

## ANTIMICROBIAL EFFICACY OF MARINE BROWN ALGAE AGAINST ORAL PATHOGENS A REVIEW

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### **ABSTRACT**

*Oral diseases are ubiquitous in nature. The offending cause could be bacterial, fungal, and viral, as a result of oxidative stress, as a form of inflammation or uncontrolled proliferation of cells. Extensive research and development have been invested in the efforts to remove the burden of oral lesion from the society. Marine brown algae have been used as food and for various industrial benefits. These algae have been studied to possess certain properties which make them a great candidate for medical research. The unique facets of these marine brown algae included the antibacterial, antifungal, antiviral, antioxidant, anti-inflammatory and anti-cancer properties. Numerous in vitro studies and a few in vivo studies proclaimed the success in employing these algae for medicinal and dental use. Within the dental horizon literature claimed the use of such organisms in the fight against caries and periodontal diseases, in impression materials and in the field of dental implant logy. Brown algae provide a much more sustainable and naturally acquired remedy than synthetic medicines and their production.*

**KEYWORDS:** *Marine Brown Algae, Antibacterial, Antioxidant, Antifungal, Antiviral, Herbal Medicine, Traditional Medicine*

### **INTRODUCTION**

The oral cavity hosts many microorganisms of which a few are pathogenic causing dental diseases.<sup>1</sup> the most common dental disease is the dental caries. Microorganisms like Streptococcus mutants, Streptococcus oralis, and Streptococcus sanguis and play contributory roles for the development of the dental disease. Periodontal breakdown is often due to plaque build up surrounding the tooth structure.<sup>2,3</sup> Plaque contains an ecosystem of microorganisms such as Fusobacterium, Porphyromonas gingivalis and Actinomyces sp .These microorganisms are causative for a variety of dental issues which could lay the seeds for more serious medical conditions and life-threatening ailments. Oral cavity has been associated with various bacterial infections in spite of the oral cavity being protected by phagocytes, the flushing of saliva and the resilient oral epithelium. Such lesions become increasingly prevalent with patients having an immune compromised state such as Acquired Immuno-Deficiency Syndrome (AIDS), transplant patients, uncontrolled diabetes and chronic corticosteroid users (cancer patients).<sup>4,5</sup>

Algae belong to the Kingdom Protista and are eukaryotic organisms. All species of algae are photosynthetic and have a simple anatomy. Similar to the terrestrial plants, algae contain pigments that aid in photosynthesis with the use of sunlight. Algae are distributed in the freshwater as well as salt water bodies of the world. They are particularly abundant in number and variety in the tropical seas of southern India in the region of the Gulf of Mannar. <sup>6</sup> Algae can be broadly split

into three main groups based on their predominant pigmentation into the green (Chlorophyta), brown (Phaeophyta) and red (Rhodophyta) algae.<sup>7</sup> The penultimate, phaeophyta or brown algae are named so due to the presence of a xanthophyll pigment called fucoxanthin giving these algae a characteristic brown appearance.<sup>8</sup> A shift in the nature of use of these brown algae has been witnessed in recent times. These brown algae used traditionally as a food source have been inoculated in various research for the identification and exploitation of the phytochemicals they contain. Few of such potent bioactive molecules include: fucoidans, sterols, glycolipids and terpenoids.<sup>9,10</sup> These compounds have been employed against common ailments affecting mankind and have returned with positive outcomes. Among the various types of algae the marine macroalgae have shown higher potential for pragmatic use in dentistry. The antimicrobial effect of these organisms and their prospective use in the field of dentistry has been reviewed using a spectrum of literature in this article.

Marine algae or seaweeds are group of organisms with little tissue differentiation that grow along the sea shores. Seaweeds are available in different forms and sizes, and ranges from unicellular microscopic organisms (microalgae) to multi-cellular of great size (macroalgae).<sup>11</sup> Humans are closely associated with these algae in numerous ways as a source of food, feed, fertilizer, medicine and as phycocolloids.<sup>12</sup> Crude extracts of algae and their components exhibit medicinal values like antimicrobial, antiviral, antifungal, anticancer, antioxidant, and anti-inflammatory properties.<sup>13</sup>

Seaweeds have lipids, proteins, minerals, dietary fibres, fatty acids, essential amino acids, omega-3, vitamins A, B, C, and E, and polysaccharides.<sup>15</sup> It also contains abundant of biologically active phytochemicals that play important roles in health-promoting effects such as polyunsaturated fatty acids, terpenoids, xanthophylls, carotenoids, phycobilins, chlorophylls, polysaccharides, vitamins, sterols, tocopherol, and phycocyanins.<sup>16</sup> Fucoxanthin, a type of xanthophyll that acts as an accessory pigment in the chloroplasts of brown seaweed, has been reported to contain numerous health benefit properties including anti-microbial and anti-cancer.<sup>17</sup> It contains high amounts of polyphenols which exhibit high potential as natural antioxidants. The polyphenols in the seaweeds have been proven as free radical scavengers and antimicrobial agents and are used in the treatment of major degenerative and deficiency diseases.<sup>18</sup>

## ANTI BACTERIAL

Brown Seaweed is a type of seaweed. Antibacterial activities have been documented in crude extracts and isolated compounds from various brown seaweed species. Kim et al.(2011), showed that the ethanolic extract of *Laminaria japonica* has antimicrobial activity against oral bacteria, with MICs of 250 and 62.5 g/mL against *Actinomyces naeslundii* and *Actinomyces odontolyticus*, respectively, and 250 and 62.5 g/mL against *Fusobacterium nucleatum* and *Porphyromonas gingivalis*, respectively.

*Actinomyces naeslundii* and *Actinomyces odontolyticus* had minimal bactericidal concentrations of 500 and 250 g/mL, respectively. A dose-dependent impact was seen, as well as a change in cell surface texture in *Actinomyces odontolyticus* and *Porphyromonas gingivalis*.<sup>19</sup>

## Anti-Viral Properties

When tested in cell cultures, extracts from *Gracilaria bursa-pastoris* and other *Gracilaria* sp were ineffective against the Herpes simplex 1 virus (HSV) and the human immunodeficiency virus (HIV).<sup>20,21</sup> These extracts yielded the proteins granin BP and citrullinyl-arginine.<sup>22,23</sup> Methanol extract from dried *Gracilaria pacifica* was effective against Sindbis virus at a concentration of 200.0 g/mL, but not against H. simplex 1 at a concentration of 400 g/mL. *Gracilaria* sp extracts and

compounds with anti-HIV activity are also potent against other retroviruses including HSV. However, because bioactive chemicals from seaweed have been little explored, the pharmacodynamic mechanisms of antiretroviral action are yet unknown.<sup>24</sup>

### **Anti Fungal Properties**

Marine brown algae had shown appreciable resistance to common fungal pathogens. Shibu et al (2019) revealed the antifungal efficacy of a marine brown algae *Sargassum wightii* against *Candida albicans*, *Candida parapsilosis*, *Fusarium* sp., *Aspergillus flavus* and *Aspergillus fumigatus*. The microbial inhibitory zones showed an increased clearance with an increase in concentration of the extract. The phytoextract prepared using ethanol as solvent showed maximum antifungal effect.<sup>25</sup> A study on the effect of brown algae *Spatoglossum asperum* had shown positive antifungal effect against common fungal dermatophytes viz. *Candida albicans*, *Candida tropicalis*, *Trichophyton mentagrophytes* and a non dermatophyte *Aspergillus flavus*. The disc diffusion method had been employed with the discs being loaded with chloroform and methanolic extracts of the algae.<sup>26</sup> This antifungal property of *Spatoglossum asperum* could be employed for oral candidiasis and aspergillosis with further research. Similarly, Selvaraj et al reported that the chloroform extract of *Stoechospermum marginatum* showed moderate antifungal activity against *Trichophyton mentagrophytes*, *Aspergillus flavus* and *Candida albicans*.<sup>27</sup> Negara BFSP et al., identified phlorotannins as biomolecules with high antifungal efficacy. Phlorotannins are specifically found in brown seaweed; they are formed by the Golgi apparatus through the acetate-malonate pathway. The phlorotannins were extracted from marine brown algae *Ecklonia cava*, *Ecklonia stolonifera*, *Sargassum ringgoldianum*, *Ishige okamurae*, *Fucus vesiculosus*, and *Eisenia bicyclis*, as well as species in the genera *Cystophora* and *Fucus*. The minimum inhibitory concentration ranged from 3.9 to 31.3 mg/mL against *C. albicans*, *E. floccosum*, and *T. mentagrophytes*.<sup>28</sup> Such biomolecules could be isolated, stabilized and used as effective antifungal medications.

### **Anti Oxidant**

By chelating metal ions, phenolic substances can act as antioxidants, limiting radical production and enhancing the antioxidant endogenous system.<sup>29</sup> Natural antioxidants derived from plants can react quickly with these free radicals, slowing or stopping the progression of oxidative damage.<sup>30</sup> Antioxidants derived from natural sources can help extend the shelf life of foods. As a result, antioxidant consumption and/or the addition of antioxidants to food components may protect the body as well as the foods against these events.<sup>31</sup>

### **Anti-Inflammatory**

According to Bhakuni, D.S et al. (1992) these seaweeds have anti-inflammatory properties Bio active molecules.<sup>32</sup> Polysaccharide fractions from *Gracilaria verrucosa* were given orally and intraperitoneally to mice at a concentration of 4.0 mg/animal and demonstrated immunopotentiating activity that stimulated phagocytosis.<sup>33,34</sup>

### **Anti Cancer Property**

The anticancer potential of crude extracts of diverse brown algae derived from various marine locations against various cancer cell lines has been studied extensively. The enzymatic extract of *Ecklonia cava*, as well as its crude polyphenolic and polysaccharide fractions, demonstrated antiproliferative activity against marine colon cancer cell line (CT-26), human leukaemia (THP-1), mouse melanoma (B-16), and human leukaemia (U-937) cells in vitro. According to the nuclear staining experiment, the polyphenolic extract had the strongest activity against CT-26 cells (IC<sub>50</sub> = 5.1 g/mL) via

apoptotic cell death.<sup>35</sup> The importance of brown algae's in vitro anticancer potential for cancer therapy was highlighted by in vivo studies on tumour suppressive activity. The antiproliferative activity of crude extracts of ten Phaeophyta species isolated from the Brittany coasts against three human cancers, human leukaemic T cell lymphoblast (Jurkat), human Burkitt's lymphoma (Daudi), and human chronic myelogenous leukaemia (K562) cells, revealed that Sargassaceae sp., Dictyota dichotoma, and Desmarestia proved efficient in preventing cell growth. Padina pavonica and Cystoseira mediterranea brown algae had a substantial inhibitory effect on human breast adenocarcinoma (MCF-7) and human prostate cancer cells (DU 145, PC-3, and LNCaP) in a crude methanol extract recovered from the Aegean Shores of Turkey<sup>36,37</sup> The anti-tumor property of brown algae is established to be as a result of its ability to maintain an antiproliferative property by propagating apoptotic cell death. Such a valuable property could yield in cancer chemotherapeutic with improved efficiency and reduced side effects.

### APPLICATIONS IN DENTISTRY

**Anticariogenic** Phenolic chemicals compounds isolated from brown algae impede bacteria's biological processes by damaging the permeability of the bacteria's cell membrane, resulting in Dental Caries.<sup>38</sup> Sargasso micracanthum, a brown seaweed, has anti cryogenic efficacy against a variety of cariogenic bacteria, including Streptococcus mutans, Streptococcus pyogenes, and Streptococcus sobrinus. Strong anti-cariogenic action was also discovered for Dictyopteris undulata against Streptococcus mutans, Streptococcus sobrinus, and Streptococcus pyogenes. Peronospora arborescens, on the other hand, was found to have inhibitory effects on Streptococcus mutans and Streptococcus sobrinus. Sargassum muticum, on the other hand, displays anticariogenic effects against Streptococcus mutans. Ishige okamurae was found to exhibit potent inhibitory effects against Streptococcus mutants and Streptococcus pyroxenes, two cryogenic bacteria<sup>39</sup>

**Periodontal Diseases:** Periodontal disease affects the ligament periodontal tissue, specifically the gingiva, as well as the buffer network that connects teeth and alveolar bones. Gingivitis and periodontitis are two diseases that are frequently present in periodontal tissues. Brown algae is one of the natural substances that can be used to treat periodontal illnesses including gingivitis and periodontitis, as it contains tannins, saponins, phenols, flavonoids, iodine, steroids, and other compounds that function as antibacterial, antiviral, antifungal, and antioxidants.<sup>40</sup>

**Impression Material:** Brown algae, Sargassum polycystum is used as an irreversible hydrocolloid (alginate) material for taking dental impressions, Potassium alginate is a common component used in standard dental impression materials. The alginate impression material was composed of potassium alginate extracted from brown algae Sargassum polycystum. Ju et al have demonstrated that the functional group of the extracted potassium alginate had the same structure as the potassium alginate.<sup>41, 42</sup>

**Dental Implants:** The potential of the marine algae and their extracts has been harnessed to the benefit of the longevity of the dental implants and to reduce complications associated with implant placements. Alginates derived from marine brown algae had been used to coat over the implant surfaces to prevent implant contamination and infection post operatively. This is owing to the nature of bacteriostasis shown by these marine products.<sup>43,44</sup> Certain other marine red algae products AlgiPore (Dentsply Friadent, Mannheim, Germany) have been employed in sinus lift surgery as an alternate to the gold standard autogenous bone grafts. Ewers R, 2005 demonstrated that the marine-derived HA material ACA, in a mixture with approximately 10% autogenous collector bone and blood or platelet rich plasma, stimulated enough new bone in 6 months to allow implant osseointegration after 6 months with a high implant survival rate.<sup>45</sup> Merino JJ et al., 2019 had

demonstrated the effective detoxification effect of chronic supplementation with marine green algae *Chlorella vulgaris* in longstanding titanium implants and dental amalgam patients.<sup>46</sup>

## CONCLUSIONS

Marine brown algae has been traditionally used in medicine and culinary products. The recent surge in research for identification of potent biomolecules from brown algae has yielded in a positive and convincing result. A plethora of application await for these medicinally superior plants. The ease of procurement, availability in large numbers and cheap rates have made research and development feasible. In lieu of synthetic medicines and their production brown algae provide a much sustainable and naturally acquired remedy. However for the real life application of such marine algae to manifest immense clinical research and development have to take place.

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