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Full Length Research Paper

Anti-inflammatory properties of *Albuca setosa* and its possible mechanism of action

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Albuca setosa **is used for the treatment of wounds, articulation problems and rheumatoid arthritis. In this study we characterized the anti-inflammatory response of *A. setosa* on inflammation induced by carrageenan, dextran, histamine, serotonin, arachidonic acid and xylene. The extract was administered orally at a dose of 150 and 300 mg/kg. The extract of *A. setosa* at both doses significantly inhibited (P< 0.01) the formation of the carrageenan-induced rat paw edema in the first, second and the third hour of inflammation (peak of inflammation) by 52, 55, 43% and 68, 84, 85% for 150 and 300 mg/kg, respectively. Concerning inflammation induced by dextran and inflammatory mediators such as histamine, serotonin and arachidonic acid, the effect of *A. setosa* was significant (P<0.01) mostly during the first and the second hours of inflammation by a maximum of inhibition of 61, 83, 50 and 47%, respectively. Results also showed that water leaf extract of *A. setosa* significantly inhibited (P< 0.05) topical edema in the mouse ear induced by xylene for 150 mg/kg by 44% but was not dose dependent. The results obtained suggest that the water leaf extract of *A. setosa* is endowed with effective anti-inflammatory activity mediated via either inhibition of phospholipase A2 (PLA2) activity or cyclooxygenase cascade and by blocking the release of vasoactive substances like histamine, serotonin and kinins.**

Key words: *Albuca setosa*, inflammation, carrageenan, dextran, histamine, serotonin.

INTRODUCTION

Albuca setosa called *inqwebeba* in xhosa is a member of the Hyacinthaceae family. It is distributed in the Eastern Cape Province of South Africa where its traditional usage is very extensive. Xhosa people (*amaXhosa*) living in an urban context in the eastern Cape Province of South Africa use *A. setosa* for cultural purposes and often access it through commercial trade at around R32 /kg depending on the availability of the plant (Dold and cocks, 2002). *A. setosa* is used as a ritual wash, an emetic, and a facial steam treatment as protection against bad luck and sorcery (Cocks, 2006). *A. setosa* is used for forms of ritual purification such as a ritual body wash (*Ukuhlamba ngeyeza*) (Cocks, 2006). Therapeutically, *A. setosa* is traditionally used as a purgative (*Ukugabha* and *Ukucima*), spraying (*Ukutshiza*), fumigating (*Ukugxotha*) and steam treatment (*Ukufutha*) (Cocks, 2006). *A. setosa* is used for the treatment of wounds, articulation problems and arthritis rheumatoid (Hutchings et al., 1996). *A. setosa* is also used as an anthelmintic, lotion for washing wounds in animal and to treat venereal diseases (Hutchings et al., 1996). Previous studies showed that *A. setosa* possess membrane stabilization properties, limit protein denaturation process and decrease white blood cell migration during acute inflammation (Umapathy et al., 2010). This present study is aimed at to evaluate the efficiency of *A. setosa* on experimental model of inflammation. In addition, we investigated the possible

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Abbreviations: PLA2, Phospholipase A2; **SAVP,** South African vaccine producers; **WSU,** Walter Sisulu University; **PG,** prostaglandin; **PGE2,** prostaglandin E2.

mechanisms involved in the healing effect of this plant.

MATERIALS AND METHODS

Plant material and extract preparation

The plant material of *A. setosa* was collected from its natural environment approximately 5 km south west of Flagstaff in the OR Tambo municipality, Eastern Cape Province of South Africa. Identification of the plant was done at the Kei Herbarium at Walter Sisulu University in Mthatha. Leaf sample of the *A. setosa* was chopped, air dried and ground to powder (pulverised). A 40 g of dried powder was macerated in distilled water and shaken for 72 h on an orbital shaker.

The mixture was filtered using a Buchner funnel and Watman No. 1 filter paper and then concentrated to dryness under reduced pressure at a maximum of 55°C using a rotating evaporator (Bibby Sterilin rotator evaporator RE-100), a brown powder yielding 5 g was obtained.

Animals

Male wistar rats and male swiss mice weighing 150 to 200 g and 25 to 30 g, respectively were provided by South African vaccine producers (SAVP). The animals were housed in the animal house of Walter Sisulu University (WSU). Also, the experiments were authorized by the ethical committee for WSU.

The animals were kept in groups of five in standard cages at room temperature in 12 h dark/12 h light control, with both food and water *ad libitum*. 12 h before experiment, animals received only water in order to avoid food interference with substances absorbed from plant extracts.

Drug

Xylene (Shalom laboratories, Durban), carrageenan, serotonin, arachidonic acid, histamine and dextran (Sigma Chemicals Company, USA) were used in the study and indomethacin (Fluka, Biochemika) was used as the standard.

Anti inflammatory activity evaluation

Carrageenan-induced paw edema

In rats, the hind paw edema was induced by a single subplantar injection 0.1 ml of carrageenan (1%, w/v in normal saline) 30 min after dosing distilled water (10 mL/kg), indomethacin (10 mg/kg) and extract (150 and 300 mg/kg).

Paw volume was measured before injection of the irritant and at 1 h intervals for 3 h thereafter with a plethysmometer (7150, Ugo Basile) (Li et al*.,* 2003). The edema was calculated from the difference between final and basal average paw volumes (mL) at different time intervals (Sanchez et al., 1998). Percent inhibition of edema (Ahmed et al., 1993; Okoli et al., 2006) was calculated using the relation:

Inhibition of edema (%) = 100 × [1- (a-x)/(b-y)],

Where; a = mean paw volume of treated rats at various time after carrageenan injection, x = mean paw volume of treated rats before formation of rat paw edema induced by carrageenan during the first, second and the third hour of inflammation carrageenan injection, b = mean paw volume of control rats at various time after carrageenan injection, y = mean paw volume of control rats before carrageenan injection.

Dextran-induced paw edema

The animals were treated similar to the case of carrageenan induced paw edema models, except that in place of carrageenan, dextran (0.1 ml, 1% w/v in normal saline) were used (Gupta et al., 2006). Percent inhibition of edema was calculated using the relation previously described.

Histamine, serotonin and arachidonic acid-induced paw edema

In these models, hind paw edema in the right foot of a rat was induced by subplantar injection of 0.1 ml of 1% freshly prepared histamine or serotonin or arachidonic acid in normal saline and the paw edema was measured as mentioned earlier (Suleyman et al., 1991). Group division and treatment of the animals were the same as the Carrageenan-induced rat paw edema. Percent inhibition of edema was calculated using the relation previously described.

Xylene-induced ear edema

Mice were allotted to groups of 5 animals each. 30 min after oral treatment of mice with distilled water (10 mL/kg), indomethacin (10 mg/kg) and extract (150 and 300 mg/kg), edema was induced in each mouse by applying a drop of xylene to the inner surface of the right ear. 15 min later, the animals were killed under ether anesthesia and circular sections of both ears were taken using a cork borer (diameter of 5 mm) and weighed. Edema was quantified as the weight difference between the two earplugs. The anti-inflammatory activity was evaluated as percent edema reduction/ inhibition in the treated animals relatively to the control animals (Asuzu et al., 1999) using the relation:

Edema reduction/inhibition (%) = 100 × [1 - (Rt-Lt)/ (Rc-Lc)],

Where; Rt = mean weight of right earplug of treated animals, Lt = mean weight of left earplug of treated animals, Rc = mean weight of right earplug of control animals, Lc = mean weight of left earplug of control animals.

Statistical analysis

Data are reported as mean ± S.E.M. and differences among treated groups were analyzed statistically by analysis of variance (ANOVA) followed by Dunnett's test. Results with $p < 0.05$ were considered significant.

RESULTS

Carrageenan-induced paw edema

The anti-inflammatory activity of water extract of *A. setosa* was measured at the dose of 150 and 300 mg/kg against acute paw edema induced by carrageenan. The

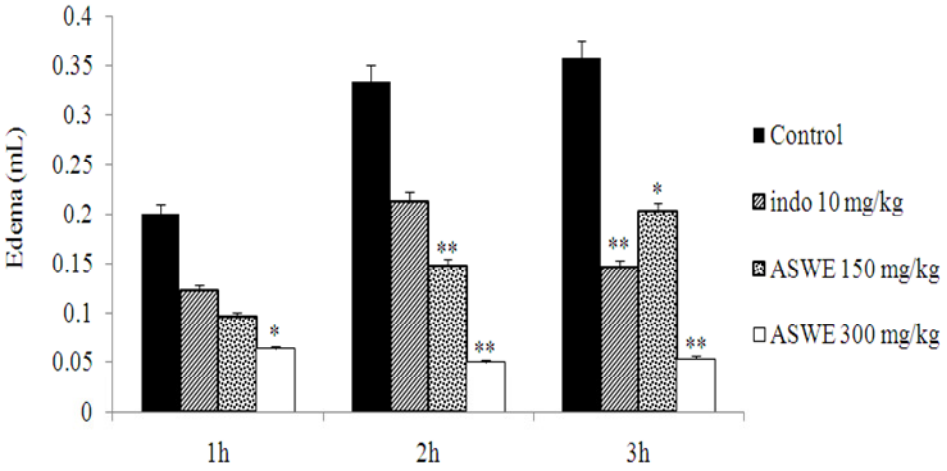

Figure 1. Effect of *A. setose* water extract on carrageenan-induced paw edema. Values are mean ± SEM. (n = 5). Variation compared to the control animals. *P<0.05, **P<0.01 ANOVA followed by Dunnett's test. ASWE: *Albuca setose* water extract, indo: indomethacin.

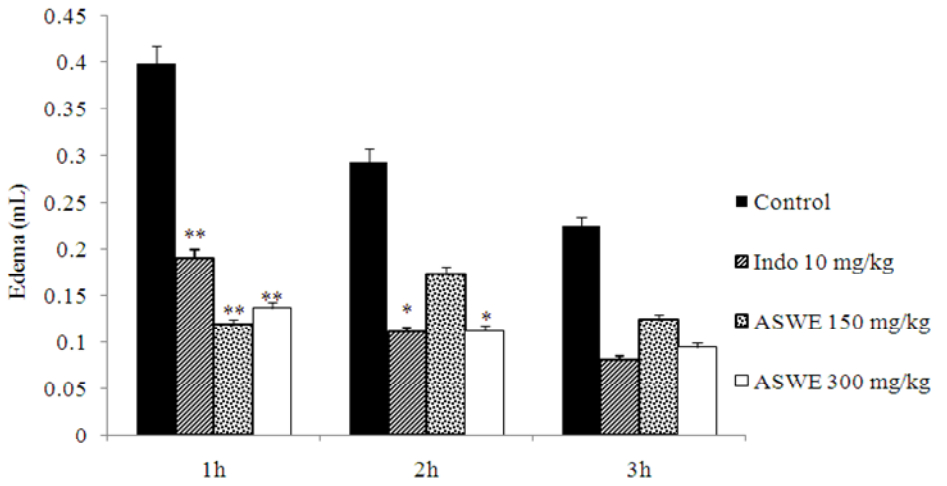

Figure 2. Effect of ASWE on dextran-induced paw edema. Values are mean ± SEM. (n = 5). Variation compared to the control animals. *P<0.05, **P<0.01 ANOVA followed by Dunnett's test. ASWE: *Albuca setose* water extract, indo: indomethacin.

results are summarized in Figure 1. The extract of *A. setosa* at both doses significantly inhibited ($p < 0.01$) the (peak of inflammation) by 52, 55, 43% and 68, 84, 85% for 150 and 300 mg/kg, respectively. The extract produced anti-inflammatory activity and the results were slightly comparable to that of indomethacin 10 mg/kg.

Dextran-induced paw edema

The anti-inflammatory activity of water extract of *A. setosa* was measured at the dose of 150 and 300 mg/kg against acute paw edema induced by dextran. The results are summarized in Figure 2. The extract produced significant ($p< 0.01$) anti-inflammatory activity at the first and the second hour of inflammation by 42, 41 and 65%, 61% for 150 and 300 mg/kg, respectively in dextran-induced paw edema in rats.

Serotonin and histamine-induced paw edema

The anti-inflammatory effect of water extract of *A. setosa*

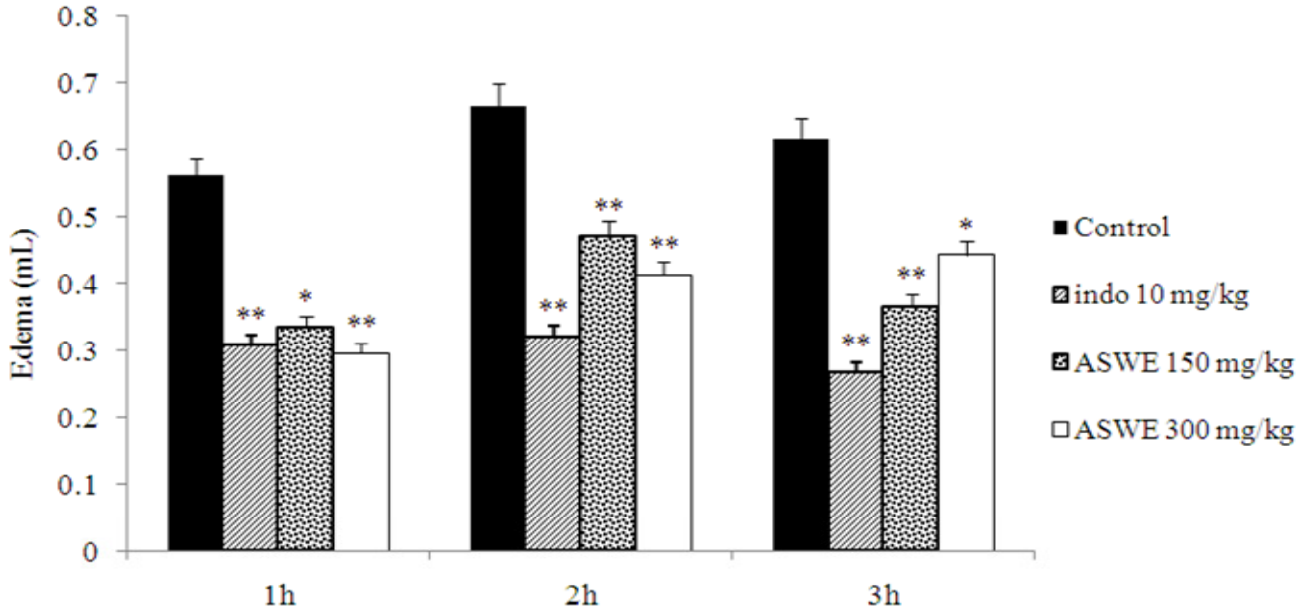

Figure 3. Effect of ASWE on serotonin-induced paw edema. Values are mean ± SEM. (n = 5). Variation compared to the control animals. * P<0.05; **P<0.01 ANOVA followed by Dunnett's test. ASWE: *Albuca setose* water extract, indo: indomethacin.

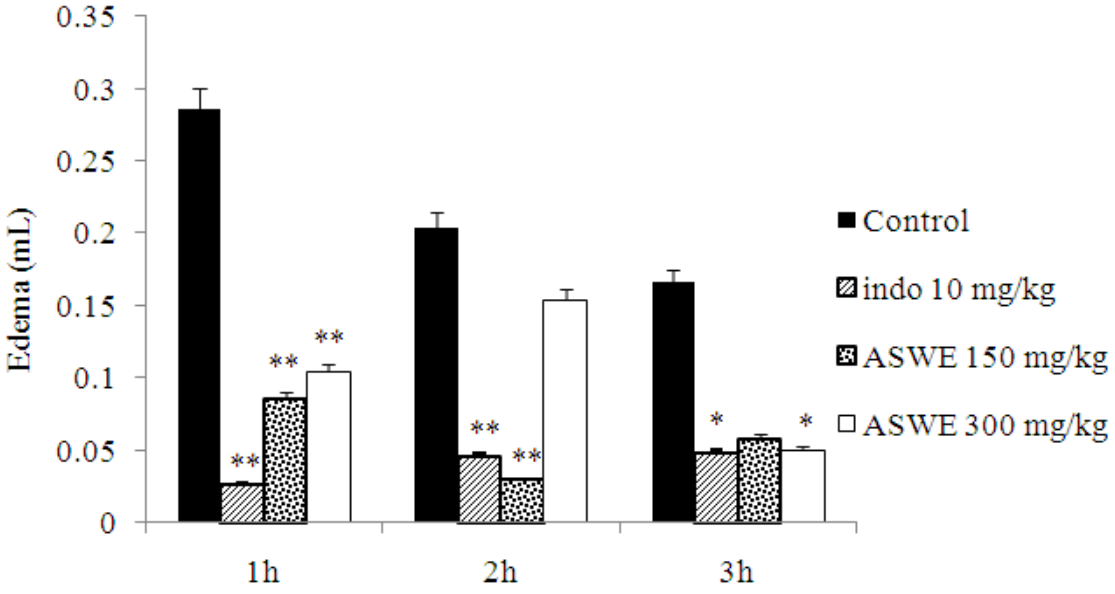

Figure 4. Effect of ASWE on histamine-induced paw edema. Values are mean ± SEM. (n = 5). Variation compared to the control animals. *P<0.05; **P<0.01 ANOVA followed by Dunnett's test. ASWE: *Albuca setose* water extract, indo: indomethacin.

against acute edema induced by phlogistic agent serotonin and histamine has been shown in Figures 3 and 4, respectively. The extract exhibited significant anti-inflammatory activity with a maximum inhibition of 50% for serotonin and 83% for histamine during the first and the second hour of inflammation.

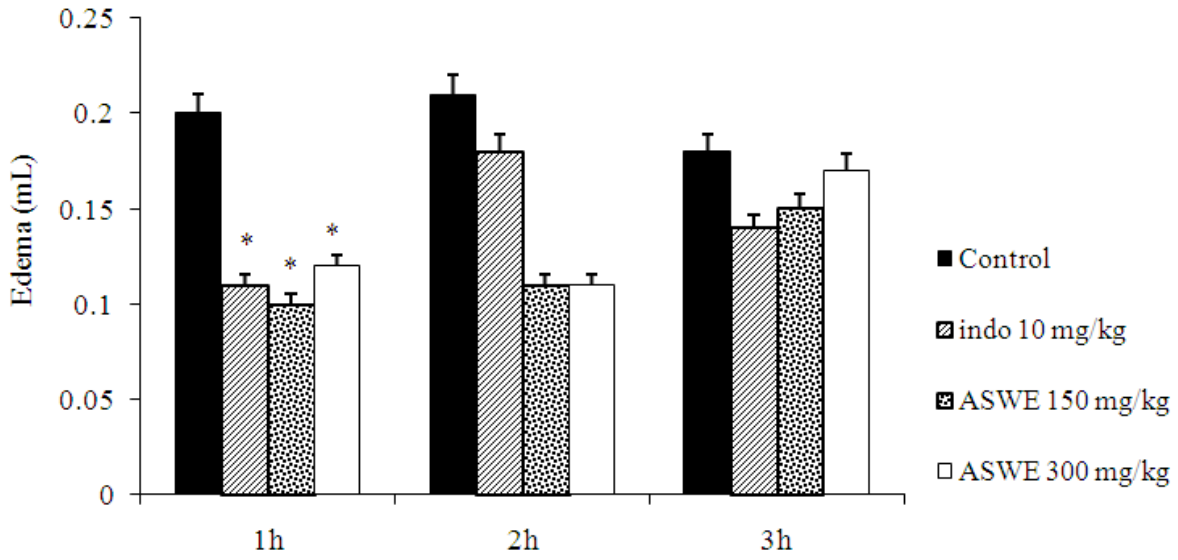

Figure 5. Effect of ASWE on arachidonic acid-induced paw edema. Values are mean ± SEM. (n = 5). Variation compared to the control animals. *, P<0.05; **, P<0.01 ANOVA followed by Dunnett's test. ASWE: *Albuca setose* water extract, indo: indomethacin.

Arachidonic acid-induced paw edema

The anti-inflammatory effect of water extract of *A. setosa* on arachidonic acid induced edema is reported in Figure 5. The extract produced significant (P< 0.05) anti-inflammatory activity at the first hour of inflammation by 47 and 36% for 150 and 300 mg/kg, respectively.

Xylene induced ear edema

Oral administration of *A. setosa* 30 min before topical application of xylene, inhibited the development of ear edema. The inhibitory effect of water extract of *A. setosa* was not dose dependent and it was significant (P< 0.05) at 150 mg/kg. The inhibition produced by indomethacin 10 mg/kg (49%) was greater than that produced by 150 (44%) and 300 mg/kg (22%) of water extract of *A. setosa* (Table 1).

DISCUSSION

A. setosa is a traditional herbal agent which has been used in the treatment and management of inflammation and painful conditions in the eastern Cape province of South Africa. However, its pharmacological actions and mechanisms have just started to be documented. Previous studies showed that *A. setosa* possess membrane stabilization properties, limit protein denaturation process and decrease white blood cell migration during acute inflammation (Umapathy et al., 2010). In the present study, we evaluated the anti-inflammatory effect of water extract of *A. setosa* on rodents using edema induced by different phlogistic agents. The extract demonstrated a potent efficiency against inflammation induced by carrageenan, dextran, serotonin, histamine, arachidonic acid and xylene.

The water extract of *A. setosa* leaves significantly inhibited the carrageenan-induced paw edema for 3 h of carrageenan challenge. Carrageenan-induced rat paw edema is a suitable experimental animal model for investigating the anti-inflammatory effect of natural products and is believed to be biphasic, the first phase (1 h) involves the release of serotonin and histamine and the second phase (over 1 h) is mediated by prostaglandin, the cylooxygenase products, and the continuity between the two phases is provided by kinins (Zhou et al., 2008). According to the result obtained it can be suggested that *A. setosa* may inhibit both phase of edema induced by carrageenan. To verify these findings, the effect of the plant extract was performed on dextran, serotonin, histamine and arachidonic acid induced paw edema.

It is well established that carrageenan and dextran induce rat paw edema by different mechanisms. Dextran is a polysaccharide of high molecular weight that induces anaphylactic reaction after injection in mice and rats extremities, which is characterized by extravasation and edema formation, as a consequence of liberation of

Table 1. Effect of ASWE on xylene-induced edema on the mouse ear.

Parameter	Dose (mg/kg)	Edema (mg)	Inhibition (%)
Control	-	5.5 ± 0.5	
ASWE	150	3.0 ± 0.5*	44
	300	4.3 ± 0.8	22
indo	10	2.7 ± 0.5*	49

Values are mean ± S.E.M. (n = 5). Variation compared to the control animals * ($P<0.05$) ANOVA followed by Dunnett's test. ASWE: *Albuca setose* water extract, indo: indomethacin.

histamine and serotonin from mast cells (Van Wauve and Goosens, 1989). The previous result showed that the extract also reduced the edema induced by histamine and serotonin. Histamine is one of the important inflammation mediators and it is a potent vasodilator substance and increases the vascular permeability (Linardi et al., 2002; Cuman et al., 2001). This study showed that all the doses of *A. setosa* effectively suppressed the edema induced by histamine, so considering that histamine is the main mediator in both models, it can be suggested that the crude extract contain compounds that are capable of inhibiting histamine liberation. *A. setosa* also suppressed the inflammation induced by serotonin which indicates that it may exhibit its anti-inflammatory action by means of inhibiting the synthesis or the release of mediators that might be involved in inflammation such as serotonin, histamine and prostaglandins.

The metabolites of arachidonic acid formed through cyclooxygenase and lipoxygenase pathways represent two important classes of inflammatory mediators. Prostaglandin (PG), prostaglandin E2 (PGE2) in particular is known to cause or enhance the cardinal signs of inflammation. Arachidonic acid provokes a rapid intense inflammatory response that is affected by lipooxygenase and cyclooxygenase inhibitors (Young et al., 1984). It has been observed earlier that the water extract of *A. setosa* inhibited the histamine, serotonin and carrageenan-induced edema which suggests that its inhibitory effect on arachidonic acid-induced edema could be partly due to inhibition of mast cell mediated release. *A. setosa* may have the potential to inhibit both cyclooxygenase and lipoxygenase pathways of arachidonic acid metabolism, which may be supplemented by its antihistaminic activity and antiserotonergic property. From previous study, *A. setosa* was confirmed to possess membrane stabilization properties (Umapathy et al., 2010). Extracts with membrane stabilizing properties are well known for their interfering activity with the early phase of the inflammatory mediators release, namely, the prevention of phospholipases release that trigger the formation of inflammatory mediators (Aitadafoun et al., 1996). To support our finding, we also evaluated the effect of *A setosa* on xylene-induced mouse ear edema.

Xylene-induced mouse ear edema formation is useful for screening and investigating the anti-inflammatory activity of test substances on the acute phase of inflammation (Xiao-Jia et al., 2008). Xylene causes instant irritation of the mouse ear, which leads to fluid accumulation and edema characteristic of the acute inflammatory response (Okoli et al., 2006). Suppression of this response is a likely indication of antiphlogistic effect. The ear edema model permits the evaluation of anti-inflammatory steroids and is less sensitive to non-steroidal anti-inflammatory agents. The effect of *A. setosa* in this model suggests the inhibition of phospholipase A2 (PLA2) (Atta et al., 1998).

Conclusion

In conclusion, water extract of *A. setosa* leaves have been confirmed to possess anti-inflammatory properties, which may provide some evidence for its folk use and further exploitation. On the other hand, it is also suggested to identify the potent fractions or ingredients responsible for the activity reported in this study. Work is in progress to isolate and characterize these ingredients for *A. setosa*.

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REFERENCES

Ahmed MM, Qureshi S, Al-bekairi AM, Shah AH, Rao RM (1993). Anti-inflammatory activity of *Caralluma tuberculata* alcoholic extract.

Fitoterapia, 64: 359-362.
Aitadafoun M, Mounieri C, Heyman SF, Binitisc C, Bon C (1996). 4-alkoxy benzamides as new potent phospholipase A2 inhibitors. J. Biochem. Pharmacol., 51: 737-742.
Asuzu IU, Sosa S, Della L (1999). The anti-inflammatory activity of *Icacina trichantha* tuber. Phytomedicine, 6: 267-272.
Atta AH, Alkohafi A (1998). Antinociceptive and anti-inflammatory effects of some Jondanian medicinal plants extracts. J. Ethnopharmacol., 60(2): 117-124.
Cocks D (2006). Cultural significance of biodiversity: the role of medicinal plants in urban African cultural practices in the Eastern Cape, South Africa. J. Ethnobiol., 26(1): 60-81.
Cuman RKN, Bersani-Amadio CA, Fortes ZB (2001). Influence of Type 2 diabetes on the inflammatory response in rats. Inflamm. Res., 50: 460-465.
Dold AP, Cocks ML (2002). The trade in medicinal plants in the Eastern Cape Province, South Africa. S. Afr. J. Sci., 98: 589-597
Gupta M, Mazumder UK, Sambath KR, Gomathi P, Rajeshwar Y, Kakoti BB, Tamil SV (2006). Anti-inflammatory, analgesic and antipyretic effects of methanol extract from *Bauhinia racemosa* stem bark in animal models. J. Ethnopharmacol., 98: 267-273.
Hutchings A, Scott AH, Lewis G, Cunningham AB (1996). Zulu Medicinal Plants: An Inventory University of Natal Press. Pietermaritzburg.
Li DW, Hyun JE, Jeong CS, Kim YS, Lee EB (2003). Anti-inflammatory activity of α-hederin methyl ester from the alkaline hydrolysate of the butanol fraction of Kalopanax pictus bark extract. Biol. Pharm. Bull., 26: 429-433.
Linardi A, Costa SKP, Da Silva GR, Antunes E (2002). Involvement of kinins, mast cells and sensory neurons in the plasma exudation and paw edema induced by staphylococcal entrotoxin-B in the mouse. Eur. J. Pharmacol., 399: 235-242.
Okoli CO, Akah PA, Nwafor SV, Anisiobi AI, Ibegbunam IN, Erojikwe O (2006). Anti-inflammatory activity of hexane leaf extract of Aspilia africana C.D. Adams. J. Ethnopharmacol., 109: 219-225.
Sanchez S, Bartrons R, Rodriguez L, Gonzalez P, Planas ME (1998). Protective effect of nifedipine against carrageenan-induced inflammation. Pharmacology, 56: 131-136.
Suleyman H, Demirezer LO, Kuruuzum A, Banoglu ZN, Gocer F, Ozbakir G, Gepdiremen A (1991). Anti-inflammatory effect of the aqueous extract from Rumex patientia L. roots. J. Ethnopharmacol., 65: 141-148.
Umapathy E, Ndebia EJ, Meeme A, Adam B, Menziwa P, Nkeh-Chungag BN, Iputo JE (2010). An experimental evaluation of *Albuca setosa* aqueous extract on membrane stabilization, protein denaturation and white blood cell migration during acute inflammation. J. Med. Plants Res., 4(9): 789-795.
Van WJP, Goosens JG (1989). Arabinolactan and dextran induced ear inflammation in mice: differential inhibition by H1-antihistamines, 5-HT-serotonin antagonists and lipoxygenase blockers. Agents Action, 28: 78-82.
Xiao-Jia HU, Hui-Zi JIN, Wen-Zheng XU, Ming C, Xiao-Hua L, Wei Z, Juan S, Chuan Z, Wei-Dong Z (2008). Anti-inflammatory and Analgesic Activities of Edgeworthia chrysantha and Its Effective Chemical Constituents. Biol. Pharm. Bull., 31(9): 1761-1765.
Young JM, Spires DA, Bedord CJ, Wagner B, Ballaron SJ, Deyoung LM (1984). The mouse ear inflammatory response to topical arachidonic acid. J. Investig. Dermatol., 82: 367-371.
Zhou M, Wang H, Suolangjiba KJ, Yu B (2008). Antinociceptive and anti-inflammatory activities of Aquilaria sinensis (Lour.) Gilg. Leaves extract. J. Ethnopharmacol., 117: 345-350.