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A systematic review on marine-derived fucoidan as a nutritional therapeutic in periodontal disease

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Abstract

Introduction: Fucoidan is a naturally occurring sulfated polysaccharide derived from brown seaweeds such as *Fucus vesiculosus*, *Laminaria japonica*, and *Undaria pinnatifida*. As a nutritive agent, fucoidan modulates tsystemic health through its bioactive components that influence metabolic, immune, and cellular functions. Its anti-inflammatory properties have a promising role in mitigating chronic low-grade inflammation, which underlies many systemic and oral diseases. Fucoidan is recently reported to possess significant antibacterial activity and the evidence regarding its use for periodontal diseases is scattered. **Objective:** Critical evaluation of the efficacy of fucoidan on periodontal pathogens using the existing evidence. **Methods:** Literature search was done on PubMed, Cochrane, Scopus, etc, according to PRISMA guidelines. Relevant articles were collected and evidence was tabulated. **Results:** The collected evidence indicated that fucoidan shows multifaceted therapeutic potential regarding periodontal diseases through multiple mechanisms like modulation of microbial virulence, reduction of inflammation, and boosting host–pathogen balance. **Conclusion:** Fucoidan exhibited promising antimicrobial, antibiofilm, and anti-inflammatory properties against periodontal pathogens.

Keywords: Fucoidan. Periodontal biofilm. Antibacterial. Antiinflammatory. Periodontal pathogens.

Introduction

Periodontal disease is a highly prevalent oral health issue primarily caused by accumulation of bacterial biofilm **[1]**. *Porphyromonas gingivalis*, *Treponema denticola*, and *Aggregatibacter actinomycetemcomitans* are reported to play a major role in both initiation and progression of periodontal inflammation and destruction **[2]**. The interaction between the triad of pathogens, host immune response, and the environmental factors together lead to periodontal inflammation, consequent tissue destruction, and eventual tooth loss. Management of periodontal diseases often necessitates managing the microbial component in addition to modulating inflammatory responses **[3]**.

Fucoidan is a sulfated polysaccharide that is derived from various brown seaweeds. In recent years, it has gained attention as a functional nutraceutical with significant health-promoting properties. As a nutritive agent, fucoidan contributes to systemic health through its bioactive components that influence metabolic, immune, and cellular functions. Unlike conventional nutrients that primarily provide energy or structural components, fucoidan acts as a bioactive dietary polysaccharide, exerting regulatory effects on physiological processes. It is rich in fucose and sulfate groups, which are responsible for its diverse biological activities. When consumed, fucoidan interacts with the gastrointestinal tract, where it may function as a prebiotic, modulating gut microbiota composition and promoting the growth of beneficial bacteria. This, in turn, enhances nutrient absorption, immune function, and overall metabolic health.

It has recently gained a significant attention due to its broad-spectrum of biological activities such as antimicrobial, anti-inflammatory, and biofilm-disrupting properties **[4,5]**. It has been used in Asian medicine in the olden days and has demonstrated effectiveness in various health applications, ranging from cancer therapy to wound healing. Its unique molecular structure of high sulfate content has led to interaction with microbial cell wall leading to its therapeutic actions such as inhibiting the adhesion and biofilm formation **[6]**.

Recent studies highlight fucoidan's efficacy against periodontal pathogens, suggesting its potential as an adjunctive treatment in periodontal therapy **[7]**. *In vitro* and *in vivo* models have shown that fucoidan not only exhibits antimicrobial properties but also modulates inflammatory pathways by downregulating pro-inflammatory cytokines such as IL-1β and TNF-α. This dual action may be of use in synergistic management of periodontal diseases in the microbial and inflammatory aspect of the disease **[8]**. Considering the potential, evidence regarding use of fucoidan for periodontal diseases is scattered. Therefore, this systematic review is done to critically evaluate the efficacy of fucoidan on periodontal pathogens.

Materials and Methods

The topic was searched in PROSPERO in which we have not registered. The protocol adhered strictly to PRISMA 2020 guidelines (Table 1) (Figure 1).

Population

- Individuals with periodontal disease (e.g., gingivitis, periodontitis)
- Studies involving periodontal pathogens (*Porphyromonas gingivalis*, *Treponema denticola*, *Aggregatibacter actinomycetemcomitans*, *Prevotella intermedia*, etc.)

Intervention

- Fucoidan (natural or synthetic sulfated polysaccharides from brown seaweed
- Fucoidan-based therapies (e.g., extracts, nanoparticles, gels, or mouthwashes)

Comparators

- Placebo or no treatment
- Standard periodontal treatments (e.g., chlorhexidine, antibiotics)
- Other natural antimicrobial agents

Outcomes

- Reduction in periodontal pathogens (quantitative microbial data, biofilm inhibition)
- Changes in clinical periodontal indices (e.g., bleeding on probing, pocket depth, clinical attachment level)
- Anti-inflammatory effects (e.g., cytokine levels, tissue inflammation)
- Safety and tolerability

Inclusion criteria

- English language articles
- Randomized controlled trials (RCTs)
- *In vitro* studies evaluating fucoidan's efficacy on periodontal pathogens
- Animal studies investigating periodontal outcomes with fucoidan
- Clinical trials and observational studies

Exclusion Criteria

- Reviews, letters and editorials
- Fucoidan tested for non-periodontal microbiological uses

Table 1. Search Strategy.

PubMed	fucoidan OR "sulfated polysaccharide" OR "brown seaweed extract" AND (periodontal OR "periodontal disease" OR periodontitis OR gingivitis OR "oral biofilm" AND "Porphyromonas gingivalis" OR "Aggregatibacter actinomycetemcomitans" OR "Treponema denticola" OR "Prevotella intermedia" AND efficacy OR antimicrobial OR antibacterial OR "biofilm inhibition" OR "anti-inflammatory"
Cochrane Library	fucoidan OR "sulfated polysaccharide" OR "brown seaweed extract" AND periodontal OR "periodontal disease" OR periodontitis OR gingivitis OR "oral biofilm" AND "Porphyromonas gingivalis" OR "Aggregatibacter actinomycetemcomitans" OR "Treponema denticola" OR "Prevotella intermedia" AND efficacy OR antimicrobial OR antibacterial OR "biofilm inhibition" OR "anti-inflammatory"

Scopus	TITLE-ABS-KEY fucoidan OR "sulfated polysaccharide" OR "brown seaweed extract" AND periodontal OR "periodontal disease" OR periodontitis OR gingivitis OR "oral biofilm" AND "Porphyromonas gingivalis" OR "Aggregatibacter actinomycetemcomitans" OR "Treponema denticola" OR "Prevotella intermedia" AND efficacy OR antimicrobial OR antibacterial OR "biofilm inhibition" OR "anti-inflammatory"
Proquest	fucoidan OR "sulfated polysaccharide" OR "brown seaweed extract" AND (periodontal OR "periodontal disease" OR periodontitis OR gingivitis OR "oral biofilm" AND "Porphyromonas gingivalis" OR "Aggregatibacter actinomycetemcomitans" OR "Treponema denticola" OR "Prevotella intermedia" AND efficacy OR antimicrobial OR antibacterial OR "biofilm inhibition" OR "anti-inflammatory"
Google Scholar	fucoidan OR "sulfated polysaccharide" OR "brown seaweed extract" AND periodontal OR "periodontal disease" OR periodontitis OR gingivitis OR "oral biofilm" AND "Porphyromonas gingivalis" OR "Aggregatibacter actinomycetemcomitans" OR "Treponema denticola" OR "Prevotella intermedia" AND efficacy OR antimicrobial OR antibacterial OR "biofilm inhibition" OR "anti-inflammatory"

Source: Own authorship.

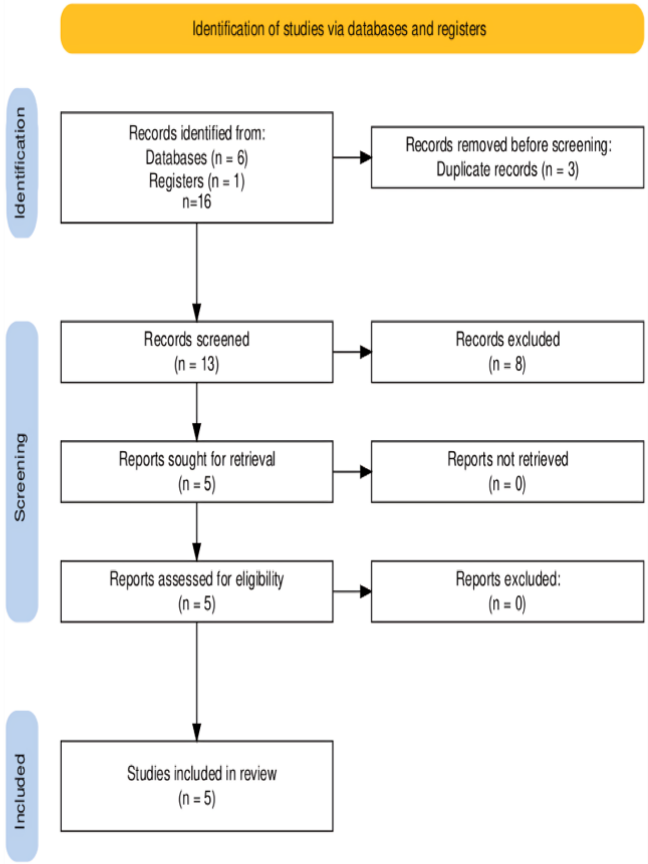

Figure 1. PRISMA Flow Chart. Source: Own authorship.

Results

Tool used to analyse risk of bias is QUIN and SYRCLE tool was used for analysing risk of bias in animal studies (Figure 2). All the *in vitro* studies reported 4 to 6 domains indicating low to moderate bias. *In vivo* studies also demonstrated low to moderate risk of bias (Tables 2-5).

Table 2. Data Extraction Table.

Author year	**Country**	**Study type**	**Population / model**	**Type of fucoidan intervention**	**Control group / comparator**	**Microbe tested**	**Outcome (key results)**
Jun et al (2018) **[9]**	Korea / Japan (authors from Korea & Japan)	*In vitro* antimicrobial & antibiofilm assays	Bacterial cultures / dental plaque bacteria	Sulfated polysaccharides (including fucoidan from Fucus vesiculosus, various fractions; tested at µg/mL concentrations)	Untreated bacteria / nocompound controls (and comparator polysaccharides)	*Streptococcus mutans, Streptococcus sobrinus* and other dental plaque bacteria tested	MICs reported between 125– 1000 µg/mL for tested strains; biofilm formation suppressed (complete inhibition of formation at ≥ ~250 µg/mL for some trains), but established biofilms were not eradicated.
Lee et al (2013) **[10]**	Korea (authors affiliated in Korea)	*In vitro* antimicrobial & synergy testing	Bacterial cultures (oral pathogens, lab strains/clinical isolates)	Fucoidan (various sources/species) alone and in combination with antibiotics (ampicillin, gentamicin)	Antibiotics alone and untreated controls	Oral pathogenic bacteria tested (including periodontal and cariogenic strains in the study)	Fucoidan alone had measurable MIC/MBC ranges; when combined with antibiotics MIC/MBC values for antibiotics were reduced (synergy) — combination reduced MIC/MBC to as little as 1/2 to 1/8 of original values.

Nagraj et al (2022) **[11]**	India	*In vitro* microbiological study (agar diffusion, MIC/MBC)	Periodontal pathogen cultures (lab isolates)	Brown seaweed (Sargassum wightii) extract (crude leaf extract; fucoidancontaining)	Untreated controls	P.Gingivalis (Pg), F.Nucleatum (Fn), *T.Forsythia (Tf) and A. Actinomycetemcomitans* (Aa).	Demonstrated zones of inhibition and MIC/MBC ranges (abstract/summary notes antibacterial efficacy; reported MICs in microgram range in available PDF).
Tang et al (2022) **[12]**	China	*In vitro* (nanomaterial development) — dentinal tubule + biofilm model	Enterococcus faecalis biofilm and infected dentinal tubule ex vivo/*in vitro* models	Fucoidanderived carbon dots (FDCDs; synthesized via hydrothermal method)	Untreated controls / conventional disinfectants	*Enterococcus faecalis* (biofilm model)	FDCDs displayed excellent inhibition of E. faecalis biofilms, penetrated dentinal tubules, and reduced bacterial load; showed good dispersibility and biocompatibility in assays.
Alsac et al (2013) **[13]**	France	*In vivo* experimental (animal) inflammatory/aneurysm model with Porphyromonas gingivalis exposure	Animal model (experimental aneurysm model with weak pathogen contamination)	Systemic/local fucoidan treatment (regimen described in paper)	Vehicle / nofucoidan controls	Porphyromonas gingivalis was used to stimulate pathology; outcomes measured were neutrophil activation and aneurysm enlargement	Fucoidan decreased neutrophil activation and limited P. gingivalis-induced aneurysm enlargement in the model.

Source: Own authorship.

Table 3. Risk of Bias for *in vitro* studies.

Mechanistic Category	Experimental Evidence (Study)	Proposed Mechanism of Action	Observed Effects / Key Results	Relevance to Periodontal Therapy
Direct Antimicrobial Activity	Jun et al., 2018; Lee et al., 2013; Nagraj et al., 2022 **[9,11,12]**	- Disruption of bacterial cell membrane integrity- Electrostatic interaction between sulfated fucoidan and bacterial surfaces- Inhibition of glucosyltransferases and other virulence enzymes	- MIC values: 125–1000 µg/mL against S. mutans, S. sobrinus, P. gingivalis, F. nucleatum, T. forsythia, A. actinomycetemcomitans- Dose-dependent inhibition of bacterial growth	Reduces bacterial load and pathogenic colonization within the periodontal pocket
Antibiofilm and Anti-Adhesion Effects	Jun et al., 2018; Tang et al., 2022 **[9,10]**	- Interference with bacterial adhesion and coaggregation- Inhibition of extracellular polymeric substance (EPS) synthesis- Surface modification preventing initial attachment	- Complete suppression of biofilm formation at ≥250 µg/mL- Fucoidan-derived carbon dots (FDCDs) disrupted E. faecalis biofilm and penetrated dentinal tubules	Prevents maturation of pathogenic biofilms and enhances disinfection of subgingival areas
Synergistic Enhancement of Antibiotic Efficacy	Lee et al., 2013 **[12]**	- Increased bacterial membrane permeability facilitating antibiotic uptake- Possible inhibition of bacterial efflux systems	- Fucoidan + antibiotics (ampicillin/gentamicin) reduced MIC/MBC by 2–8× compared to antibiotics alone	Enables lower antibiotic dosage, reducing resistance risk and enhancing clinical efficacy
Anti-Inflammatory / Immunomodulatory Effects	Alsac et al., 2013 **[13]**	- Binding to selectins and modulation of leukocyteendothelial adhesion- Suppression of neutrophil activation and oxidative burst- Downregulation of proinflammatory cytokines (IL-1β, TNF-α)	- Reduced neutrophil activation and limited P. gingivalis-induced aneurysm expansion	Controls hostmediated tissue destruction in chronic periodontitis
Antioxidant Cytoprotective Properties	Tang et al., 2022; Lee et al., 2013 **[10,12]**	- Scavenging of ROS and RNS species- Chelation of metal ions contributing to oxidative stress	- Reduced oxidative damage markers; maintained biocompatibility in cytotoxicity assays	Protects gingival fibroblasts and osteoblasts from oxidative injury in inflamed tissues
Biocompatibility Regenerative Potential	Tang et al., 2022 (FDCDs) **[12]**	- Fucoidan supports cell adhesion and proliferation- Promotes angiogenesis and collagen synthesis when incorporated in scaffolds	- Excellent cytocompatibility observed; no significant toxicity in cell culture	Potential for incorporation in membranes, hydrogels, or nanoparticles for periodontal regeneration
Structure–Function Correlation	All studies	- Sulfation degree, molecular weight, and source species influence activity- Lowmolecular-weight, highly sulfated fractions show enhanced antimicrobial potency	- Variation in bioactivity across studies due to structural heterogeneity	Highlights need for standardized extraction, purification, and compositional profiling

Source: Own authorship.

Table 4. Risk of Bias for Animal Studies.

Studies	Clearly stated aim/hypothesis	Sample size calculation/justification	Randomization of samples	Standardization of materials & methods	Blinding of outcome assessor	Reproducibility (replicates/independent repeats)	Statistical analysis appropriateness	Outcome reporting completeness	Funding/conflict of interest
Jun JY et al., 2018 [9]	L	H	U	L	H	L		L	U
Lee KY et al., 2013 [10]	L	H	U	L	H	L	L	L	U
Nagraj BK et al., 2022 [11]	L	H	H	L	H	U	L	L	U
Tang S et al., 2022 [12]	L	H	U	L	H	L	L	L	L

Note: L-Low; H-High; U-Unclear. Source: Own authorship.

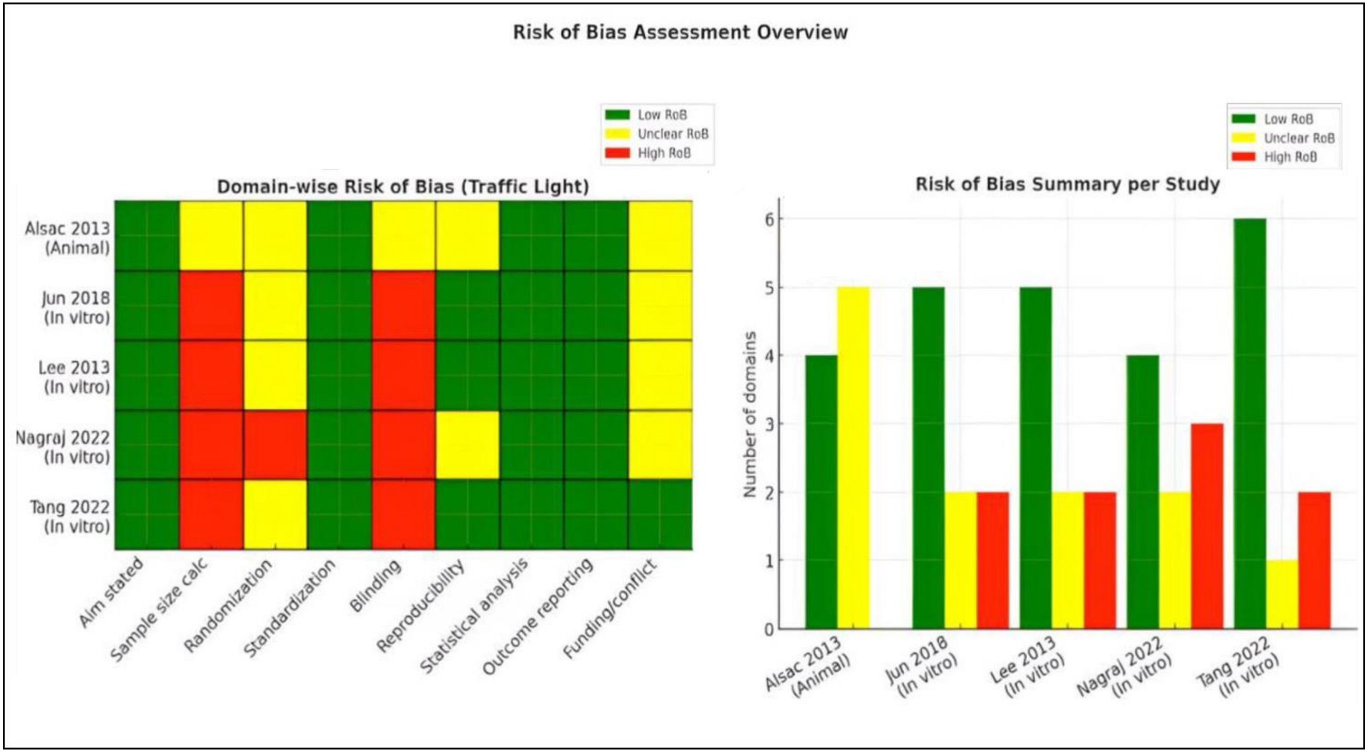

Figure 2. Risk of bias summary. Source: Own authorship. Note: L-Low; H-High; U-Unclear.

Table.5 Mechanistic Summary of Fucoidan Actions on Periodontal Pathogens and Host.

Study	Sequence generation	Baseline characteristics	Allocation concealment	Random housing	Blinding (caregivers/investigators)	Random outcome assessment	Blinding (outcome assessor)	Incomplete outcome data	Selective outcome reporting	Other bias
Alsac JM et al., 2013 [13]	U	L	U	U	U	U	U	L	L	U

Note: L-Low; H-High; U-Unclear. Source: Own authorship.

Discussion

This systematic review focussed on collecting the evidences related to efficacy of fucoidan against periodontal pathogens. It clearly emphasised on its antimicrobial propertties with information on anti-inflammatory and biofilm-disruptive mechanisms that have been reported. As can be observed no human study has been reported and only *in vitro* and *in vivo* stuides are available in current point of time. The collected evidence indicates that fucoidan shows multifaceted therapeutic potential regarding periodontal diseases through multiple mechanisms like modulation of microbial virulence, reduction of inflammation, and boosting host–pathogen balance.

With regard to antimicrobial properties, all *in vitro* studies demonstrated that fucoidan had appreciable antimicrobial effect against key oral pathogens. Jun et al. (2018) **[9]** showed that fucoidan fractions reduced the growth and biofilm formation of by *Streptococcus mutans* and *S. sobrinus*, with thier MIC values ranging from 125 to 1000 µg/mL. This study revealed that cariogenic plaque inhibition was more during biofilm initiation rather than eradication of mature biofilms. Therefore, fucoidan has the potential to interfere with bacterial adhesion and thereby early colonization. In other words, it can be said that fucoidan exhibits extracellular polymeric substance (EPS) matrix disruption and surface attachment, leading to discouragement of microbial plaque.

Lee et al. (2013) **[10]** showed synergistic effects between fucoidan and conventional antibiotics viz. ampicillin and gentamicin in co-administration reduced the MIC and MBC of antibiotics by 8 times. Therefore, fucoidan has potential to increase antibiotic efficacy probably by affecting the bacterial membrane permeability. Further it may also have interference in the resistance mechanisms of the flora. This is of great advantage as it can reduce the dosage requirements of antibiotics and can postpone resistance development.

In similar lines, Nagraj et al. (2022) **[11]** have confirmed the antibacterial activity of *Sargassum wightii* extracts with fucoidan against periodontal pathogens viz. *P. gingivalis, F. nucleatum, T. forsythia,* and *A. actinomycetemcomitans*. While the data was from agar diffusion and MIC/MBC assays, together these emphasize the fucoidan's broad-spectrum antimicrobial potential against species implicated in periodontitis.

Tang et al. (2022) **[12]** reported a novel nanomaterial formulation about the action of fucoidan-derived carbon dots against the *Enterococcus faecalis*. It was reported that the novel material inhibited biofilm formation and disrupted existing biofilms. While the review focussed on periodontal pathogens, studies on other pathogens were included to show the biofilm disruptive properties of fucoidan. In addition to antimicrobial action, fucoidan has shown profound immunomodulatory effects that are relevant to periodontal inflammation. Alsac et al. (2013) **[13]** reported that systemic or local administration of fucoidan significantly reduced neutrophil activation and reduced the aneurysm enlargement in a *P. gingivalis*-induced inflammatory model. Eventhough this study described aneurysmal aspect of *P. gingivalis* rather than gingival context, the chronic immune activation characteristic of periodontitis was similated and hence was included in the review. From the mechanistic point of view, fucoidan's sulfate groups possibly can bind to selectins and modulate leukocyte adhesion. Its antioxidant activity counteracts reactive oxygen species of periodontal tissue destruction. These multifacted properties place fucoidan as biofunctional material for periodontal management (Table 5).

In this systematic review, overall methodological quality of *in vitro* studies was of moderate risk of bias, with good quality in clarity in study aims and standardization of experimental conditions. *In vivo* study by Alsac et al., (2013) **[13]**, unclear risk was seen in several domains, despite outcome data being complete and selective reporting being minimal. Considering the antimicrobial aspect, it causes disruption of bacterial membranes and inhibition of glucosyltransferases. With regard to anti-biofilm effects, it interferes with matrix formation and bacterial coaggregation. From anti-inflammatory point of view modulation of cytokine secretion and inhibition of neutrophil infiltration was reported along with potentiation of conventional antimicrobials. From all the collected information and considering the moderate risk of bias leading to acceptance of evidence from the studies, it can be seen that fucoidan is a promising candidate for treatment of periodontal diseases. However, it needs to be optimised for molecular weight, sulfation degree, and extraction source for standardising the bioactivity before clinical translation. Future research must focus on well-designed *in vivo* periodontal models and controlled clinical trials.

Limitations

More number of clinical trials should be considered and periodontal regenerative potential is to be supported with clinical studies.

Conclusion

Within the limitations of the review evidence, fucoidan exhibits promising antimicrobial, antibiofilm, and anti-inflammatory properties against periodontal pathogens. Standardization of extraction methods and structural characterization are essential before clinical application. In the context of oral and periodontal health, fucoidan's nutritive properties are particularly significant. By reducing systemic inflammation and oxidative stress, it may indirectly support periodontal health. Additionally, its ability to enhance collagen synthesis, promote fibroblast proliferation, and stimulate osteoblastic activity contributes to tissue repair and regeneration. As a dietary supplement or incorporated into functional foods, fucoidan may therefore serve as a supportive agent in maintaining periodontal integrity and preventing disease progression. It has tremendous potential in biomaterials science, microbiology, and clinical periodontology.

CrediT

Author contributions: **Conceptualization-** All authors; **Data curation-** B Bhuvaneswari, S Gopalakrishnan, U Arunmozhi; **Formal Analysis-** All authors; **Investigation-** All authors; **Methodology-** B Bhuvaneswari; **Supervision-** Thodur Madapusi Balaji; **Writing - original draft-** All authors; **Writing-review & editing-** All authors.

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Conflict of Interest

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Similarity Check

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Application of Artificial Intelligence (AI)

Not applicable.

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It was performed.

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