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ANTI-INFLAMMATORY ACTIVITY AND CHEMICAL COMPOSITION OF THE ESSENTIAL OILS FROM *SENECIO FLAMMEUS*

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ABSTRACT

Many species from *Senecio* genus have been used in traditional medicine, and their pharmacological activities have been demonstrated. This study investigated the chemical composition and anti-inflammatory activities of essential oils from *Senecio flammeus.* A total of 48 components representing 98.41 % of the total oils were identified. The main compounds in the oils were α-farnesene (11.26 %), caryophyllene (8.69 %), n-hexadecanoic acid (7.23 %), and α-pinene (6.36 %). The anti-inflammatory activity of the essential oils was evaluated in rodents (10–90 mg/kg bw) in classical models of inflammation [carrageenan-induced paw edema, 12-O-tetradecanoyl-phorbol-13-acetate (TPA)-induced ear edema, and cotton pellet-induced granuloma]. The essential oils at doses of 10, 30, and 90 mg/kg bw significantly reduced carrageenan-induced paw edema by 17.42 % ($P < 0.05$), 52.90 % ($P < 0.05$), and 66.45 % ($P < 0.05$) 4 h after carrageenan injection, respectively, and significantly reduced myeloperoxidase activity ($P < 0.05$). The essential oils (10, 30, and 90 mg/kg) also produced a significant dose-dependent response to reduce TPA-induced ear edema by 20.27 % ($P < 0.05$), 33.06 % ($P < 0.05$), and 53.90 % ($P < 0.05$), respectively. The essential oils produced significant dose-response anti-inflammatory activity against cotton pellet-induced granuloma that peaked at the highest dose of 90 mg/kg (49.08 % wet weight and 47.29 % dry weight). Results demonstrate that the essential oils of *S. flammeus* were effective in the treatment of both acute and chronic inflammatory conditions, thereby supporting the traditional use of this herb.

Keywords: *Senecio flammeus,* chemical composition, essential oil, anti-inflammatory activity

INTRODUCTION

Inflammation is a protective host response to foreign antigenic challenge or tissue injury that, if unopposed, can lead to loss of tissue structure and function. An aberration of these mechanisms may favor the development of various illnesses. Thus, properly regulated inflammatory responses are necessary for healthy immune function. Clinical treatment of inflammatory diseases is dependent on non-steroidal or steroidal chemical therapeutics (Rainsford, 2007). However, the use of steroidal drugs as anti-inflammatory agents is also becoming highly controversial because of their multiple side effects (Schäcke et al., 2002). The screening and development of new agents with more powerful anti-inflammatory activities and fewer side effects are still in progress, and much hope is given for finding anti-inflammatory drugs from indigenous medicinal plants. The use of plant extracts and components has become increasingly important for scientific research and industrial applications in recent years.

The genus *Senecio*, which belongs to the tribe *Senecioneae*, is the largest and most

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complex genus of the family *Asteraceae*. This genus includes more than 1500 species worldwide, and more than 160 species are distributed in China (Shi et al., 2013). Some of these species have been used in Chinese traditional or folk medicines for their improvement of eyesight, detumescence, anti-inflammation, and vermifuge properties. A series of studies demonstrated the antimicrobial activity of essential oils from various *Senecio* species (Pérez et al., 1999; El-Shazly et al., 2002), but studies on the anti-inflammatory potential of essential oils from this genus are highly limited.

Senecio flammeus, a perennial herb, is extensively distributed in northwestern and southwestern China, Russia, Siberia, Korea, Japan, and Korea. It has been used in Chinese folk medicine for the treatment of inflammation and ulcers. As of this writing, no report on the phytochemical and biological properties of *S. flammeus* has been published. Therefore, this paper is the first to describe the profile of essential oils of *S. flammeus* (SFEO). This study aimed to determine the chemical composition of SFEO, and evaluate their anti-inflammatory activity in vivo.

MATERIALS AND METHODS

Plant material

S. flammeus plants were collected from the Wutai Mountains, Shanxi Province, China in June 2011, and identified by Dr. Xun Gong. The plants were dried in the shade (at room temperature). The voucher specimen (No. 724095) was deposited in the Kuming Institute of Botany, Chinese Academy of Sciences.

Isolation of essential oils

The air-dried plant materials (500 g) of *S. flammeus* were chopped and subjected to hydrodistillation for 5 h using a Clevenger-type apparatus. The obtained oils were dried over sodium sulfate for 24 h, filtered, and stored at 4 °C in sealed brown glass vials until analysis.

Preparation of test samples for bioassay

To assess the anti-inflammatory activity, test samples were administered orally to test animals after being suspended in a mixture of distilled H_2O and 1 % Tween 80. Animals of the control group received the same experimental handling as those of the test groups, except drug treatment was replaced with appropriate volumes of the dosing vehicle. Indomethacin (10 mg/kg) in 1 % Tween 80 was used as a reference drug.

Animals

Male and female Sprague–Dawley rats (5 week) and Kunming mice (5 week) were obtained from the Laboratory Animal Center of Sun Yat-sen University. The animals were housed in autoclaved polyethylene cages (four rats in each group per cage), and maintained on a 12 h:12 h light: dark cycle. The temperature and relative humidity of the animal room were maintained at 23 ± 2 °C and 50 %–70 %, respectively.

The animals were quarantined and acclimatized for a week before treatment. Rats of either sex weighing 160–200 g or mice of either sex weighing 25–30 g were randomly selected and assigned to the treatment and control groups using a computer randomization process.

GC–FID analysis

An Agilent HP-6890 gas chromatograph (Agilent Technologies, Palo Alto, CA, USA) with an HP-5 5 % phenylmethylsiloxane capillary column (30 m × 0.25 mm i.d., 0.25 μm film thickness) and equipped with an FID detector was used for GC–FID analysis. Helium gas at a constant flow rate of 1 mL/min was used as the carrier gas. The injector and mass transfer line temperatures were set at 250 °C and 280 °C, respectively. The essential oil solution (1 μL) in hexane was injected and analyzed under the following column conditions: initial column temperature at 40 °C for 1 min, which was then increased to 250 °C at a 3 °C/min heating ramp, and then subsequently maintained at 250 °C for 20 min.

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GC–MS analysis

Quantitative and qualitative analyses of the essential oils were performed using a GC-MS 6890-5975 system (Agilent Technologies, Palo Alto, CA, USA) equipped with an HP-5 MS fused silica capillary column (30 m × 0.25 mm i.d., 0.25 µm film thickness). For GC–MS detection, an electron ionization system with 70 eV ionization energy was used. Helium gas was used as the carrier gas at a constant flow rate of 1 mL/min. The injector and mass transfer line temperatures were set at 250 °C and 280 °C, respectively. Essential oil solution (1 µL) in hexane was injected and analyzed under the following column conditions: initial column temperature at 40 °C for 1 min, which was increased to 250 °C at a 3 °C/min heating ramp, and then maintained at 250 °C for 20 min. The Kovats indices were calculated for all volatile components using a homologous series of n-alkanes (C_8–C_{25}) on the HP-5 MS column. The major oil components were identified via co-injection with standards (whenever possible), and confirmed through the Kovats indices using the Wiley (V.7.0) and National Institute of Standards and Technology (NIST) V.2.0 GC–MS library. The relative concentration of each compound in the essential oil was quantified based on the peak area integrated in the analysis program.

Carrageenan-induced paw edema

Rats of either sex were divided into five groups of eight animals each. The first group (negative control) received the vehicle only. Animals of the second, third, and fourth groups were treated orally with SFEO at doses of 10, 30, or 90 mg/kg, respectively. The fifth group (positive control) received 10 mg/kg indomethacin. At 30 min after drug administration, edema was induced by injecting 0.1 mL of 1 % carrageenan in normal saline into the plantar aponeurosis of the right hind paw. Hind paw volume (an index of swelling) was measured using a plethysmograph before injection and 1, 2, 3, 4, 5, and 6 h after carrageenan injection (Winter et al., 1962). The difference between the initial and subsequent paw volume readings was the actual edema volume. The percent inhibition of inflammation was calculated using the formula:

$$\% \text{ inhibition} = 100 (1 – Vt / Vc)$$

where Vc represents the edema volume in the control, and Vt refers to the edema volume in the group treated with the tested oils or indomethacin.

Myeloperoxidase (MPO) activity was measured in paw tissue samples obtained from animals after the end (6 h) of edema measurements. These samples were homogenized in 50 mM phosphate buffer (pH 6.0) containing 0.5 % hexadecyl-trimethylammonium bromide. The supernatants were mixed with a solution of o-dianisidine dihydrochloride (0.167 mg/mL in 50 mM phosphate buffer) containing 0.005 % H_2O_2. The changes in absorbance at 460 nm were measured with a microplate reader. The results were expressed as units of MPO (UMPO)/mg tissue, in which one UMPO is defined as the amount of enzyme that degrades 1 µmol H_2O_2/min (Bradley et al., 1982).

12-O-tetradecanoyl-phorbol-13-acetate (TPA)-induced ear edema

Mice of either sex were divided into five treatment groups of eight animals each. The negative control group received the vehicle only. Animals of the second, third, and fourth groups were treated orally with SFEO at doses of 10, 30, or 90 mg/kg, respectively. The positive control group received 10 mg/kg indomethacin. At 30 min after oral treatment, edema was induced by applying 2.5 µg of TPA dissolved in 20 µL of acetone to the inner surface of the right ear. Acetone was applied to the left ear as the control. After 6 h, the mice were killed under ether anesthesia, and both ears were removed and weighed (De Young et al., 1989). The percent inhibition of inflammation was calculated using the formula:

$$\% \text{ inhibition} = 100 (1 – Vt / Vc)$$

where Vc represents the edema volume in the control, and Vt refers to the edema

volume in the group treated with the tested oils or indomethacin.

Cotton pellet-induced granuloma

Rats of either sex were divided into five groups of eight animals each. Inflammation was induced by the method of Mosquera et al. (2011) with slight modifications. The animals were anesthetized with ketamine (50 mg/kg, i.m.). The back skin was shaved and disinfected with 70 % ethanol, and an incision was made in the lumbar region. Subcutaneous tunnels were formed by blunted forceps, and a sterilized, pre-weighed cotton pellet (15 ± 1 mg) was placed on both sides in the scapular region. The animals were treated orally with distilled water as the negative control, indomethacin (10 mg/kg) as the positive control drug, or 10, 30, or 90 mg/kg SFEO daily for 7 d. On day 8, the animals were sacrificed, and pellets were dissected. The pellets were dried in an oven at 60 °C until the weight stabilized. The net dry weights (initial minus final) were determined. Wet and dry contents were determined using the following formulae:

Wet content = weight of the cotton pellet (wet) – weight of the cotton pellet (dry)

Dry content = weight of the cotton pellet (dry) – actual weight of the cotton pellet.

Statistical analysis

Data are presented as means ± standard deviation (SD). For statistical analysis, data were analyzed by one-way ANOVA, followed by a Duncan post-hoc for pair-wise comparisons between groups. A significant difference between groups was set at $P < 0.05$.

RESULTS AND DISCUSSION

Steam distillation of 500 g of dried plant material yielded 1.9 mL (0.38 %, v/w) of yellow oils with a distinct smell. The oil samples were analyzed via GC–FID and GC–MS. The components were identified based on their retention index values, and by comparing their mass spectra with those reported in the literature. GC–MS analysis of SFEO found 48 components, representing 98.41 % of the oils (Table 1). The composition of SFEO was as follows: 18.38 % monoterpene hydrocarbon fraction, 30.23 % sesquiterpene hydrocarbon fraction, 17.62 % oxygenated monoterpene fraction, 13.70 % oxygenated sesquiterpenoid fraction, 2.55 % phenylpropanoid fraction, and 15.93 % others. The main components of the oils were α-farnesene (11.26 %), caryophyllene (8.69 %), n-hexadecanoic acid (7.23 %), and α-pinene (6.36 %).

SFEO differed from other species of the genus *Senecio* by the percentages of monoterpenoids and sesquiterpenoids present. Analyses of the oils of *S. flammeus* showed that the species was predominantly sesquiterpenoid, but other species, such as *S. farfarifolius* (Baser and Demirci, 2004), *S. leucostachys* (Mirza and Baher, 2008), *S. nutans* (De Feo et al., 2003), *S. squalidus* (Chalchat et al., 2004), and *S. polyanthemoides* (Oladipupo and Adebola, 2009), were predominantly monoterpenoid.

However, some main components of SFEO resembled those of other species. Farnesene is the major component in essential oils of *S. platyphyllus* (Usta et al., 2009) and *S. trapezuntinus* (Osman et al., 2008). Caryophyllene is the major component in essential oils of *S. polyanthemoides* (Oladipupo and Adebola, 2009), *S. platyphyllus* (Usta et al., 2009), *S. pandurifolius* (Kahriman et al., 2011), and *S. vernalis* (Nori-Shargh et al., 2008). α-Pinene is the major component in essential oils of *S. furfarifolium* (Baser and Demirci. 2004), *S. graveolens* (Pérez et al., 1999), *S. vernalis* (Usta et al., 2009), *S. polyanthemoides* (Oladipupo and Adebola, 2009), *S. mustersii* (Luz et al., 2010), *S. nutans* (De Feo et al., 2003), and *S. inaequidens* (Andreani et al., 2013). The current results indicate that SFEO contained some components relatively similar to those of other *Senecio* species.

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Table 1: Chemical composition of essential oils of *Senecio flammeus*

Peak no.	RI [a]	Components	% RA [b]	Identification Methods [c]
		Monoterpene hydrocarbons	18.38	
1	931	α-Thujene	2.35	MS, RI, Co
2	937	α-Pinene	6.36	MS, RI, Co
3	973	α-Sabinene	2.06	MS, RI
4	992	β-Myrcene	3.21	MS, RI, Co
5	1015	α-Terpinene	0.68	MS, RI
6	1059	γ-Terpinene	1.35	MS, RI
7	1088	Terpinolene	2.37	MS, RI, Co
		Oxygenated monoterpenes	17.62	
8	1037	Eucalyptol	3.35	MS, RI
9	1102	Linalool	3.34	MS, RI, Co
10	1109	Thujone	2.78	MS, RI
11	1162	Lyratol	2.29	MS, RI
12	1255	Geraniol	1.58	MS, RI
13	1342	Piperitenone	1.61	MS, RI
14	1365	Piperitenone oxide	2.67	MS, RI
		Sesquiterpene hydrocarbons	30.23	
15	1349	α-Cubebene	0.57	MS, RI
16	1364	Cyclosativene	0.62	MS, RI
17	1368	Ylangene	1.38	MS, RI
18	1388	β-Cubebene	2.31	MS, RI
19	1399	Cedrene	1.02	MS, RI
20	1408	α-Cedrene	0.39	MS, RI
21	1418	Caryophyllene	8.69	MS, RI, Co
22	1428	cis-Thujopsene	0.65	MS, RI
23	1450	Aromadendrene	0.26	MS, RI
24	1482	Germacrene D	1.69	MS, RI
25	1495	Bicyclogermacrene	0.38	MS, RI
26	1505	α-Farnesene	11.26	MS, RI, Co
27	1514	γ-Cadinene	0.39	MS, RI
28	1540	α-Calacorene	0.62	MS, RI
		Oxygenated sesquiterpenes	13.70	
29	1496	Dihydro-β-agarofuran	0.31	MS, RI
30	1575	Spathulenol	0.68	MS, RI
31	1583	Caryophyllene oxide	1.35	MS, RI
32	1594	Carotol	0.72	MS, RI, Co
33	1606	Humulene epoxide II	0.45	MS, RI
34	1642	τ-Muurulol	0.75	MS, RI
35	1658	7-epi-α-Eudesmol	0.27	MS, RI
36	1682	α-Bisabolol	1.41	MS, RI
37	1714	6-Isopropenyl-4,8a-dimethyl-1,2,3,5,6,7,8,8a-octahydro-naphthalen-2-ol	5.63	MS, RI, Co
38	1740	(2Z.6E) Farnesol	0.78	MS, RI
39	1788	Drimenol	1.35	MS, RI
		Phenylpropanoids	2.55	
40	1024	p-Cymene	0.56	MS, RI
41	1165	Benzoic acid	0.31	MS, RI, Co
42	1304	Carvacrol	0.63	MS, RI, Co
43	1410	Methyl eugenol	1.05	MS, RI

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Table 1 (cont.): Chemical composition of essential oils of *Senecio flammeus*

Peak no.	RI [a]	Components	% RA [b]	Identification Methods [c]
		Others	15.93	
44	1332	Myrtenyl acetate	0.61	MS, RI
45	1366	Neryl acetate	0.48	MS, RI
46	1924	Hexadecanoic acid, methyl ester	5.36	MS, RI, Co
47	1969	n-Hexadecanoic acid	7.23	MS, RI, Co
48	2115	Phytol	2.25	MS, RI, Co
		Total identified (%)	98.41	

[a] Retention index (RI) relative to n-alkanes on the HP-5 MS capillary column
[b] Relative area (peak area relative to the total peak area)
[c] MS = mass spectrum, Co = co-injection with standard compound

The anti-inflammatory effect of SFEO was investigated using classical acute inflammatory models, including paw edema, ear edema, and peritonitis. This study revealed that SFEO significantly ameliorated the inflammatory response in rodent models.

Carrageenan-induced paw edema is the most prominent experimental model in the search for new anti-inflammatory drugs and evaluation of anti-inflammatory effects of natural products (Posadas et al., 2004). We found that the administration of SFEO significantly reduced carrageenan-induced paw edema. The effects of SFEO and indomethacin on carrageenan-induced rat paw edema are summarized in Table 2. Injection of carrageenan into the sub-plantar tissue of the right hind paw of rats in the control group caused edema development, which peaked (1.68 ± 0.10 mL in paw volume) 3 h after post-phlogistic agent injection. The effect of SFEO was dose-dependent from the first hour to the sixth hour with a peak effect (66.45 % inhibition) produced at 90 mg/kg during the fourth hour. This effect was less than but not significantly different ($P < 0.05$) from that produced by 10 mg/kg indomethacin (68.39 % inhibition). The effects of essential oils at 90 mg/kg and indomethacin were also time-dependent until the sixth hour.

Table 2: Effect of essential oils of *S. flammeus* on carrageenan-induced rat paw edema

Treatment	Dose (bw)	Increase in paw volume (mL)					
		1 h	2 h	3 h	4 h	5 h	6 h
Control	10 mL/kg	0.57±0.06 (-)	1.42±0.07 (-)	1.68±0.10 (-)	1.55±0.08 (-)	1.17±0.10 (-)	0.72±0.08 (-)
Indomethacin	10 mg/kg	0.31±0.02[a] (45.61)	0.51±0.04[a] (64.08)	0.56±0.05[a] (66.67)	0.49±0.04[a] (68.39)	0.38±0.04[a] (67.52)	0.31±0.03[a] (56.94)
Essential oil	10 mg/kg	0.52±0.04[ab] (8.77)	1.26±0.07[ab] (11.27)	1.30±0.10[ab] (22.62)	1.28±0.09[ab] (17.42)	0.97±0.08[ab] (17.09)	0.53±0.06[ab] (26.39)
Essential oil	30 mg/kg	0.43±0.06[ab] (24.56)	0.83±0.08[ab] (41.55)	1.08±0.08[ab] (35.71)	0.73±0.09[ab] (52.90)	0.67±0.06[ab] (42.74)	0.42±0.05[ab] (41.67)
Essential oil	90 mg/kg	0.38±0.04[ab] (33.33)	0.66±0.08[ab] (53.52)	0.73±0.09[ab] (56.54)	0.52±0.07[a] (66.45)	0.43±0.06[a] (63.25)	0.35±0.06[a] (51.39)

Values are expressed as mean ± SD ($n = 8$)
Figures in parentheses indicate percentage inhibition of edema development
[a] $P < 0.05$ vs. control group
[b] $P < 0.05$ vs. indomethacin group

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The inflammatory response by carrageenan in the rodent hind paw is a multimediated phenomenon (Vinegar et al., 1976). In the beginning of carrageenan injection, the paw volume markedly increases in relation to histamine and serotonin (Geen, 1974), after which the increase in vascular permeability is maintained by the release of kinins up to 2.30 h; from 2.30 h to 6 h, the mediators appear to be prostaglandins and NO, the release of which is closely associated with the migration of leukocytes into the inflamed site (Castro et al., 1968; Di Rosa et al., 1971). The second phase of edema is sensitive to most clinically effective anti-inflammatory agents (Smucker et al., 1967). These data suggest that SFEO could inhibit increased microvascular permeability (edema) and leukocyte influx, but the action mechanisms involved should be further investigated.

The inhibitory leukocyte effect promoted by the essential oils was associated with a marked reduction in MPO. SFEO (10, 30, and 90 mg/kg) markedly inhibited ($P < 0.05$) the carrageenan-induced increase in MPO activity in the paws of rats compared with that in the vehicle-treated group (Table 3). Similarly, indomethacin inhibited ($P < 0.05$) carrageenan-induced MPO activity.

Table 3: Effect of essential oils of *S. flammeus* on myeloperoxidase activity

Treatment	Dose (bw)	UMPO/mg tissue
Control	10 mL/kg	9.03±0.87
Indomethacin	10 mg/kg	0.58±0.11[a]
Essential oil	10 mg/kg	4.32±0.51[ab]
Essential oil	30 mg/kg	1.37±0.38[ab]
Essential oil	90 mg/kg	0.67±0.26[a]

Values are expressed as mean ± SD (n = 8)
[a] $P < 0.05$ vs. control group
[b] $P < 0.05$ vs. indomethacin group

The decrease in MPO may be attributed to the inhibitory effect on both neutrophil- and mononuclear-activated influxes, because MPO can reflect the activation and chemotaxis of both neutrophils and mononuclei at the site of injury induced by carrageenan (Fröde and Medeiros, 2001).

Mouse ear edema induced by TPA has been used as an animal model for testing anti-inflammatory activity. SFEO significantly ($P < 0.05$) reduced the TPA-induced ear edema that peaked at 90 mg/kg (53.90 %). However, the level of inhibition observed at this dose was significantly lower than that produced by 10 mg/kg indomethacin (63.45 %) (Table 4).

Extensive experimental evidence has shown that exposure of skin to TPA induces a pleiotropic tissue response that encompasses a strong inflammatory reaction similar to that observed in several skin diseases (Hvid et al., 2008; Verma et al., 2006). Some findings suggested that eicosanoids have an important function in TPA-induced skin inflammation (Rao et al., 1993). The mechanism of the TPA-induced increase in eicosanoids is not completely known but may include the activation of protein kinase C (Wang et al., 2001), mitogen-activated protein kinases, and nuclear factor-kB, as well as the generation of mediators, such as tumor necrosis factor-a, interleukin-1b, keratinocyte-derived chemokine, macrophage inflammatory protein-2, and prostaglandins (Cataisson et al., 2005; Medeiros et al., 2007; Otuki et al., 2005).

To assess the efficacy of SFEO and indomethacin against the proliferative phase of inflammation, in which tissue degeneration and fibrosis occur, cotton pellet-induced granuloma test was performed. The effects of SFEO and indomethacin on the proliferative phase of inflammation are summarized in Table 5. SFEO was responsible for the anti-inflammatory effect, which could be calculated depending on the moist and dry weights of cotton pellets. According to these results, the anti-proliferative effects of SFEO (90 mg/kg) and indomethacin (10 mg/kg bw) were calculated as 47.29 % and 48.64 % ($P < 0.05$), respectively. After drying, the anti-proliferative effects were calculated based on the dry weights of pellets. The inhibition of inflammation by SFEO and indomethacin were 47.29 % and 48.64 % ($P < 0.05$), respectively.

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Table 4: Effect of essential oils of *S. flammeus* on 12-O-tetradecanoyl-phorbol-13-acetate-induced ear edema

Treatment	Dose (bw)	Increase in ear weight (mg)	Inhibition (%)
Control	10 mL/kg	42.32±0.37	-
Indomethacin	10 mg/kg	15.47±0.21[ab]	63.45
Essential oil	10 mg/kg	33.74±1.22[ab]	20.27
Essential oil	30 mg/kg	28.33±1.07[ab]	33.06
Essential oil	90 mg/kg	19.51±0.86[ab]	53.90

Values are expressed as mean ± SD (*n* = 8)
[a] P < 0.05 vs. control group
[b] P < 0.05 vs. indomethacin group

Table 5: Effect of essential oils of *S. flammeus* on cotton pellet-induced granuloma

Treatment	Dose (bw)	Wet content of granuloma (mg)	Inhibition (%)	Dry content of granuloma (mg)	Inhibition (%)
Control	10 mL/kg	228.6±13.2	–	51.6±3.3	–
Indomethacin	10 mg/kg	113.2±8.5[a]	50.48	26.5±3.6[a]	48.64
Essential oil	10 mg/kg	178.6±13.9[ab]	21.87	40.8±2.7[ab]	20.93
Essential oil	30 mg/kg	145.4±11.7[ab]	36.40	33.3±3.4[ab]	35.47
Essential oil	90 mg/kg	116.4±10.6[a]	49.08	27.2±2.7[a]	47.29

Values are expressed as mean ± SD (*n* = 8)
[a] P < 0.05 vs. control group
[b] P < 0.05 vs. indomethacin group

The cotton pellet-induced granuloma model is widely used to assess the transudative, exudative, and proliferative events during chronic inflammation (Williams and Williams, 1983). Inflammation involves the proliferation of macrophages, neutrophils, and fibroblasts, as well as the multiplication of small blood vessels, which are the basic sources for the formation of a highly vascularized reddish mass known as granulation tissue (Bhattacharya and Nag Chaudhuri, 1992). Thus, a decrease in granuloma weight may be due to the ability of SFEO to reduce the number of fibroblasts and synthesis of collagen and mucopolysaccharide, which are natural proliferative markers of granulation tissue formation (Ionac et al., 1996).

CONCLUSION

This paper provides evidence of the anti-inflammatory activity of SFEO. Our findings are the first to show that SFEO possesses anti-inflammatory properties, providing a scientific basis for the ethnobotanical uses of SFEO in treating inflammatory disorders. Further detailed investigation is currently underway to characterize the active agents responsible for the observed effects, and estimate the anti-inflammatory mediators for confirming the mechanism.

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