



**A REVIEW ON PHARMACOLOGICAL IMPORTANCE OF MARINE
PHYTOCONSTITUENTS (CAULERPA SPECIES) IN INFLAMMATORY DISORDERS**

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ABSTRACT

Inflammations of the joints and other tissues observed in many diseases were reported to subside by using drugs from biological sources and these drugs are considered relatively safe. In this review, we focus to assess and state the feasibility of using Caulerpin, a phyto-constituent from marine sea weed *Caulerpa* species for its antinociceptive and anti-inflammatory actions and further prospective lines of works are discussed.

KEYWORDS: Marine algae, anti-inflammatory, Caulerpin.

INTRODUCTION

Seaweed is a relatively easy to obtain adequate, reliable and most importantly renewable supplies by aquaculture. Among the marine organism's seaweed is a promising candidate for drug production. Several metabolized products of polyunsaturated fatty acids i.e, oxylipins resembles human eicosanoid hormones and anomalous products of these compounds underlie several diseases related to inflammation. Hence eicosanoids and their derivatives have wide attention in the search of anti-inflammatory drugs (Radhika et al., 2013).

In the event of discovery of synthetic drugs for anti-inflammatory effects with due side effects, alternate, safe and effective drugs for inflammation from biological sources is becoming indispensable (Kaboli et al., 2001). Besides, non-steroidal anti-inflammatory drugs (NSAIDs) had been reported to contribute to mortality annually (Clegg et al., 2006; Wolf et al., 1999; Singh, 1998).

Nowadays, searches of natural medicinal herbs against inflammatory diseases, especially from marine organisms, Seaweed attracting the attention of many scientists and other countries in the world with the ability to withstand fluctuation in salinity around them, strong tidal current, variation in light intensity and constant

fluctuation in temperature, which are reflected by its adaptive properties influence its physical/morphological and biochemical constituents (Ehrlich, 2010) and it serves as an important source of bioactive compounds of medicinal value (Veena et al., 2007),

Analytical studies of microalgae indicate the presence of various bioactive compounds having anti-inflammatory potential (Bhakuni and Rawat, 2005). A vast number of scientific researchers on anti-inflammatory effect of seaweed encompass the medicinal activities of macroalgae which necessitates to narrow down to specific ones and focus on the further in-depth investigation will pave for future drug development with least toxicity effects (Irwandi and Hammed, 2011).

Among the three-main division of marine macroalgae (Chlorophyta, Phaeophyta, and Rhodophyta) *Caulerpa* is Chlorophyta genre in the family Caulerpaceae, widely distributed in tropical areas and more than 90 species of this green algae had been reported. This algae species was considered as valuable sources of structurally diverse bioactive compounds and remain largely unexploited in pharmaceutical areas (Wang et al. 2014). Secondary metabolites of *Caulerpa* species produce possible antinociceptive and anti-inflammatory activities (Everton et al., 2009).

In this review articles, we focused on the role of different phytoconstituents from *Caulerpa* species in inflammatory-related disorders and explore the feasibility of developing new active pharmacological agents for new drug development in drug research.

Caulerpa cupressoides

Purified lectin from the green marine algae *Caulerpa cupressoides* (*Cc*) exhibits the potential nociceptive and anti-inflammatory effect in Swiss male mice by using 0.8% acetic acid, 1% formalin-induced animal models. It represents an important marine phytoconstituents for future studies (Vanderlei *et al.*, 2010) as a novel antinociceptive and anti-inflammatory agent. In 2012, Rodrigues *et al.*, were reported the antinociceptive and anti-inflammatory property of three sulfated polysaccharides (SPs) fractions from *C. cupressoides* such as Cc-SP1, Cc-SP2, and Cc-SP3 using *in-vivo* models, the anti-inflammatory effect showed by decreasing neutrophils migration in induced area with the addition of anticoagulant and anti- and pro-thrombotic effect (Rodrigues *et al.*, 2012).

Caulerpa kempfii

Jones *et al.*, were established anti-inflammatory and antinociceptive effect phytoconstituents of *Caulerpa kempfii* genetic defect inflammation and immunoregulation by using albino mice in 2014. Matta *et al.*, 2015 revealed the potential anti-inflammatory effect of *Caulerpa kempfii* on hexane, ethyl acetate, and hydro-alcohol fractions.

Caulerpa mexicana

The sulfated polysaccharides of the *Caulerpa mexicana* (Cm-SPs) show the nociceptive and inflammatory effect (Carneiro *et al.*, 2014). Literature reveals the Cm-SPs represents for the pain and inflammatory agents as promising natural modulatory agents, since, it was reducing the second phase response in formalin test but didn't show a significant antinociceptive effect in hot-plate test.

Caulerpa racemosa

Indole alkaloids possess an indole ring its structure and present substitutions in a different position of the indole rings. Indole compounds are related to the metabolism of tryptophan and significant complex physiological role include those related to melatonin and serotonin (5-hydroxytryptamine) (Williams, 2001).

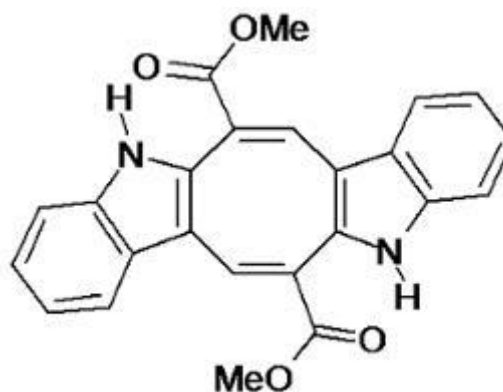


Figure-1: Structure of Caulerpin.

Caulerpin is a bisindolic alkaloid has an extra eight-member ring between the two indole rings which are incorporated directly with the carbonyl group with important biological activities such as antinociceptive and anti-inflammatory actions (De Souza *et al.*, 2009), antitumor, growth regulator and the plant root growth stimulant properties (Everton *et al.*, 2009).

Phytoconstituents form *Caulerpa racemosa* such as bis-indole alkaloids, sesquiterpenes, diterpenes, and sterols were responsible for inflammatory activity with additional pharmacological activities such as anti-tumor and antinociceptive activity (Ornano *et al.*, 2014). Sulfated polysaccharides of the *C. racemosa* possess the anti-inflammatory effect through the emoxigenase-1 pathway by the decrease in a number of leukocytes in the peritoneal cavities and reduced the levels of myeloperoxidase in the rat tissue with antinociceptive effect (Ribeiro *et al.*, 2014). Secondary metabolites of *C. racemosa* is Caulerpenyne (CPN) was recorded for its antiproliferative and apoptotic effects on two well-known neuroblastoma cell lines, SHSY5Y and Kelly. (Cavas *et al.*, 2006).

Caulerpa sertularioides

The potential anti-inflammatory effect of *Caulerpa sertularioides* extracts (methanolic, acetate, hexane and chloroform) showed by the inhibitions of leukocyte migration into the peritoneal cavity in carrageenan-induced peritonitis test, phytoconstituents exhibits the other pharmacological activities like antinociceptive activity (Da Matta *et al.*, 2011), antioxidant and antiproliferative activity (Osuna *et al.*, 2016), antibacterial activity (Esquer *et al.*, 2016).

S. No.	<i>Caulerpa</i> sps.	Pharmacological Activity	Method	Report	References
1	<i>Caulerpa racemosa</i>	Assessing function of seaweed extract	Effect of purified extracts on neuroblastoma cell lines	Secondary metabolites recorded for its antiproliferative and apoptotic effects on neuroblastoma cell lines,	Canvas et al., 2006
2	<i>Caulerpa racemosa</i>	Anti-inflammatory and antinociceptive effect	Caulerpin-metabolite on biological activity on murine models	Potential on Anti-inflammatory and antinociceptive effect confirmed and further studies continuing	Souza et al 2009
3	<i>Caulerpa racemosa</i>	Anti-inflammatory	Inhibition of carrageenan-induced paw edema with the extracts	Maximum inhibition of paw edema revealing the anti-inflammatory effect	Radhika et al 2013
4	<i>Caulerpa racemosa</i>	Molecular pattern	Phytochemical analysis	Anti-tumor, anti-inflammatory and antinociceptive actions inferred for <i>Caulerpa racemosa</i>	Ornano et al. 2014
5	<i>Caulerpa racemosa</i>	Assessing the effect of sulphated polysaccharides of <i>C.racemosa</i> (CrII)	In Swiss mice and Wistar rats the involvement of hemoxigenase-1 (HO-1) studied for its anti-inflammatory effect	CrII caused decreased and inflammation	Ribeiro et al. 2014
6	<i>Caulerpa cupressoides</i>	Assessing the effect Lectin from <i>C. cupressoides</i>	Extract on Swiss mice to observe the physiological effect	Probability on Anti-inflammatory and antinociceptive effect of <i>Caulerpa cupressoides</i> confirmed and need for further studies mentioned	Vanderlei et al. 2010
7	<i>Caulerpa cupressoides</i>	blood coagulation and thrombosis	Invivo effect – anti-coagulation and anti-/pro thrombotic effect on rats	Anti-inflammatory effect indicated by the reduction in paw-edema	Rodrigues et al. 2012
8	<i>Caulerpa kempfii</i>	Anti-inflammatory and antinociceptive effect	Extractions used to study the effect	Anti-inflammatory and antinociceptive actions observed	Matta et al. 2015
9	<i>Caulerpa Mexicana</i>	Anti-inflammatory and antinociceptive actions	Assessing anti-inflammatory and antinociceptive actions in Swiss mice	Cm-SPs seems to be a natural modulatory agent for pain and inflammatory condition	Carneiro et al 2014
10	<i>Caulerpa sertularioides</i>	Anti-inflammation	Assays of Extraction of <i>Caulerpa sertularioides</i> in laboratory mice	Anti-inflammatory and antinociceptive effect of <i>Caulerpa sertularioides</i> confirmed	Da Matta et al.2011
		Chemo- preventive activities of seaweeds	Extracts on anti-mutagenic activity anti-proliferative activity	highest antiproliferative inhibition	Osuno et al. 2016
		Extract effect of <i>C. sertularioides</i> on bacteria	Effect of extract on shrimp mortality due to vibriosis	Activation of antioxidant enzymes by the extracts	Esquer et al. 2016
		Anti-inflammatory effect of <i>C. sertularioides</i>	Extracts on antiproliferative inhibition	High yield of Extracts with antiproliferative inhibition	Ruiz et al. 2016

CONCLUSION

The lessening effects of extracts of *C.sertularioides* that triggers factors of RA is expected to lessen the disease progression and the production of allele-chemicals by *C.sertularioides* present in Indian Oceans needs to be explored further as there is possibility of relationship between production of bio-derivatives and its environment. Studies on the role *C. sertularioides* on autoimmune reaction and on major cells, fibroblasts, primary mediators and other cytokines, growth factors, reactive oxygen species, hydrolytic enzymes further, can be expected to offer lead drug(s) for synthesizing of novel drugs which will be a favorable choice in pharmacologic therapy for RA in future.

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