known that most of the analgesic drugs possess antipyretic activity. The leaves extract of *oxalis dehradunensis* Raizada revealed marked antipyretic activity in brewer's yeast- induced pyrexia in rats. In the present study the initial rise of temperature after 18 hrs of subcutaneous yeast injection was above 38ºC.There was significant difference between the initial mean basal temperature of the different groups and the mean temperature between the groups of pyrexia rats, after 18 hours of yeast injection. Rectal temperature of pyrexia rats were lowered significantly with the test drug and standard drug when compared with control group. Standard drug Paracetamol is more potent than the test extracts.[18] No toxicity was seen in the test drugs treated groups after 24 hours of experiment so the test drug is a safe antipyretic agent.

CONCLUSION

From the above discussion it can be concluded that the leaves extract of *oxalis dehradunensis* Raizada possess both analgesic and antipyretic activity. So we can say that herbal extract may be remunerative effect with lower side effect as compare to standard drug (Diclofenac sodium and Paracetamol) for the management of analgesia and pyretic respectively.

ACKNOWLEDGEMENT

I am thankful to Dr. Tirath Kumar Asst Prof. Kumaun University, Bhimtal campus for guiding me and providing laboratory facilities for my research work.

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