ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/IJISRT24AUG1423

Recent Advances in the Therapeutic Potential of Fucoidan: A Comprehensive Review

Pavithra M
Department of Periodontics,
Tagore Dental College and hospital,
Rathinamangam, Melakottaiyur Post, Chennai-600127.

Dr. Bhuvaneswari Birla Bose
Professor and HOD,
Department of Periodontics,
Tagore Dental College and Hospital,
Rathinamangam, Melakottaiyur Post, Chennai-600127.

Dr. Juala Catherine
Reader,
Department of Periodontics,
Tagore Dental College and Hospital,
Rathinamangam, Melakottaiyur Post, Chennai-600127.

Abstract:- Fucoidan, a polysaccharide primarily comprised of l-fucose and sulfate groups possesses a unique chemical structure that underpins its notable therapeutic potential. Its remarkable biological functions such as antioxidant, anticarcinogenic, antiviral, anticoagulant, antithrombotic, immunoregulatory, and anti-inflammatory properties have gained substantial recognition in the global food and pharmaceutical industries. This review highlights recent advancements in understanding fucoidan's potential biological activities that could innovate treatments for oral infections and inflammatory diseases. A systematic search for relevant articles published between January 2000 and July 2024 was conducted across multiple databases, including PubMed, Scopus, Web of Science, and Google Scholar. Manual searches of references listed in the identified publications were conducted to ensure thorough coverage of the subject. The inclusion criteria focused on peer-reviewed articles in English-language, encompassing meta-analysis, randomized clinical trials, cohort studies, case-control studies and in vitro studies. Exclusion criteria comprised abstracts, opinion pieces, review articles not providing original analysis, and studies not directly addressing the therapeutic effects of fucoidan. This rigorous selection process aims to encapsulate the most significant and recent scientific evidence regarding the therapeutic applications of fucoidan. Fucoidans, with their diverse pharmacological properties, hold promising therapeutic potential which could emerge as a novel therapeutic option for treating wide range of diseases. Fucoidans have demonstrated anti-inflammatory properties, which may be beneficial in reducing inflammation related to periodontal diseases and other oral conditions. We anticipate that this review will serve as a foundational guide and inspire continued product development centered on fucoidan.

Clinical relevance to interdisciplinary dentistry:

- **Fucoidan, a polysaccharide rich in fucose holds wide pharmacological effects**
- **Enhancement of oral health outcomes through anti-inflammatory properties**
- **Antimicrobial activity against oral pathogens**
- **Wound healing property may aid in periodontal diseases.**

Keywords:- *Immunity; Inflammation; Leukocyte; Polysaccharides.*

I. INTRODUCTION

The marine environment recognized for its abundant chemical and biological diversity, acts as a distinctive source for cosmetics, dietary supplements, agrochemicals, and pharmaceuticals.[1] Recently, marine algae identified for their nutritional and medicinal value, contain bioactive compounds effective against allergies, cancer, hypertension, inflammation, obesity, oxidative stress, and thrombosis.[2,3,4] In the field of antimicrobial research, marine algae have been thoroughly investigated globally, revealing potential candidates such as algal lectins, halogenated furanones, bromo-diterpenes, phlorotannins, and sesquiterpenes.[5,6] The first extraction of fucoidan from brown algae species, such as Laminaria digitata, Ascophyllum nodosum, and Fucus vesiculosus, occurred in 1913. [7] This polysaccharide is highly hygroscopic and carries a negative charge.[8]

Fucoidan, which is rich in fucose, is located in the intercellular spaces and fibrillar cell walls of brown algae.[9] Its efficacy varies depending on the specific algal species, source and method of administration.[9]

The bioactivity of fucoidans is primarily determined by their structural characteristics, including fucose & sulfate content, sulfation position, and the substitution patterns of monomeric units in the backbone.[10,11] This review examines both the established and emerging cellular functions of fucoidan, offering a conceptual framework to support its ongoing development and application.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/IJISRT24AUG1423

II. MATERIALS AND METHODS

Studies on fucoidan published from January 2000 to July 2024 were searched across various databases, including PubMed, Scopus, Web of Science and Google Scholar. Manual searches of references from these publications ensured comprehensive coverage. The inclusion criteria focused on peer-reviewed articles in English-language, encompassing meta-analysis, randomized clinical trials, cohort studies, case-control studies and in vitro studies. Exclusions were abstracts, opinion pieces, non-analytical reviews, and studies not focused on fucoidan's therapeutic effects. This stringent selection process was designed to capture the most relevant and recent data on fucoidan's therapeutic potential.

III. SOURCES OF FUCOIDAN

Fucoidan can be sourced from various marine organisms, including sea cucumbers [12] and brown algae.[13] Numerous algae and invertebrates have been identified for their fucoidan content. Species such as Fucus vesiculosus, Chorda filum, Sargassum stenophyllum, Fucus distichus, Caulerpa racemosa, Dictyota menstrualis, Ascophyllum nodosum, Fucus evanescens, Fucus serratus, Padina gymnospora, Kjellmaniella crassifolia, Hizikia fusiforme, and Analipus japonicus have been identified for their fucoidan content.[14] Various studies have reported different extraction methods to obtain distinct types of fucoidan from these sources. [14]

IV. STRUCTURE OF FUCOIDAN

Commercially available fucoidan derived from Fucus vesiculosus consists of 44.1% fucose, 31.1% ash and 26.3% sulfate with trace amounts of amino glucose. [17] Its specific rotation, [α]D, is recorded at -123°.[15,16] Through methylation and alkali treatment analyses, Conchie and O'Neill identified the primary structural unit as 1,2-α-fucose, with most sulfate groups attached to the C-4 position of the fucose units.[17,18] Anno et al. successfully isolated L-fucose 4-sulfate from fucoidan, and the IR spectrum confirmed that the sulfate group is attached to the axial C-4 position of the L-fucopyranose unit.[19]

The structural model of fucoidan from Fucus vesiculosus proposed by Conchie was widely accepted for four decades. However, in 1993, Pankter et al. revised this model using GC/MS data from methylation analysis. [17,18] They proposed that the core region of fucoidan primarily comprises a polymer of α-(1→3)-linked fucose units, with sulfate groups attached to the C-4 position of some of these residues. Additionally, they suggested that fucose units are attached to this polymer, creating branched points approximately every 2-3 fucose residues within the chain (see Figure 1). [17,18] Patankar and co-workers also offered insights into the possible reasons for the discrepancies observed by Conchie. [20]

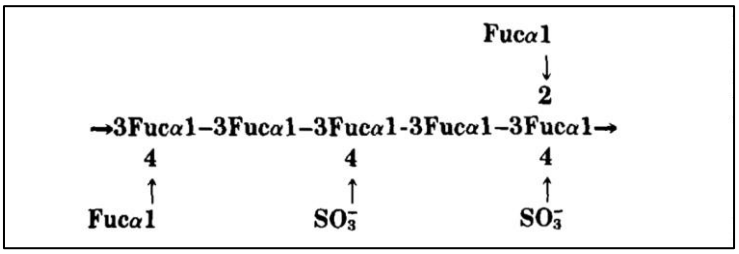

Fig 1. Pankter Model for the Structure of Fucoidan.[20]

Firstly, there was a variance in the preparation method. Conchie's research used fucoidan extracted with hot water, while Pankter used acid extraction, which has become the standard in commercial preparations.[20] Their methylation methods also differed. Additionally, Conchie analyzed the fucoidan structure based on the chromatographic and chemical characteristics of methylated products, whereas Pankter verified these products using Gas Chromatography-Electron Ionization Mass Spectrometry (GC-EIMS).[20]

Bilan et al. found that fucoidans obtained from the brown seaweedsFucus evanescens C. Ag, Fucus serratus L and Fucus distichus primarily comprised of fucose, sulfate, and acetate. [21,22]

The fucoidan from Fucus evanescens C.Ag. featured a linear backbone made up of alternating 3- and 4-linked α-L-fucopyranose 2-sulfate residues, structured as →3)-α-L-Fucp(2SO3−)-(1→4)-α-L-Fucp(2SO3−)-(1→.[23] In some instances, additional sulfate groups were located at position 4 of the 3-linked fucose residues, while other hydroxyl groups were randomly acetylated.[23]

The fucoidan from Fucus distichus was composed of repeating disaccharide units: →3)-α-L-Fucp-(2,4-di-SO3−)-(1→4)-α-L-Fucp-(2SO3−)-(1→. Although this fucoidan displayed a regular structure, the presence of random acetylation and some under-sulfation of the disaccharide units may somewhat obscure this regularity.[21]

Fucoidan from Fucus vesiculosus exhibits a simpler chemical composition compared to most fucoidans, which are more complex. In 1962, Schweiger isolated a polysaccharide from Macrocytis pyrifera, which showed a fucose-to-galactose ratio of 18:1.[21] This finding was the first to suggest that fucoidan is not just a fucan sulfate but a heteropolymer containing fucose, galactose, and small amounts of xylose. Later studies identified additional sugars such as mannose, xylose, glucose and glucuronic acid

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/IJISRT24AUG1423

(GlcA) in fucoidans from various brown seaweeds, further complicating structural analysis.[21]

V. BIOACTIVITY OF FUCOIDANS

A. Anticoagulant and Antithrombotic Activity

Anticoagulants are valuable in treating conditions like deep vein thrombosis, atrial fibrillation, disseminated intravascular coagulation (DIC), post heart-valve replacement etc.,[24] Heparin is a commonly used anticoagulant owing to its distinctive polyanionic properties but its clinical effectiveness is limited by the risk of causing hemorrhages and heparin-induced thrombocytopenia.[25] Alternative drugs with diminished side effects are therefore imperative, prompting the exploration and development of safer and more efficacious anticoagulants.[26] Fucoidan exhibits noteworthy anticoagulant effects, emerging as one of the most researched compounds in this regard. However, the mechanisms underlying these effects are intricate and contingent upon its structure.[27]

Nishino et al. extensively tested the anticoagulant activities of fucoidans from nine brown seaweed species, assessing parameters such as thromboplastin time (TT), activated partial thromboplastin time (APTT), and anti-factor Xa activity, and compared them with heparin (167 units/mg). [28] All fucoidans showed varying levels of thromboplastin time (TT) activity, ranging from 0 to 35 units/mg, and activated partial thromboplastin time (APTT) activity, ranging from 12 to 38 units/mg. However, anti-factor Xa activity was minimal across all fucoidans.[28] Notably, among the fucoidans tested, the sample from E. kurome showed the highest activity levels for both APTT (38 units/mg) and TT (35 units/mg). In contrast, the fucoidans from H. fusiforme exhibited APTT and TT activities of 25 units/mg and 22 units/mg, respectively. [28] Additionally, the F-4 fraction of fucoidan extracted from L. angustata var. longissima demonstrated an anti-thrombin activity of 200 units/mg, exceeding the activity of heparin, which generally measures around 140 units/mg.[29]

Cumashi et al. investigated the anticoagulant properties of fucoidans extracted from nine different species of brown algae. [30] Notably, all fucoidans—except those from Cladosiphon okamuranus, which contain substantial amounts of 2-O-α-D-glucuronopyranosyl branches within the linear (1→3)-linked poly-α-fucopyranoside chain—showed anticoagulant activity when evaluated using activated partial thromboplastin time (APTT). [30] Furthermore, only the fucoidans extracted from Laminaria saccharina, Fucus serratus, Laminaria digitata, Fucus evanescens, and Fucus distichus displayed strong antithrombin activity in platelet aggregation tests..[30] Evidence indicates that the anticoagulant efficacy of fucoidan is significantly influenced by several factors, such as its molecular weight (Mw), sulfate/total sugar ratio, degree of sulfation, sulfation pattern, and glycoside branching.[31]

Fucoidan and its derivatives demonstrate greater anticoagulant activity than low molecular weight heparin fractions (LMWF), highlighting the crucial role of molecular weight (Mw) and conformation in their effectiveness. [32] Chandía et al. effectively synthesized low molecular weight heparin fractions (LMWF) through free radical depolymerization, exhibiting notable anticoagulant activity.[32] Fucoidans hold potential applications, including anticoagulant and antithrombotic medications, with minimal side effects. Fucoidan can function as a valuable research tool for studying and discerning interconnected events like coagulation, bleeding, thrombosis, and platelet aggregation.

B. Anti-Tumour and Immunomodulatory Activity

The immunomodulatory activity of fucoidan is currently an active area of research. Fucoidan exhibits various pharmacological effects, including antiviral and antitumor activities by modulating cellular immune functions which is fucoidan's primary mechanism of action. Fucoidan binds to receptors such as Toll-like receptors (TLRs) on dendritic cells, macrophages, and other monocytes, stimulating the release of proinflammatory factors, chemokines and cytokines, thereby enhancing the immune response.[33] Fucoidan as an adjuvant, enhances protein expression and cytokine production in spleen conventional dendritic cells (cDCs), potentially benefiting tumour vaccine development.

Fucoidan boosts the positive impact of lactic acid bacteria on immune functions by improving the Th1/Th2 response.[33] Fucoidans derived from Laminaria japonica and Eisenia bicyclis have demonstrated effectiveness in combating sarcoma.[34] In vitro studies show that fucoidan from Laminaria japonica inhibits the growth of hepatoma QGY7703 cells, suppresses proliferation, and induces apoptosis in human lymphoma HS-Sultan cell lines.[34] Additionally, fucoidans from Laminaria saccharina, Fucus serratus, Laminaria digitata, Fucus distichus, and Fucus vesiculosus significantly reduced the adhesion of MDA-MB-231 breast carcinoma cells to platelets, helping to mitigate tumor metastasis..[30]

Alekseyenko et al. investigated the antitumor and antimetastatic effects of Fucus evanescens in mice with transplanted Lewis lung adenocarcinoma. A 10 mg/kg dose improved the antimetastatic effects of cyclophosphamide without affecting its antitumor activity, while a higher dose of 25 mg/kg increased its cytotoxic effects.[35] Additionally, fucoidans prevent tumor cells from adhering to various substrates.

Fucoidan markedly reduced the growth of peripheral blood mononuclear cells from ATL patients and HTLV-1-infected T-cell lines, while leaving normal cells largely unaffected.[34] It also stimulates the production of interferon-gamma (IFN-γ) and interleukin-1 (IL-1) in vitro, and enhances various immune cell functions, thereby boosting the antibody response to sheep red blood cells (SRBC) in vivo.[34] As biological response modifiers, polysaccharides like fucoidan enhance immune responses.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/IJISRT24AUG1423

In addition to directly inhibiting tumor cell growth, fucoidans also hinder the development and spread of tumor cells by enhancing the body's immune response.[34] It directly exerts cytotoxic effects on tumor cells, particularly on human HS-Sultan cells, by engaging caspase and ERK pathways.[34] Additionally, it boosts the number of macrophages and facilitates tumor destruction through type 1 T-helper (Th1) cell and NK cell responses.[34]

Studies have shown that fucoidan can effectively treat gastrointestinal ulcers caused by oral aspirin by modulating the immune response and decreasing inflammation. Fucoidan from Fucus vesiculosus stimulates the production of IL-6 and TNF-α in peritoneal macrophages.[33] However, the relationship between the structure of fucoidan and its immune regulatory activity remains debated. Khil'chenko et al. demonstrated that sulfate and acetyl groups significantly influence the immunomodulatory activity of fucoidan, reducing inflammatory cytokine release [33] laying the foundation for its development as a novel polysaccharide immunomodulator and tumor therapy agent.

C. Antiviral Activity

In the search for natural antiviral agents with carbohydrate properties, research on sulfated polysaccharides has shown antiviral effects both in vitro and in vivo. Fucoidan, in particular, compared to existing antiviral drugs exhibits antiviral effects with relatively low cytotoxicity.[36] he antiviral effectiveness of fucoidan largely depends on its structural features, such as sulfate group content, degree of sulfation, monosaccharide composition, molecular conformation, molecular weight (Mw) and stereochemistry.[37,38] The sulfate content and molecular weight (Mw) are crucial factors for antiviral activity, with evidence suggesting that higher Mw and sulfate content enhance this activity.[39] In particular, a sulfate group at the C-4 position of the (1–3)-linked fucopyranosyl unit appears essential for fucoidan's anti-HSV activity.[40]

Fucoidan has attracted interest for its broad-spectrum antiviral activity, as well as its low toxicity and resistance. It inhibits viral attachment to host cells by interacting with the positively charged regions of viral envelope glycoproteins, which are essential for virus binding, thus disrupting the infection process.[40]

Reports indicate that fucoidan's antiviral activity is due to its ability to enhance the phagocytic function of immune cells and stimulate humoral immunity. Fucoidan derived from Laminaria japonica demonstrates antiviral effects against both RNA and DNA viruses. Remarkably, fucoidan exhibits substantial antiviral effects against poliovirus III, ECHO6 virus, adenovirus III, coxsackie B3 virus, and coxsackie A16. It effectively prevents the development of cytopathic effects (CPE) and protects cultured cells from infections caused by these viruses. [43] Fucoidans extracted from Undaria pinnatifida (Mekabu), Stoechospermum marginatum, Undaria pinnatifida, Adenocystis utricularis, and Cystoseira indica demonstrate antiviral activities against both HSV-1 and HSV-2, without inducing cytotoxicity in Vero cell cultures.[46]

Additionally, fucoidans inhibit the replication of enveloped viruses such as human cytomegalovirus (HCMV) and human immunodeficiency virus (HIV).[44] Electron microscopy frequently shows agglutinated virions when they are mixed with fucoidan.[47] Orally administered fucoidan may suppress viral replication and bolster both innate and adaptive immune defense functions.[48]

Fucoidans, abundant in dietary brown seaweed products are consumed in Asia. Doh-ura et al. have shown that fucoidan derived from commonly consumed brown algae exhibits antiprion activity, delaying the onset of disease when administered following enteral prion infection.[49] Despite their potent antiviral activity in vitro, fucoidans face bioavailability challenges in vivo, like other polyanions.[50] Thus, enhancing fucoidan's therapeutic efficacy may require employing drug delivery systems. In conclusion, fucoidan shows great potential as a highly effective antiviral compound with low toxicity. Its broad-spectrum antiviral activity, coupled with appropriate drug delivery strategies, could pave the way for its expanded application in clinical settings.

D. Anti-Inflammatory Activity

The inflammatory response reflects the body's defense mechanism against inflammatory agents. Although excessive inflammation can be harmful and lead to tissue damage, it is essential for protecting the body against disease when properly regulated. [33] During the inflammatory response, the production of nitric oxide (NO) and the expression of inflammatory factors are heightened. Numerous human diseases are associated with inflammatory responses, including atherosclerosis, inflammatory disorders, diabetes, neurodegenerative diseases, chronic autoimmune conditions, and age-related illnesses. [33] Fucoidans extracted from nine different species of brown algae showed an ability to inhibit leucocyte recruitment in a rat inflammation model. The effectiveness of these fucoidans was not significantly influenced by their fucose and sulfate content or other structural features of their polysaccharide backbones. [33]

Fucoidan has been shown to inhibit the release of nitric oxide (NO) triggered by bacterial lipopolysaccharide, effectively reducing inflammation. Furthermore, fucoidan functions as a ligand for macrophage scavenger receptor A, facilitating its uptake by macrophages and the subsequent suppression of NO production. In addition, fucoidan's anti-inflammatory effects are also evident in its ability to inhibit leukocyte migration to inflamed tissues.[34]

Mekabu fucoidan helps reduce pulmonary inflammation and decrease Th2-dominated responses, indicating its potential for treating allergic inflammation. Yang et al. studied the effects of fucoidan on inducible nitric oxide synthase (iNOS) expression in the macrophage cell line RAW264.7 and found that a low concentration of fucoidan (10 μg/ml) enhanced the basal iNOS expression in

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/IJISRT24AUG1423

inactive macrophages. [33] Additionally, they discovered that fucoidan inhibited the release of nitric oxide (NO) in RAW264.7 cells stimulated by lipopolysaccharide (LPS). [33] This inhibition of activator protein 1 (AP-1) activation by fucoidan may be related to its NO-blocking and anti-inflammatory effects.[33]

Studies have shown that fucoidan derived from wakame decreases cyclo-oxygenase-2 expression in rabbit articular chondrocytes in a manner that is dependent on both dose and time, demonstrating its anti-arthritis effects.[33] Fucoidan has the ability to modulate the inflammatory response in individuals with advanced cancer. Additionally, fucoidan can work synergistically to boost the effectiveness of anti-inflammatory medications. For instance, chitosan nanoparticles loaded with ciprofloxacin and coated with fucoidan have proven effective in treating intracellular and biofilm infections caused by Salmonella.[33] Fucoidan, being a macromolecular substance, shows promising potential as a direct drug or food adjuvant compared to other small molecule anti-inflammatory drugs.[33]

E. Angiogenesis

Angiogenesis, essential for development, reproduction, and tissue repair, depends on a precise balance between pro-angiogenic factors and inhibitors. [33] When this balance is disrupted, the vascular system's ability to repair damaged blood vessels is impaired, highlighting the need for both pro-angiogenic and anti-angiogenic therapies.[33] The process involves proliferation, differentiation, and migration of mature endothelial cells, governed by various angiogenic factors such as vascular endothelial growth factor (VEGF), platelet-derived growth factor and fibroblast growth factor (FGF).[33]

Fucoidan, derived from brown seaweeds like Sargassum fusiforme, shows potential in cancer treatment by inhibiting angiogenesis. It disrupts angiogenesis by regulating endothelial cell plasminogen activator inhibitor 1 and VEGF. Furthermore, fucoidan affects chemokine CXCL12 and matrix metalloproteinases (MMPs) to restrict cell migration. Persulfated fucoidan also reduces basement membrane degradation, cell migration, and angiogenesis in human umbilical vein endothelial cells (HUVECs) on matrigel.

Furthermore, fucoidan exhibits pro-angiogenic effects by modulating heparin-binding growth factors, such as fibroblast growth factor (FGF-2). [33] At antithrombotic concentrations, it enhances FGF-2-induced angiogenesis by regulating angiogenic surface proteins expressions, notably α6. Low molecular weight fucoidan (LMWF) supports FGF-2-induced angiogenesis in human endothelial cells, which may assist in blood remodelling in ischemic regions. Recent research indicates that fucoidan activates C-Jun N-terminal kinase (JNK) and p38 through the AKT/MMP-2 signaling pathway in HUVECs.

Structural factors, particularly molecular weight (Mw), play a crucial role in determining fucoidan's pro-angiogenic and anti-angiogenic activities. For example, natural fucoidan with an Mw of 47.5 kDa and high sulfation levels effectively inhibits angiogenesis, while a derivative with lower Mw and reduced sulfate content shows diminished inhibitory effects. Fucoidan extracted from the marine brown alga L. japonica, with a molecular weight (Mw) of 30 kDa and high sulfate content, shows strong inhibition of angiogenesis. In contrast, fucoidan with an Mw of 15–20 kDa and low sulfation does not effectively inhibit tube formation in HUVECs, highlighting the importance of Mw and sulfation in fucoidan's anti-angiogenic properties. Generally, an Mw range of 20 to 30 kDa seems to be critical for its effectiveness.

F. Osteogenic Property

Fucoidan has been shown to boost the activity of various factors, such as basic fibroblast growth factor (FGF) and bone morphogenetic protein (BMP), by shielding molecules from enzymatic degradation and improving their interaction with specific receptors.[51]Studies has also associated fucoidan with bone and tissue regeneration, with the sulfate ester group of L-fucose playing a crucial role in these regenerative properties..[52] Recent studies have reinforced this finding, with research into biomaterials using poly L-glycolic acid and fucoidan showing that scaffolds incorporating fucoidan demonstrated enhanced osteogenic potential.[53]

Additionally, Igondjo et al. showed that fucoidan stimulated the expression of osteogenic differentiation markers, including collagen type I, alkaline phosphatase and mineral deposition, while also enhancing cell proliferation, thereby highlighting fucoidan's osteoconductive properties.[54] These findings indicate that fucoidan holds significant potential as a biomaterial for both bone regeneration and the creation of artificial bone in clinical settings.

G. Antibacterial property

Ke-Xin Yu et al conducted a study that demonstrated fucoidan's antibacterial activity against S. aureus through an antibacterial susceptibility test..[59] The effectiveness of fucoidan was attributed to its lower molecular weight compared to other antibacterial compounds, which was achieved through depolymerization methods as demonstrated by Omid Ashayerizadeh and colleagues.[55] Research by Maria Consuelo and her team has demonstrated that fucoidan possesses potent antibacterial properties, particularly against pathogens such as Salmonella enterica and Listeria monocytogenes.[56] The efficacy of fucoidan in inhibiting bacterial growth was found to depend on factors such as concentration, temperature, and exposure time to the pathogens. Additionally, Thangapandi Marudhupandi and coworkers explored fucoidan's antibacterial properties against human pathogenic agents like Salmonella typhi and Vibrio cholerae suggesting that it could serve as a safe antibiotic for treating various bacterial infections. [57] Their findings underscored the need for further research to elucidate the precise mechanism of action. Moreover, a study involving multiple bacterial strains including S. aureus, E. coli, B. licheniformis and S. epidermidis revealed that E. coli was particularly susceptible to fucoidan

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/IJISRT24AUG1423

compared to other strains. [58] These collective findings highlight the broad spectrum of antibacterial activity exhibited by fucoidan and its potential as an alternative antibiotic in combating bacterial infections.

VI. FUCOIDANS IN DENTISTRY

Fucoidans have shown promising potential in various applications within dentistry. Studies have demonstrated their antimicrobial activity against oral pathogens, making them potentially useful in combating dental caries and periodontal diseases. [59] The study on fucoidan extracted from Cladosiphon okamuranus Tokida revealed that highly purified fucoidan can alleviate chronic colitis in murine models by reducing interleukin-6 production in colonic epithelial cells.

Given the systemic effects of inflammation, this finding may suggest potential benefits for managing inflammatory conditions in the oral cavity, such as gingivitis and periodontitis. Chronic colitis involves inflammation and damage to the colonic mucosa.

The ability of fucoidan to ameliorate colitis implies its potential role in promoting mucosal healing. This could be relevant to oral mucosal conditions, including oral ulcers and mucositis, where promoting healing is essential.[60] Fucoidans have been found to possess anti-inflammatory properties that may help in reducing inflammatory conditions in the oral cavity, such as periodontal diseases and oral mucositis. [61 62] Additionally, fucoidan has been studied for its potential to enhance wound healing, which could be advantageous for managing oral wounds, such as those occurring after dental procedures.[59] Studies have assessed the biocompatibility of fucoidans for potential applications in dental materials, such as coatings for dental implants or scaffolds for tissue engineering.[63] This provides a starting point for exploring the potential uses of fucoidans in dentistry and their associated research findings.

VII. CONCLUSION

Fucoidan holds significant therapeutic potential, but comprehensive validation is needed to confirm its specific properties. Key research areas include pharmacokinetics, uptake, and biodistribution. Clinical trials are limited due to varied experimental models and a lack of comparative studies. Fucoidan's anti-inflammatory, antimicrobial, wound healing and immune-modulating effects show promise in dentistry for treating periodontal diseases and oral mucositis. Although initial results are promising, further detailed invivo and clinical trials are needed to establish safety and effectiveness. Despite challenges, fucoidan shows promise in inflammation modulation, cancer inhibition, viral suppression, and immune enhancement, potentially becoming a valuable natural therapy.

➢ *Financial Support And Sponsorship:*
Nil.

➢ *Conflicts Of Interest:*
There are no conflicts of interest.

REFERENCES

[1]. Blunt JW, Copp BR, Hu WP, Munro MH, Northcote PT, Prinsep MR. Marine natural products. Natural product reports. 2007;24(1):31-86.
[2]. Wang T, Ólafsdóttir GR, Jónsdóttir R, Kristinsson HG, Johannsson R. Functional and nutraceutical ingredients from marine macroalgae. Handbook of seafood quality, safety and health applications. 2010 Oct 1:508-21.
[3]. Alasalvar C, Miyashita K, Shahidi F, Wanasundara U, editors. Handbook of seafood quality, safety and health applications. John Wiley & Sons; 2011 Jun 15.
[4]. de Jesus Raposo MF, De Morais AM, De Morais RM. Marine polysaccharides from algae with potential biomedical applications. Marine drugs. 2015 May 15;13(5):2967-3028.
[5]. Swamy MA. Marine algal sources for treating bacterial diseases. Advances in food and nutrition research. 2011 Jan 1;64:71-84.
[6]. Jun JY, Nakajima S, Yamazaki K, Kawai Y, Yasui H, Konishi Y. Isolation of antimicrobial agent from the marine algae Cystoseira hakodatensis. International journal of food science & technology. 2015 Apr;50(4):871-7.
[7]. Mak W. Extraction, characterization and antioxidant activity of Fucoidan from New Zealand Undaria pinnatifida (Harvey) Suringar (Doctoral dissertation, Auckland University of Technology).2021
[8]. Cui K, Tai W, Shan X, Hao J, Li G, Yu G. Structural characterization and anti-thrombotic properties of fucoidan from Nemacystus decipiens. Int J Biol Macromol. 2018;120:1817-1822.
[9]. Ale MT, Mikkelsen JD, Meyer AS. Important determinants for fucoidan bioactivity: A critical review of structure-function relations and extraction methods for fucose containing sulfated polysaccharides from brown seaweeds. Mar Drugs. 2011 Oct;9(10):2106-30.
[10]. Fernando IPS, Dias M, Madusanka DMD, Han EJ, Kim MJ, Heo SJ, Lee K, Cheong SH, Ahn G. Low molecular weight fucoidan fraction ameliorates inflammation and deterioration of skin barrier in fine dust stimulated keratinocytes. Int J Biol Macromol. 2021; 168:620-630.
[11]. Jayawardena TU, Sanjeewa KK, Nagahawatta DP, Lee HG, Lu YA, Vaas A, Abeytunga DT, Nanayakkara CM, Lee DS, Jeon YJ. Anti-Inflammatory Effects of Sulfated Polysaccharide from Sargassum swartzii in Macrophages via Blocking TLR/NF-κB Signal Transduction. Mar Drugs. 2020;18(11):601.
[12]. Mansour MB, Balti R, Yacoubi L, Ollivier V, Chaubet F, Maaroufi RM. Primary structure and anticoagulant activity of fucoidan from the sea cucumber Holothuria polii. Int J Biol Macromol. 2019;121:1145-1153.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/IJISRT24AUG1423

[13]. Zhao Y, Zheng Y, Wang J, Ma S, Yu Y, White WL, Yang S, Yang F, Lu J. Fucoidan extracted from Undaria pinnatifida: Source for nutraceuticals/functional foods. Mar Drugs. 2018;16(9):321.
[14]. Luthuli S, Wu S, Cheng Y, Zheng X, Wu M, Tong H. Therapeutic effects of fucoidan: A review on recent studies. Marine drugs. 2019 Aug 21;17(9):487.
[15]. Black WAP, Dewar ET, Woodward FN. Manufacture of algal chemicals. IV. Laboratory-scale isolation of fucoidin from brown marine algae. J Sci Food Agric. 1952;3:122-129.
[16]. Nishino T, Nishioka C, Ura H. Isolation and partial characterization of a novel amino sugar-containing fucan sulfate from commercial Fucus vesiculosus fucoidan. Carbohydr Res. 1994;255:213-224.
[17]. Conchie J, Percival EGV. Fucoidin part II. The hydrolysis of a methylated fucoidin prepared from Fucus vesiculosus. J Chem Soc. 1950;827-833.
[18]. O'Neill AN. Degradative studies on fucoidan. J Am Chem Soc. 1954;76:5074-5076.
[19]. Anno K, Seno N, Ota M. Isolation of L-fucose 4-sulfate from fucoidan. Carbohydr Res. 1970;13:167-169.
[20]. Patankar MS, Oehninger S, Barnett T. A revised structure for fucoidan may explain some of its biological activities. J Biol Chem. 1993;268:21770-21776.
[21]. Bilan MI, Grachev AA, Ustuzhanina NE, Shashkov AS, Nifantiev NE, Usov AI. A highly regular fraction of a fucoidan from the brown seaweed Fucus distichus L. Carbohydr Res. 2004;339:511-517.
[22]. Bilan MI, Grachev AA, Shashkov AS, Nifantiev NE, Usov AI. Structure of a fucoidan from the brown seaweed Fucus serratus L. Carbohydr Res. 2006;341:238-245.
[23]. Bilan MI, Grachev AA, Ustuzhanina NE. Structure of a fucoidan from the brown seaweed Fucus evanescens C.Ag. Carbohydr Res. 2002;337:719-730.
[24]. Mourao PAS, Pereira MS. Searching for alternatives to heparin—Sulfated fucans from marine invertebrates. Trends Cardiovasc Med. 1999;9:225-232.
[25]. Suleria HAR, Masci PP, Zhao KN, Addepalli R, Chen W, Osborne SA, Gobe GC. Anti-coagulant and anti-thrombotic properties of blacklip abalone (Haliotis rubra): In vitro and animal studies. Mar Drugs. 2017;15:240.
[26]. Moll S, Roberts HR. Overview of anticoagulant drugs for the future. Semin Hematol. 2002;39:145-157.
[27]. Zayed A, Hahn T, Rupp S, Kramer R, Ulber R. Fucoidan as a natural anticoagulant, antiviral and anti-cancer drug. Naunyn-Schmiedebergs Arch Pharmacol. 2018;391
[28]. Nishino T, Nagumo T. Sugar constituents and blood-anticoagulant activities of fucose-containing sulfated polysaccharides in nine brown seaweed species. Nippon Nogeikagaku Kaishi. 1987;61:361-363.
[29]. Kitamura K, Matsuo M, Yasui T. Fucoidan from brown seaweed Laminaria angustata var. longissima. Agric Biol Chem. 1991;55(2):615-616.
[30]. Cumashi A, Ushakova NA, Preobrazhenskaya ME, D'Incecco A, Piccoli A, Totani L, Tinari N, Morozevich GE, Berman AE, Bilan MI, Usov AI, Grachev AA, Sanderson CJ, Kelly M, Rabinovich GA, Iacobelli S. A comparative study of the anti-inflammatory, anticoagulant, antiangiogenic, and antiadhesive activities of nine different fucoidans from brown seaweeds. Glycobiology. 2007;17:541-552.
[31]. Nishino T, Nagumo T, Kiyohara H, Yamada H. Studies on polysaccharides from Ecklonia kurome. 2. Structural characterization of a new anticoagulant fucan sulfate from the brown seaweed Ecklonia kurome. Carbohydr Res. 1991;211:77-90.
[32]. Chandia NP, Matsuhiro B. Characterization of a fucoidan from Lessonia vadosa (Phaeophyta) and its anticoagulant and elicitor properties. Int J Biol Macromol. 2008;42:235-240.
[33]. Wang Y. Biological activities of fucoidan and the factors mediating its therapeutic effects: a review of recent studies. Int J Biol Macromol. 2021;156:1235-1243.
[34]. Li B, Lu F. Fucoidan: Structure and bioactivity. Mar Drugs. 2020;18(9):419.
[35]. Lin Y, Qi X, Liu H, Xue K, Xu S, Tian Z. The anti-cancer effects of fucoidan: A review of both in vivo and in vitro investigations. Cancer Cell International. 2020 May 7;20(1):154.
[36]. Queiroz KCS, Medeiros VP, Queiroz LS, Abreu LR, Rocha HAO, Ferreira CV, et al. Inhibition of reverse transcriptase activity of HIV by polysaccharides of brown algae. Biomed Pharmacother. 2008;62:303-307.
[37]. Adhikaria U, Mateub CG, Chattopadhyaya KC, Pujolb A, Damonteb EB, Ray B. Structure and antiviral activity of sulfated fucans from Stoechospermum marginatum. Phytochemistry. 2006;67:2474-2482.
[38]. Thuy TTT, Ly BM, Van TTT, Quang NV, Tu HC, Zheng Y. Anti-HIV activity of fucoidans from three brown seaweed species. Carbohydr Polym. 2015;115:122-128.
[39]. Genga Raj SR, Ng CH, Mohd-Said S, Yu KX. Antibacterial potential of aqueous extracts and compounds from selected Brown seaweeds. INNOSC Theranostics Pharmacol Sci. 2019;2(1):29–3
[40]. Duarte MER, Noseda DG, Noseda MD, Tulio S, Pujol CA, Damonte EB. Inhibitory effect of sulfated galactans from the marine alga Bostrychia montagnei on herpes simplex virus replication in vitro. Phytomedicine. 2001;8:53-58.
[41]. Lee JB, Hayashi K, Hashimoto M, Nakano T, Hayashi T. Novel antiviral fucoidan from sporophyll of Undaria pinnatifida (Mekabu). Chem Pharm Bull (Tokyo). 2004;52:1091-1094.
[42]. Harden EA, Falshaw R, Carnachan SM, Kern ER, Prichard MN. Virucidal activity of polysaccharide extracts from four algal species against herpes simplex virus. Antivir Res. 2009;83:282-289.
[43]. Li F, Tian TC, Shi YC. Study on anti virus effect of fucoidan in vitro. J N Bethune Univ Med Sci. 1995;21:255-257.

ISSN No:-2456-2165 https://doi.org/10.38124/ijisrt/IJISRT24AUG1423

[44]. Zong AZ, Cao HZ, Wang FS. Anticancer polysaccharides from natural resources: A review of recent research. Carbohydr Polym. 2012;90:1395-1410.
[45]. Hemmingson JA, Falshaw R, Furneaux RH, Thompson K. Structure and antiviral activity of the galactofucan sulfates extracted from Undaria pinnatifida (Phaeophyta). J Appl Phycol. 2006;18:185-193.
[46]. Mandal P, Mateu CG, Chattopadhyay K, Pujol CA, Damonte EB, Ray B. Structural features and antiviral activity of sulphated fucans from the brown seaweed Cystoseira indica. Antivir Chem Chemother. 2007;18:153-162.
[47]. Lapshina L, Reunov A, Nagorskaya V, Zvyagintseva T, Shevchenko N. Inhibitory effect of fucoidan from brown alga Fucus evanescens on the spread of infection induced by tobacco mosaic virus in tobacco leaves of two cultivars. Russ J Plant Physiol. 2006;53:246-251.
[48]. Hayashi K, Nakano T, Hashimoto M, Kanekiyo K, Hayashi T. Defensive effects of a fucoidan from brown alga Undaria pinnatifida against herpes simplex virus infection. Int Immunopharmacol. 2008;8:109-116.
[49]. Doh-ura K, Kuge T, Uomoto M, Nishizawa K, Kawasaki Y, Iha M. Prophylactic effect of dietary seaweed fucoidan against enteral prion infection. Antimicrob Agents Chemother. 2007;51:2274-2277.
[50]. Luscher-Mattli M. Polyanions—A lost chance in the fight against HIV and other virus diseases? Antivir Chem Chemother. 2000;11:249-259
[51]. Pereira J, Portron S, Dizier B, Vinatier C, Masson M, Corre P, et al. The in vitro and in vivo effects of a low-molecular-weight fucoidan on the osteogenic capacity of human adipose-derived stromal cells. Tissue Eng Part C Methods. 2011;17(0):557–68.
[52]. D P, S GP, J C, Amm G, L P. Fucoidan - a valuable source from the ocean to pharmaceutical. Front Drug Chem Clin Res. 2020;3(1):1–4.
[53]. Yoo YI, Ko KW, Cha SG, Park SY, Woo J, Han DK. Highly effective induction of cell-derived extracellular matrix by macromolecular crowding for osteogenic differentiation of mesenchymal stem cells. J Ind Eng Chem. 2022;107:391–400.
[54]. Igondjo Tchen Changotade S, Korb G, Bassil J, Barroukh B, Willig C, Colliec-Jouault S, et al. Potential effects of a low-molecular-weight fucoidan extracted from Brown algae on bone biomaterial osteoconductive properties. J Biomed Mater Res A. 2008;87(3):666–75. doi:10.1002/jbm.a.31819
[55]. Ashayerizadeh O, Dastar B, Pourashouri P. Study of antioxidant and antibacterial activities of depolymerized fucoidans extracted from Sargassum tenerrimum. Int J Biol Macromol. 2020;151:1259–1266.
[56]. Poveda-Castillo GDC, Rodrigo D, Martinez A, Pina-Perez M. Bioactivity of Fucoidan as an antimicrobial agent in a new functional beverage. Beverages. 2018;4(3):64–13.
[57]. Marudhupandi T, Kumar TTA. Antibacterial effect of fucoidan from Sargassum wightii against the chosen human bacterial pathogens. Int Curr Pharm J. 2013;2(10):156–158.
[58]. Ayrapetyan ON, Obluchinskaya ED, Zhurishkina EV, Skorik YA, Lebedev DV, Kulminskaya AA, et al. Antibacterial properties of fucoidans from the Brown algae fucus vesiculosus l. of the barents sea. Biology. 2021;10(1):67–17.
[59]. Maeda H, Hosokawa M, Sashima T, Funayama K, Miyashita K. Fucoxanthin from edible seaweed, Undaria pinnatifida, shows antiobesity effect through UCP1 expression in white adipose tissues. Biochem Biophys Res Commun. 2007;332(2):392–397.
[60]. Shibata H, Kimura-Takagi I, Nagaoka M, Hashimoto S, Sawada H, Ueyama S. Highly purified fucoidan derived from Cladosiphon okamuranus Tokida ameliorates murine chronic colitis through the down-regulation of interleukin-6 production on colonic epithelial cells. Clin Exp Immunol. 2013;173(3):491–498.
[61]. Fitton JH, Stringer DN, Karpiniec SS. Therapies from fucoidan: An update. Mar Drugs. 2015;13(9):5920–5946.
[62]. Hyun JH, Kim SC, Kang JI, Kim MK, Boo HJ, Kwon JM, et al. Apoptosis inducing activity of fucoidan in HCT-15 colon carcinoma cells. Biol Pharm Bull. 2015;28(2):44–47.
[63]. Ale MT, Mikkelsen JD, Meyer AS. Important determinants for fucoidan bioactivity: A critical review of structure-function relations and extraction methods for fucose-containing sulfated polysaccharides from brown seaweeds. Mar Drugs. 2011;9(10):2106–2130.