Research Article

EVALUATION OF ANTI-INFLAMMATORY AND WOUND HEALING ACTIVITY OF THE MARINE ALGA *SYMPHYOCLADIA LATIUSCULA*

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ABSTRACT

The aim of the current study was to evaluate the anti-inflammatory and wound healing activity of poly phenols from the marine macro red alga *Symphyclocladia latiuscula*. *Symphyclocladia latiuscula*, a marine red alga, is traditionally used for food and for the treatment of inflammatory diseases including rheumatism and rheumatoid arthritis. Since there is no systematic evaluation of its anti-inflammatory activity hence, the study was carried out with the objective of evaluating anti-inflammatory and wound healing activity of this alga. The dried powder of *Symphyclocladia latiuscula* was extracted with 90% methanol and poly phenols were isolated. The anti-inflammatory activity and wound healing potential were determined with poly phenols in Wistar rats using carrageenan induced paw edema, carrageenan induced pleurisy and splinted wound model respectively. Rats were fed with poly phenols of *Symphyclocladia latiuscula* at a dose of 100 mg/kg and 200 mg/kg p.o. The administration of rats with 100 mg and 200 mg of poly phenols inhibited inflammation and accelerated wound healing. The paw volume, exudate volume, leukocyte number, protein and MDA were decreased and SOD was increased and there was an increase in rate of wound contraction and decrease in period of epithelization. Histopathological analysis further evidenced the wound healing activity. The maximum activities were observed with 200 mg/kg of poly phenols which was more than that of the standard drug. Results from the study suggest that *Symphyclocladia latiuscula* possess both anti-inflammatory and wound healing activity and hence could be useful in the development of natural anti-inflammatory agents.

Keywords: *Symphyclocladia latiuscula*, anti-inflammatory, wound healing, carrageenan, poly phenols.

INTRODUCTION

Inflammation is defined as the local response of living mammalian tissues to injury from any agent. It is a body defense reaction in order to eliminate or limit the spread of injurious agent, followed by removal of the necroses cells and tissues.¹ At present, most inflammatory diseases are treated with conventional anti-inflammatory drugs, such as steroidal anti-inflammatory drugs (SAIDs) and non-steroidal anti-inflammatory drugs (NSAIDs). However, prolonged use of these drugs produces many adverse effects.² Aspirin can cause stomach bleeding, acetaminophen can cause liver damage,³ inhibition of cyclooxygenase-1 (COX-1) increases the chances of bleeding,⁴ COX-2 inhibitor can cause heart problem.³ Hence, we aimed to discover new anti-inflammatory agents with fewer adverse effects, that could be developed for long-term administration.

Wounds are an unnatural break, tear, or defect in the skin, caused by thermal/physical injury, or an underlying pathological condition.⁵ Wound healing is a dynamic process involving complex interactions between cellular, molecular, biochemical and physiological activities which result in the regeneration and replacement of injured connective tissue at the wound site.⁶ This dynamic system requires the coordination of various components including inflammatory cells, vascular cells, epidermal cells, extracellular matrix (ECM), proteolytic enzymes, as well as inhibitors.⁷ Following injury, an inflammatory response occurs and the cells below the dermis (the deepest skin layer) begin to increase collagen (connective tissue) production. Later, the epithelial tissue (the outer skin) is regenerated.⁸

Symphyclocladia latiuscula (Harvey) Yamada is a marine macro red alga distributed along the coasts of Northern China, Korea, and Japan.⁹ The people of China, Korea and Japan use this alga as an edible component in their diet.¹⁰ Previous chemical studies on this species have resulted a variety of bioactivities, such as antibacterial, antifungal, free-radical-scavenging, aldose reductase inhibitory, antiviral, anticancer and Taq DNA polymerase inhibitory activities.¹¹ But there is no systematic evaluation of anti-inflammatory activity and wound healing potential of this alga. Hence, we have made an attempt to evaluate the anti-inflammatory and wound healing activity of this marine red alga *Symphyclocladia latiuscula*.

MATERIALS AND METHODS

Chemicals and Reagents

Folin-Ciocalteu reagent, carrageenan and gallic acid were purchased from Sigma Aldrich. All other chemicals and reagents like methanol, n-hexane, acetonitrile, ibuprofen, dexamethasone, diclofenac sodium, thiopentone sodium, etc. were of high analytical grade and obtained from Vasa Scientific Company, Bangalore, India. Ultrapure water was used for the experiments.

Collection of algal material

The marine alga *Symphyclocladia latiuscula* was collected from the coast of Northern China by hand picking during the month of May. Algal samples were cleaned from epiphytes, extraneous matter and necrotic were removed. Samples were washed thoroughly with deionized water, dried in shade, cut into fine

pieces and then ground in a grinder to reach fine powder shape. The voucher specimen (Batch No. ACPL/CSH07/141101) was deposited at Rajiv Gandhi University of Health Sciences, Bangalore, India. Also, a copy has been preserved for the future reference at Karnataka College of Pharmacy, Department of Pharmacology and Bangalore.

Extraction and Isolation

500 gm of powdered algae material was subjected to successive extraction in a Reflux condenser using 1 liter of methanol for 3 hours at a temperature of 70°C for 3 times adding fresh methanol each time. Each time liquid layer was collected. Finally, all the three layers of liquid were mixed and preceded for distillation. The final product was filtered using Whatman Filter Paper (WFP) 1. The extract thus obtained was transferred to separating funnel containing same volume of n-hexane and shaken vigorously for few minutes allowing liquids to separate. This was done for 5 times. Each time fresh n-hexane was added. The n-hexane layer was discarded, and aqueous layer was precipitated with acetonitrile to obtain the poly phenols. The product was concentrated using vacuum rotary evaporator at 40-50°C to obtain the dried extract. This dried extract was stored at 4°C in an airtight container until further use. Henceforth the poly phenols of *Symphyclocladia latiuscula* will be referred to as SLP throughout the paper.¹²

Test for Poly phenols (Folin-Ciocalteu Method)

The poly phenolic compound (20 µl) was mixed with 250 µl of dd H₂O and 250 µl of Folin-Ciocalteu reagent (Phenol reagent). Then 500 µl of 35% Na₂CO₃ was added followed by incubation at ambient temperature in the dark for 20 min. Blue color was observed which confirms the presence of poly phenols in the extract.¹³

Animals and Ethics Statement

Wistar rats of either sex weighing 200-250 g were used for the experiment. They were maintained in standard laboratory conditions at room temperature (22 ± 2 °C) and relative humidity (30-70%) with 12 h light/dark cycle. The animals were fed with conventional pellet diet and free access to water *ad libitum*. Animals were obtained from the animal house of Karnataka College of Pharmacy, Bangalore, India. The study protocols were approved by the Institutional Animal Ethics Committee (IAEC) (Ref. No: KCP-IAEC/4/18-19/4/8.9.2018). Studies were performed in accordance with the guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Government of India and New Delhi.

Acute Oral Toxicity

Female Albino Wistar rats were used in the study. Acute oral toxicity was performed as per OECD-423 guidelines.¹⁴ The animals were fasted overnight with water *ad libitum*. The starting dose of 5 mg/kg of poly phenols was administered orally to three animals in each group. If mortality was observed in two or three animals, then the dose administered was assigned as a toxic dose. If mortality was observed in one animal, then the same dose was repeated again in three animals to confirm the toxic dose. If mortality was not observed, the procedure was repeated for further higher doses such as 50, 300, and 2000 mg/kg body weight. Animals were observed individually after dosing at least once during the first 30 minutes, periodically during the first 24 hours, with special attention given during the first 4 hours and daily thereafter, for a total of 14 days.

Carrageenan induced paw edema for Anti-inflammatory activity

The anti-inflammatory activity was examined in rats, according to the method of Winter *et al.*¹⁵ Rats were taken and divided into 5 groups, each consisting of 6 animals. The testing activity was carried out only in the sub plantar region of the right hind paw by administration of carrageenan (s. c.) as the inducing agent. The paws in all the animals were marked with ink at the level of lateral malleolus. The various groups of animals were starved for overnight with only water before administering the drug. The various groups of animals were administered as follows:

- Normal group; Normal saline (10 ml/kg p.o.)
- Diseased group; 0.1 ml of 1% w/v Carrageenan in saline (s.c.)
- Standard group; Ibuprofen (200 mg/kg p.o.) 1 hr before injecting 0.1 ml of Carrageenan
- Low dose group; SLP (100 mg/kg p.o.) 1 hr before injecting 0.1 ml of Carrageenan
- High dose group; SLP (200 mg/kg p.o.) 1 hr before injecting 0.1 ml of Carrageenan

The increase in paw volume was measured by using mercury plethysmometer. Paw volume was measured immediately before and once an hour for 6 h after carrageenan injection. The anti-inflammatory effect was calculated as percentage inhibition in edema, obtained at each time interval using the following formula and reported.

$$\% \text{ inhibition of edema} = [1 - V_t/V_c] \times 100$$

Where, V_t is increase in paw volume in treated group and V_c is increase in paw volume in control group.

Carrageenan induced Pleurisy for Anti-inflammatory activity

The carrageenan induced pleurisy was determined in rats by the method of Mikami and Miyasaka.¹⁶ The grouping was similar to above model and the animals were administered as follows:

- Normal group; Normal saline (10 ml/kg p.o.)
- Diseased group; 0.2 ml of 1% Carrageenan in saline
- Standard group; Dexamethasone (2.5 mg/kg i.p.) 1 hr before injecting 0.2 ml of Carrageenan
- Low dose group; SLP (100 mg/kg p.o.) 1 hr before injecting 0.2 ml of Carrageenan
- High dose group; SLP (200 mg/kg p.o.) 1 hr before injecting 0.2 ml of Carrageenan

One hour after the last administration of drug, rats were lightly anaesthetized by thiopentone sodium (40 mg/kg i.p.), and then 0.2 ml of 1% carrageenan in normal saline was injected into the pleural cavity of each rat. 4 h after injection, rats were lightly anaesthetized, and blood samples were taken by cardiac puncture. The serum was separated and stored at -20°C for measurement of Malondialdehyde (MDA) and Superoxide Dismutase (SOD). Animals were then killed by an overdose of ether, and pleural cavities were exposed. The exudate volume was measured, and the pleural cavity was washed with 2 ml ice-cold phosphate-buffered saline (pH 7.2) with heparin (5 U/ml). The exudates and washing were combined as the pleural exudates for the measurement of total protein. Exudates contaminated with blood were discarded. The total leukocyte number in the pleural exudates was counted in a Neubauer chamber.

Splinted wound model for Wound healing activity

The wound healing activity was evaluated according to the method described by Morton and Malone.¹⁷ Rats were divided into 4 groups, each consisting of 6 animals. The fur on the dorsal thoracic region was removed. Then they were anesthetized by thiopentone sodium (40 mg/kg i.p.). 30 min later, two full thickness wound of circular area 19.62 mm² was made on the depilated ethanol sterilized dorsal thoracic region using biopsy punch. Animals were allowed to recover from anesthesia and housed individually in sterile cages. The animals were administered with Diclofenac Na (10 mg/kg i.p.) twice daily for a period of 3 days to avoid death due to pain. The drug was applied to the wounds once daily and the wounds were dressed using fresh cotton gauge and leucoplast tape. This was done till the wound got completely healed (usually it takes 12-14 days).

- Control group; Simple ointment
- Standard group; 10% povidone iodine ointment
- Low dose group; 100 mg/kg *Symphocladia latiuscula* poly phenols (SLP)
- High dose group; 200 mg/kg *Symphocladia latiuscula* poly phenols (SLP)

The wound area and period of epithelization were determined. Also, biochemical parameters, namely hydroxyproline,¹⁸ hexosamine¹⁹ and total protein contents²⁰ were determined from granulation tissue excised on the 15th day.

Histopathological Studies

Rats were sacrificed by high dose of chloroform on 15th day after beginning of experiment. The skin specimen of wound area was taken and preserved in 10% neutral formalin, processed and blocked with paraffin. 5 µm thick sections of tissue were taken and stained with hematoxylin and eosin (H and E) for further histopathological interpretations. Tissue sections were quantitatively assessed under a light microscope for congestion, edema, inflammatory cell infiltration, fibroblast proliferation, angiogenesis, epithelization, and collagen deposition.

Statistical analysis

All observations were expressed as mean ± SEM and calculation of the statistical significance (P value) was done by using ANOVA followed by Dunnett's test. A value of $p < 0.05$ was considered to be statistically significant.

RESULTS

Acute Oral Toxicity

No signs of toxicity or mortality were observed at 2000 mg/kg dose level. Hence, the LD₅₀ was found to be greater than 2000 mg/kg. 1/10th and 1/20th of this dose were selected (i.e. 200 mg/kg and 100 mg/kg respectively) and the experiment was carried out.

Effect of SLP on Carrageenan induced paw edema

SLP showed dose dependent inhibition after oral treatment as mentioned in Table 1. Up to 3 h, there was no significant reduction in the inflammation in any treatment group. The percent

inhibition against carrageenan induced edema was significant and found to be 25.64 % and 43.38 % by SLP at a dose of 100 mg/kg and 200 mg/kg ($p < 0.01$, $p < 0.001$) at the end of 6th h. The standard drug Ibuprofen showed the inhibition of inflammation by 41.02 % at 6th h which was more significant than 100 mg/kg of SLP ($p < 0.001$). The SLP at 200 mg/kg showed the strongest anti-inflammatory activity when compared among all groups.

Effect of SLP on Carrageenan induced pleurisy

The SLP showed decrease in inflammation after oral treatment as mentioned in Table 2. The oral treatment with 100 mg/kg and 200 mg/kg of SLP were effective in comparison with the diseased group as it significantly decreased the serum level of MDA, increased the levels of SOD, reduced the volume of pleural exudates, inhibited the production of total protein in the pleural exudates and reduced total leukocyte migration ($p < 0.001$, $p < 0.01$, $p < 0.05$). Dexamethasone, used as the reference drug, showed a similar effect on MDA, SOD and total protein, but it was significantly more potent on exudate volume and leukocyte number ($p < 0.001$). Both 100 mg/kg and 200 mg/kg of SLP were more effective than dexamethasone in decreasing MDA and total protein and increasing SOD.

Effect of SLP on Wound healing activity

A significant increase in the wound-healing activity was observed in rats treated with SLP compared to that of control group as shown in Table 3. SLP treated rats showed a significant reduction in the wound area with a percentage wound contraction being 41.51% and 53.28% at 4th day and 95.69% and 98.34% at 12th day ($p < 0.001$, $p < 0.01$, $p < 0.05$) at a dose of 100 mg/kg and 200 mg/kg respectively. The standard drug 10% povidone iodine contracted the wound area by 91.82% ($p < 0.05$) while wound area contraction in control group was 86.66% at the end of 12th day. Visual inspection of the wounds treated with SLP showed no evidence of bleeding, pus or inflammation at any time and all wounds healed without incident. The wounds treated with SLP were found to contract much faster.

Both the doses of SLP treated rats also showed significant reduction in the period of epithelization compared to that of the control group as shown in Table 4. The period of epithelization was less in SLP treated rats being 13.33 days and 14 days at 200 mg/kg and 100 mg/kg whereas standard group and control group had 14.83 and 15.16 days. Also, the wounds treated with 100 mg/kg and 200 mg/kg of SLP significantly increased the hydroxyproline, hexosamine and total protein contents in the granulation wound tissues of experimental rats compared with the control group ($p < 0.001$, $p < 0.01$, $p < 0.05$) as shown in Table 5.

Histopathological Analysis of Wounds

The histopathological analysis of the wounds treated with SLP showed better migration and proliferation of endothelial cells and thus better wound healing than that of standard and control groups. Treatment with SLP led to reduced congestion, edema, poly morpho nuclear leukocytes and mononuclear leukocyte infiltration which were present in control wounds. The SLP treated wounds showed re-epithelization, angiogenesis, fibroblast and collagen deposition faster than standard and control groups as shown in Table 6. The histopathological results of wounds of various groups are shown in Figure 1.

Table 1: Anti-inflammatory effect of SLP on Carrageenan induced Paw edema

Groups	1 hr	2 hr	3 hr	4 hr	5 hr	6 hr
Normal	0.010 ± 0.004	0.005 ± 0.002	0.010 ± 0.003	0.008 ± 0.004	0.008 ± 0.003	0.005 ± 0.003
Diseased	1.015 ± 0.004 ^{###}	1.210 ± 0.004 ^{###}	1.308 ± 0.003 ^{###}	1.205 ± 0.002 ^{###}	1.093 ± 0.002 ^{###}	0.975 ± 0.002 ^{###}
Ibuprofen (200 mg/kg)	0.620 ± 0.004 ^{***} (38.91%)	0.677 ± 0.002 ^{***} (44.04%)	0.735 ± 0.002 ^{***} (43.80%)	0.675 ± 0.002 ^{***} (43.98%)	0.605 ± 0.002 ^{***} (44.64%)	0.575 ± 0.002 ^{***} (41.02%)
100 mg/kg SLP	0.810 ± 0.005 ^{**} (20.19%)	0.855 ± 0.002 ^{**} (29.33%)	0.905 ± 0.002 ^{**} (30.81%)	0.832 ± 0.002 ^{**} (30.95%)	0.775 ± 0.002 ^{**} (29.09%)	0.725 ± 0.002 ^{**} (25.64%)
200 mg/kg SLP	0.635 ± 0.002 ^{***} (37.43%)	0.683 ± 0.002 ^{***} (43.55%)	0.733 ± 0.002 ^{***} (43.96%)	0.653 ± 0.002 ^{***} (45.80%)	0.595 ± 0.002 ^{***} (45.56%)	0.552 ± 0.002 ^{***} (43.38%)

Note: The figures in the parenthesis represent percentage inhibition of paw edema
n = 6 for all groups, values are expressed as mean ± SEM.

^{###}p < 0.001 when compared with normal group; ^{***}p < 0.001, ^{**}p < 0.01 when compared with diseased group

Table 2: Anti-inflammatory effect of SLP on Carrageenan induced Pleurisy

Groups	MDA (nmol/ml)	SOD (U/ml)	Exudate vol ^m (ml)	Protein (mg/ml)	Leukocyte no. (10 ³ /μl)
Normal	6.63 ± 0.76	240.10 ± 7.02	0.04 ± 0.02	15.10 ± 1.20	46.20 ± 12.0
Diseased	11.56 ± 1.15 ^{###}	202.20 ± 6.69	1.66 ± 0.11 ^{###}	30.3 ± 2.33 ^{###}	115.50 ± 13.0 ^{###}
Dexamethasone (2.5 mg/kg)	9.0 ± 2.20 ^{**}	220.40 ± 10.0	0.64 ± 0.13 ^{***}	23.00 ± 3.51 ^{**}	60.7 ± 12.5 ^{***}
100 mg/kg SLP	8.8 ± 2.06 ^{**}	221.30 ± 14.58	1.00 ± 0.19 ^{**}	21.30 ± 3.66 ^{**}	100.5 ± 16.3 [*]
200 mg/kg SLP	8.5 ± 1.98 ^{**}	225.60 ± 13.02	0.90 ± 0.17 ^{**}	18.00 ± 3.40 ^{***}	72.5 ± 15.5 ^{**}

n = 6 for all groups, values are expressed as mean ± SEM

^{###}p < 0.001 when compared with normal group

^{***}p < 0.001, ^{**}p < 0.01, ^{*}p < 0.05 when compared with diseased group

Table 3: Effect of SLP on wound area contraction

Groups	Day 0 (mm ²)	Day 4 (mm ²)	Day 8 (mm ²)	Day 12 (mm ²)
Control	19.782 ± 0.058	15.406 ± 0.060 (22.12%)	8.139 ± 0.037 (58.85%)	2.638 ± 0.032 (86.66%)
Povidone I ₂	19.809 ± 0.048	12.918 ± 0.061 [*] (34.78%)	6.272 ± 0.044 [*] (68.33%)	1.620 ± 0.022 [*] (91.82%)
100 mg/kg SLP	19.862 ± 0.106	11.616 ± 0.080 ^{**} (41.51%)	4.673 ± 0.034 ^{**} (76.47%)	0.855 ± 0.020 ^{**} (95.69%)
200 mg/kg SLP	19.809 ± 0.063	9.253 ± 0.053 ^{***} (53.28%)	3.235 ± 0.027 ^{***} (83.66%)	0.328 ± 0.011 ^{***} (98.34%)

Note: The figures in the parenthesis represent percentage of wound contraction

n = 6 for all groups, values are expressed as mean ± SEM

^{***}p < 0.001, ^{**}p < 0.01, ^{*}p < 0.05 when compared with control group

Table 4: Effect of SLP on period of Epithelization

Groups	Period of epithelization (days)
Control	15.16 ± 0.029
Povidone I ₂	14.83 ± 0.020
100 mg/kg SLP	14 ± 0.045
200 mg/kg SLP	13.33 ± 0.036

N = 6 for all groups, values are expressed as mean ± SEM

Table 5: Effect of SLP on Biochemical Parameters

Groups	Hydroxyproline (mg/g tissue)	Hexosamine (mg/g tissue)	Protein (mg/g tissue)
Control	45.7 ± 1.5	0.3 ± 0.04	115.4 ± 6.0
Povidone I ₂	48.3 ± 3.8	0.4 ± 0.02 [*]	118.6 ± 4.7
100 mg/kg SLP	52.5 ± 4.3 [*]	0.5 ± 0.03 ^{**}	130.5 ± 4.5 [*]
200 mg/kg SLP	55.6 ± 3.8 [*]	0.6 ± 0.03 ^{***}	143.8 ± 5.4 ^{**}

n = 6 for all groups, values are expressed as mean ± SEM

^{***}p < 0.001, ^{**}p < 0.01, ^{*}p < 0.05 when compared with control group

Table 6: Quantitative histopathological changes on day 15 after Skin wounding

Groups	Congestion	Edema	Infiltration		Necrosis	Fibroblasts	Angiogenesis	Epithelialization
			PMNLs	Monocytes				
Control	+	+	+	++	+	+	++	+
Povidone I ₂	+	+	+	++	-	++	++	++
100 mg/kg SLP	-	-	-	+	-	+++	+++	++
200 mg/kg SLP	-	-	-	+	-	+++	+++	+++

+: slight; ++: moderate; +++: marked; -: absent; PMNL: poly morphonuclear leukocyte

Figure 1: Histopathological changes on day 15 after wounding of a section of skin; control group showing a non epithelialized wound surface with the presence of necrosis (A); rats treated with povidone-iodine showing migrating epithelium at the edge (B); rats treated with poly phenols of *Symphyocladia latiuscula* showing wound surface with well-organized thick epithelium and fibrosis (C and D). Haematoxylin and eosin stain; scale bar = 100 µm

CONCLUSION

Inflammation is well orchestrated response to deleterious stimuli including tissue injury, and infection. It is elicited to restore normal condition of tissue or body. Inflammation has been indicated as a major cause in the development of several diseases in humans including neurological, cardiovascular, intestinal, dental, and renal disorders. Carrageenan is the phlogistic agent of choice for testing anti- inflammatory agents. The edematous response that occurs 0–2 h after carrageenan injection has been correlated with the exudative stage of inflammation, which is featured with the release of histamine, serotonin, and bradykinin. The late phase, occurring about 3 h after carrageenan exposure when edema reaches its peak volume, is characterized by the presence of prostaglandins

In the present study, we investigated the anti-inflammatory activity of SLP using carrageenan induced paw edema and carrageenan induced pleurisy and wound healing activity using splinted wound model. We found that oral treatment with SLP inhibits the inflammatory response, as judged by decrease in carrageenan-induced paw edema and decrease in volume of

pleural exudate, leukocyte number, total protein, MDA and increase in level of SOD. The results showed that SLP had potent effect on increasing the serum level of SOD, which implies that SLP scavenges oxygen radicals by enhancing the activities of antioxidant enzymes.

Wound healing is not a simple linear process in which growth factors trigger cell growth but is instead an integration of dynamic interactive processes involving cells, the ECM, and their receptors and soluble mediators. Collagen is a major component of connective tissue, and the repair process depends on regulated collagen production, accumulation, and subsequent maturation. The results of this study indicated that topical application of SLP had significant wound healing activity. Enhanced levels of hydroxyproline, hexosamine and total protein in treated rats provided strength to the regenerated tissue. The extract treated wounds exhibited marked dryness of wound margins with tissue regeneration and reduced wound area compared with controls, indicating the healing potential of the *Symphyocladia latiuscula*. Wound contraction is mediated by specialized myofibroblasts found in the granulation tissue. A greater degree of re-epithelialization and fibroblastic deposition observed in extract

treated wounds signifies the pro-healing effect of *Symphyclocladia latiuscula*.

The anti-inflammatory activity may be due to its ability to neutralize free radicals which are the main players in inflammation. It may have also suppressed the activation of pro inflammatory cytokines including NF-kB, TNF- α , IL-1 β and IFN- γ and the activity of cyclo oxygenase enzymes which are involved in inflammation. These results suggest that *Symphyclocladia latiuscula* possesses considerable anti-inflammatory and wound healing activity and may become a potential source of natural anti-inflammatory agent and therapeutic agent for wound healing and their associated complications.

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