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Anti-inflammatory, Antipyretic and Analgesic Activities of Ethanol Extract of *Seriphidium kurramenses*

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Seriphidium kurramenses traditionally medicinal plant usually not present in Pakistan is used in different biological activities to cure various ailments. However, scare studies are present on *S. kurramenses* regarding to its medicinal importance to treat fever, inflammation and pain. The purpose of present study is to investigate the anti-inflammatory, antipyretic and analgesic effects of *S. kurramenses* stem and leaves in ethanolic extract on albino rats. Methodi anti-inflammatory actions were evaluated by injecting carrageenan in rats which caused edema. *S. kurramenses* produced significant (P<0.005) reduction in edema at 200 and 50mg/kg doses with respective percentages (90, 81%) of leaf and stem extract as compared to standard (diclofenac, 90%) and control (normal saline, 100%) groups. Meanwhile, antipyretic activity was examined by inducing brewer's yeast in albino rats which induced pyrexia. *S. kurramenses* showed significant reduction (P<0.005) at different doses of ethanolic extract (50mg/kg, 50mg/kg) with respective percentages of leaf (95%) and stem extract (100%) as compared to standard (brewer's yeast 81%) and control

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groups (normal saline 100%). Similarly, analgesic test was assessed by injecting acetic acid which induced writhing movements and these movements were reduced (>0.005) at different doses of ethanolic extract (400mg/kg, 400mg/kg) with respective percentages of leaf and stem extracts (52%, 56%) as compared to standard (diclofenac, 48%) and control groups (100%). It is concluded that the extract of *S. kurramenses* exhibit significant (P<0.005) results in case of anti-inflammatory and antipyretic activities but insignificant (>0.005) in analgesic activity.

Keywords: Anti-inflammatory; antipyretic; analgesic; Seriphidium kurramenses leaf; stem.

1. INTRODUCTION

Artemisial maritimal and *Artemisial kurramense* (Qazlib) are the various synonyms of *Seriphidium kurramenses*. At Pakistan Afghanistan border, in upper Kurram agency medicational flora sproutes including *S. kurramenses* which is an economical medicational flora [1]. Genus *Seriphidium* has been categorized into four groups and subgenera like *Seriphidium besser, Tournefort, Absinthium de cand, Dracunculus besser* which found in North America. According to WHO, 80% people in underdeveloped world utilize medicational flora to cure illnesses. In developed states, utilization of herbal medication is increasing day by day. Due to overpopulation, huge amount of flora species are in danger of extinction [2].To fulfill the needs of primary health care, medicinal plants are utilized in various developing countries. There are four main objectives for traditional medicines like, ensuring access, quality, efficacy, enhancing safety, and forming policy [3]. This strategy has been expected various outcomes like, medicinal flora must be sustainably utilized for western health care, the practices for the utilization of medicinal flora must be more basic and trained enhancing the availability of traditional medicines, herbal medicines must be safely monitored, information about traditional medicines must be preserved and recorded, recognition of traditional medicines enhancing by the support of Government and integration of traditional medicines with primary health care services [4]. Genus *Seriphidium* has commercially highest priority for specie *S. kurramenses*, and is utilized in medication in various states for elution of very significant ingredients known as santonin used in various beneficial oils [5]. Furthermore, majority of components like α-thujone 1,8-cineole, β-caryophyllene and β-thujone give importance to the flora of genus *Seriphidium* [6]. *S. kurramense* is also an important medicative drug which is utilized as thelmintic and in neurotransmitter and insecticidal purposes, to cure edema, fever and writhing [7]. *S. kurramenses* plant was not screened for its medicinal purposes although it is medically important [8]. So, the aim of present study is to evaluate the different activities on this plant in ethanol extract to analyze the anti-inflammatory, antipyretic and analgesic activities of *S. kurramenses* leaf and stem extract in ethanol to cure inflammation, fever and pain.

2. MATERIALS AND METHODS

2.1 Preparation of Extract

S. kurramenses stem and leaves were soaked in sterile glass bottles. Leaves and stem were immersed in ethanol. They were placed at room temperature and whatsman filter paper was used to filter the mixtures. Mixtures were placed for 7 days after pouring to Petri-dish.

2.2 Experimental Animals

Analgesic, anti-inflammatory and antipyretic activities were performed using albino rats of either female or male sex (160-200g). For experimental studies, all the rats were purchased from university of Veterinary and Animal Sciences (UVAS) Lahore. Polypropylene cages were used to kept the rats in University of Lahore Animal house.

2.3 Experimental Drugs

Normal saline, diclofenac, *S. kurramenses* leaf and stem extract, carrageenan, yeast, paracetamol, acetic acid, distilled water.

2.4 Evaluation of Anti-inflammatory Activity

48 albino rats were divided into 4 groups. Each group contained 12 rats.

Group 1:- Rats were treated with normal saline in control group.

Group 2:- Rats were treated with diclofenac (100mg/kg) in standard group.

Group 3:-Rats were treated with aqueous extract of *S. kurramenses* leaf in experimental design group.

Group 4:-Rats were treated with *S. kurramenses* stem extract in experimental design group.

Firstly, carrageenan was injected into sub-planter region of paw to all groups of rats and paw was measured before and after injection. Carrageenan was induced with respective doses 50, 100, 200 and 400mg/kg. Rat paw caused edema. *S. kurramenses* stem and leaf extract with doses of 50, 100, 200 and 400 mg/kg, while standard drug diclofenac with doses of 12.5, 25, 50 and 100mg/kg were injected 3 hr after the carrageenan injection. After the interval of 4hr, paw volume was measured.

Anti-inflammatory activity was calculated by given formula

$$\% \text{ inhibition} = \frac{(Co - Ct) - (Ct - Co)}{(Co - Ct)} X100$$

Where,

C_o= Initial reading of paw

Co- C_t= volume of hind paw of control group

Ct-Co = volume 0f hind paw of treated group after carrageenan injection

2.5 Antipyretic Activity

In this model, rats were divided as discussed earlier in anti-inflammatory activity. Firstly, rats were treated with normal saline (2ml/kg) in control group. In standard group, rats were treated with brewer's yeast and normal saline (below the nape of neck). In experimental design group, rats were treated with stem and leaf extract of *S. kurramenses* with respective doses of 50mg/kg, 100mg/kg, 200mg/kg and 400mg/kg. By inducing brewer's yeast, pyrexia was developed. In standard group, doses of paracetamol were injected in intraperitoneal tissue while in experimental design group rats were treated with injections of leaf and stem extract. Thermometer was used to measure the temperature (rectum) of rats with interval 2 hrs.

Antipyretic activity was calculated by given formula

$$\text{Percent reduction} = \frac{B - Cb}{B - A} X100$$

B = temperature after pyrexia induction

C_b=temperature after 1,2 and 3 hour

A = normal body temperature

2.6 Analgesic Activity

In analgesic model, all rats were divided same like above manner. Writhing process in rats occurred due to the injection of acetic acid with doses of 50, 100, 200 and 400mg/kg in standard and experimental design groups according to their body weight. The extract of leaf and stem were injected 1 hr before, and standard drug diclofenac were given 1/2 hr before the administration of acetic acid (intraperitoneal). The whole activity took 20 minutes.

Analgesic activity was calculated by given formula

$$\text{Analgesic activity} = \frac{Nc - Nt}{Nc} X100$$

Were,

Nc shows the control group writhes, while Nt shows the treated group writhes.

2.7 Statistical Analysis

Statistical analysis was performed using ANOVA, the significance of difference was accepted at $P<0.005$ data was presented as mean ± S. D.

3. RESULTS

3.1 Anti-inflammatory Activity

In anti-inflammatory activity, the ethanolic extract of leaf of *S. kurramenses* showed significant results P<0.005, as compared to stem of *S. kurramenses*. In inflammation assay, the maximum percentage inhibition of leaf showed at 200mg/kg dose that is 90% as compared to standard and control that was 90% and 100% respectively (Table 1).

3.2 Antipyretic Activity

In antipyretic activity the ethanolic extract of stem and leaf of *S. kurramenses* showed significant results P<0.005. The maximum percentage inhibition of stem and leaf were showed in 50mg/kg dose that is 100% and 95% as compared to standard and control groups that were 81%, 100% respectively (Table 2).

3.3 Analgesic Activity

In analgesic activity stem and leaf extract of *S. kurramenses* showed insignificant results >0.005, at doses of 50mg/kg, 100mg/kg, 200mg/kg and 400mg/kg (Table 3).

4. DISCUSSION

The ethanolic extract of different plants shows efficient analgesic and antipyretic activities [9] and also have most potent effects as anti-inflammatory activity. *S. kurramenses* is novel plant and has potential to reduce edema, fever and pain in anti-inflammatory, antipyretic and analgesic activities [10] [11]. Experimental conclusions demonstrated that *S. kurramenses* leaf, in ethanolic extract show significant anti-inflammatory and antipyretic activities. Leaf of *S. kurramenses* reduced paw edema and fever. These conclusions administered its medicinal importance [4]. According to our findings, ethanolic leaf extract of *S. kurramenses* at dose of 200mg/kg showed significant results (P<0.005) and percentage inhibition was 90% as compared to control group in anti-inflammatory activity. Carrageenan secretes histamine, bradykinin and prostaglandins, so total permeability of blood vessels was increased by hydroxytryptamine [12]. In antipyretic activity, yeast induces fever in rats due to the proteins present in yeast which caused cytokines inflammatory disease [13]. These proteins interlinked with lipopolysaccharide-binding proteins starts manufacturing and secretion of prostaglandins and it was confirmed that pyrexia caused due to prostaglandins mediators. Prostaglandins level can be decreased by using paracetamol (400mg/kg) it helps to reduce fever in rats [11]. In our findings, ethanolic extract of *S. kurramenses* provided same results like paracetamol which helps in reduction of fever by inhibiting the release of cytokines and by synthesizing prostaglandins. In present study, *S. kurramenses* was used to reduce the writhing movements in rats at different doses of ethanolic extract by mediating the inhibition of prostaglandins. Nerve endings excite and secretion of endogenous substances induce writhing with acetic acid in antinociceptive effect that results in pain. Pain receptors induces pain by endogenous mediators to interact with prostaglandins causes sensitization of pain [11]. Acetic acid caused constriction of abdomen by liberating bradykinins, prostaglandins, serotonin and other endogenous substances like histamine [14]. *S. kurramenses* is novel plant and leaf and stem showed significant results (P<0.005) in antipyretic and anti-inflammatory activities at doses of (50, 200mg/kg) with respective percentages of 100, 95 and 90% [11].

Table 1. Anti-inflammatory activity of *Seriphidium kurramenses*

Group	Dose (mg/kg)	Paw size (mm) Mean ±S.D				% inhibition
		1hr	2hr	3hr	4hr	
Control	50mg/kg	1.450±0.636	1.200±0.424	0.710±0.975	0.005±0.007	0%
	100mg/kg	1.350±0.070	1.200±0.000	0.800±0.424	0.015±0.007	0%
	200mg/kg	1.300±0.000	1.050±0.070	0.800±0.282	0.300±0.282	0%
	400mg/kg	1.900±0.141	1.500±0.000	1.350±0.070	0.550±0.070	0%
Standard	50 mg/kg	1.500±0.000	1.350±0.070	0.600±0.141	0.400±0.141	76%
	100mg/kg	0.850±0.494	0.900±0.141	0.650±0.070	0.400±0.141	88%
	200mg/kg	1.600±0.565	1.050±0.070	0.850±0.212	0.550±0.070	90%
	400mg/kg	1.450±0.070	1.000±0.000	0.750±0.070	0.800±0.565	100%
Leaf	50 mg/kg	1.300±1.141	1.100±0.000	1.000±0.000	0.750±0.212	76%
	100mg/kg	1.550±0.636	1.200±0.282	0.950±0.212	0.850±0.212	31%
	200mg/kg	1.900±0.141	1.350±0.070	1.050±0.070	0.750±0.353	90%
	400mg/kg	1.950±0.212	1.650±0.212	1.350±0.070	1.100±0.000	57%
Stem	50 mg/kg	0.850±0.070	0.800±0.000	0.650±0.070	0.550±0.070	81%
	100mg/kg	1.300±0.141	1.050±0.212	0.500±0.141	0.250±0.212	41%
	200mg/kg	0.900±0.848	1.450±0.070	0.600±0.141	0.400±0.141	72%
	400mg/kg	1.900±0.141	1.500±0.000	0.950±0.212	0.550±0.070	30%

Anti-inflammatory activity of S. kurramensesleaf and stem
Values are mean ±S.D; n=4 in each group P<0.005 compare to control group

Table 2. Antipyretic activity of *Seriphidium kurramenses*

Group	Temperature	Dose (mg/kg)	Body temp (^{o}c) Mean ±S.D				% inhibition
			0hr	0.5hr	1hr	2hr	
Control	37^{o}C	50 mg/kg	37.50±0.14	37.35±0.07	37.20±0.00	37.05±0.07	0%
		100 mg/kg	37.65±0.07	37.45±0.07	37.20±0.00	37.00±0.00	0%
		200 mg/kg	37.75±0.07	37.55±0.21	37.35±0.21	37.15±0.07	0%
		400 mg/kg	37.90±0.00	37.75±0.07	37.55±0.07	37.25±0.07	0%
Standard	38.3^{o}C	50 mg/kg	37.85±0.21	37.55±0.07	37.45±0.07	37.15±0.21	81%
		100 mg/kg	37.90±0.42	37.45±0.07	37.25±0.07	37.01±0.00	30%
		200 mg/kg	38.35±0.07	37.30±0.00	37.10±0.00	37.00±0.00	30%
		400 mg/kg	38.00±0.28	37.50±0.14	37.30±0.00	37.10±0.00	22%
Leaf	37.8^{o}C	50 mg/kg	37.95±0.07	37.65±0.21	37.35±0.07	37.20±0.00	95%
		100 mg/kg	37.65±0.21	37.50±0.14	37.25±0.21	37.10±0.00	19%
		200 mg/kg	37.85±0.07	37.50±0.00	37.20±0.14	37.05±0.07	11%
		400 mg/kg	37.40±0.00	37.25±0.07	37.15±0.07	37.10±0.00	63%
Stem	37.7^{o}C	50 mg/kg	38.00±0.00	37.65±0.35	37.40±0.28	37.15±0.07	100%
		100mg/kg	37.80±0.00	37.55±0,07	37.35±0.07	37.15±0.07	42%
		200 mg/kg	38.00±0.00	37.60±0.14	37.30±0.14	37.10±0.00	11%
		400 mg/kg	37.55±0.07	37.20±0.00	37.10±0.14	37.05±0.07	63%

Antipyretic activity of S. kurramenses, leaf and stem

Values are mean ±S.D; n=4 in each group P<0.005 compare to control group

Table 3. Analgesic activity of *Seriphidium kurramenses*

Group	Dose (mg/kg)	Writhing Mean ±S.D	% inhibition
		20 (mints)	
Control	50 mg/kg	17.00±2.82	0%
	100 mg/kg	15.00±4.24	0%
	200 mg/kg	15.50±0.70	0%
	400 mg/kg	12.50±2.12	0%
	50 mg/kg	13.50±2.12	20%
Standard	100 mg/kg	13.50±0.70	10%
	200 mg/kg	17.00±1.41	9%
	400 mg/kg	18.50±0.70	48%
	50 mg/kg	11.00±1.41	35%
Leaf	100 mg/kg	15.50±0.70	3%
	200 mg/kg	17.00±1.41	9%
	400 mg/kg	19.00±1.41	52%
	50 mg/kg	14.00±2.82	17%
stem	100mg/kg	12.50±3.53	16%
	200 mg/kg	15.00±1.41	3%
	400 mg/kg	19.50±0.70	56%

Analgesic activity of S. kurramenses leaf and stem.
Values are mean ±S.D; n=4 in each group P>0.005 compare to control group

5. CONCLUSION

From the above findings, it is determined that ethanolic extract of *Seriphidium kurramenses* can be used in allelopathy to cure fever, pain and inflammation. From overall results, we concluded that *S. kurramenses* show significant results in antipyretic and anti-inflammatory activity. We study *S. kurramenses* on the basis of their phytochemicals like alkaloids, saponins, tanins, steroids, flavonoids, cardiac glycosides, anthraquonone and phenolic. In future perspective, *S. kurramenses* plant use clinically to cure inflammation and fever. *Seriphidium kurramenses* is a novel plant and there is scarce data and a lot of more work is needed for its potential effects as anti-inflammatory and antipyretic activities.

CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that they have no known competing financial interests OR non-financial interests OR personal relationships that could have appeared to influence the work reported in this paper.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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