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Synergistic effect of fucoidan with antibiotics against oral pathogenic bacteria

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ABSTRACT

Background: Fucoidan is a sulphated polysaccharide that is primarily extracted from brown seaweeds; it has been broadly studied in recent years due to its numerous biological properties, including anticoagulant, antithrombotic, antitumour and antiviral activities.

Objective and design: In this study, fucoidan was evaluated against oral bacteria, either alone or with antibiotics, via the broth dilution method and checkerboard and time-kill assay.

Results: Minimum inhibitory concentration/minimum bactericidal concentration (MIC/MBC) values for the fucoidan against all the tested bacteria ranged between 0.125 and 0.50/0.25 and 1.00 mg ml⁻¹, for ampicillin 0.125 and 64/0.5 and 64 µg ml⁻¹ and for gentamicin 2 and 256/4 and 512 µg ml⁻¹, respectively. Furthermore, the MIC and MBC were reduced to one half-eighth as a result of the combination of the fucoidan with antibiotics. One to 3 h of treatment with MIC₅₀ of fucoidan with MIC₅₀ of antibiotics resulted from an increase of the rate of killing in colony forming units (CFUs) ml⁻¹ to a greater degree than was observed with alone.

Conclusion: These results suggest that fucoidan is important in the antibacterial actions of the agents.

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1. Introduction

The microbial composition of dental biofilms includes over 700 species of bacteria and archaea, which all exist in a relatively stable environment called microbial homeostasis.¹ Dental plaque biofilms are responsible for many of the diseases common to the oral cavity including dental caries, periodontitis, gingivitis and the less common peri-implantitis (similar to periodontitis, but with dental implants); however, biofilms are present on healthy teeth as well.² In contrast, the

accumulation of dental biofilms, which is accompanied by a change in bacterial composition, leads to the onset of dental diseases such as dental caries, gingivitis, periodontitis, etc.³ The bacterial composition often changes from a scanty biofilm dominated by Gram-positive bacteria, usually found in healthy individuals, to an increased number of Gram-negative anaerobic rods, usually observed in periodontitis.⁴

Infection due to multidrug-resistant pathogens is routinely complicated to deal with because of virulence factors and because of a relatively limited choice of antimicrobial agents. Thus, it is extremely important to find novel

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Table 1 – Antibacterial activity of fucoïdan and antibiotics in oral bacteria.

Samples	Fucoïdan (mg ml ⁻¹)			Ampicillin	Gentamicin
	MIC ₅₀ <	MIC ₉₀ <	MIC/MBC	MIC/MBC (µg ml ⁻¹)	
<i>S. mutans</i> ATCC 25175 ^a	0.062	0.25	0.25/0.50	0.125/0.5	8/16
<i>S. sanguinis</i> ATCC 10556	0.125	0.50	0.50/1.00	0.5/1	64/64
<i>S. sobrinus</i> ATCC 27607	0.125	0.25	0.25/0.50	0.5/1	4/8
<i>S. ratti</i> KCTC 3294 ^b	0.062	0.25	0.25/0.50	0.5/1	16/32
<i>S. criceti</i> KCTC 3292	0.062	0.25	0.25/0.50	1/2	8/16
<i>S. anginosus</i> ATCC 31412	0.125	0.25	0.25/0.50	1/2	32/32
<i>S. gordonii</i> ATCC 10558	0.125	0.50	0.50/1.00	0.5/1	32/32
<i>A. actinomycetemcomitans</i> ATCC 43717	0.125	0.50	0.50/1.00	64/64	4/8
<i>F. nucleatum</i> ATCC 51190	0.062	0.25	0.25/0.50	2/4	2/4
<i>P. intermedia</i> ATCC 49049	0.062	0.25	0.25/0.25	4/8	16/32
<i>P. gingivalis</i> ATCC 33277	0.031	0.125	0.125/0.25	0.5/1	256/512

^a American Type Culture Collection (ATCC).
^b Korean collection for type cultures (KCTC).

antimicrobials or new techniques that are effective for the treatment of infectious diseases caused by drug-resistant microorganisms.^{5,6} Plant-derived antimicrobials have a long history of providing the much-needed novel therapeutics.^{7,8}

The pharmacological effects of such mixtures could be as a result of the total sum of different classes of compounds with diverse mechanisms of action. There have been reports of the total contents of an herbal product showing a significantly

Table 2 – Synergistic effects of fucoïdan with ampicillin against oral bacteria.

Strains	Agent	MIC/MBC ^a		FIC/FBC	FICI/FBCI ^c	Outcome
		Alone	Combination ^b			
<i>S. mutans</i> ATCC 25175	Fucoïdan	0.25/0.50	0.062/0.125	0.25/0.25	0.5/0.5	Synergistic/ synergistic
<i>S. sanguinis</i> ATCC 10556	Ampicillin	0.0625/0.25	0.0156/0.0625	0.25/0.25		
<i>S. sobrinus</i> ATCC 27607	Fucoïdan	0.50/1.00	0.125/0.50	0.25/0.5	0.5/1.0	Synergistic/ additive
<i>S. ratti</i> KCTC 3294	Ampicillin	0.25/1.0	0.0625/0.5	0.25/0.5		
<i>S. criceti</i> KCTC 3292	Fucoïdan	0.25/0.50	0.062/0.125	0.25/0.25	0.5/0.75	Synergistic/ additive
<i>S. anginosus</i> ATCC 31412	Ampicillin	0.0156/0.0625	0.0039/0.0313	0.25/0.5		
<i>S. gordonii</i> ATCC 10558	Fucoïdan	0.25/0.50	0.062/0.125	0.25/0.25	0.5/0.5	Synergistic/ synergistic
<i>A. actinomycetemcomitans</i> ATCC 43717	Ampicillin	0.0156/0.125	0.0039/0.0313	0.25/0.25		
<i>F. nucleatum</i> ATCC 51190	Fucoïdan	0.25/0.50	0.062/0.125	0.25/0.25	0.5/0.5	Synergistic/ synergistic
<i>P. intermedia</i> ATCC 49049	Ampicillin	0.0625/0.25	0.0156/0.0625	0.25/0.25		
<i>P. gingivalis</i> ATCC 33277	Fucoïdan	0.50/1.00	0.125/0.25	0.25/0.25	0.5/0.5	Synergistic/ synergistic
	Ampicillin	0.0625/0.25	0.0156/0.0625	0.25/0.25		
	Fucoïdan	0.50/1.00	0.125/0.50	0.25/0.5	0.5/0.75	Synergistic/ additive
	Ampicillin	8/16	2/4	0.25/0.25		
	Fucoïdan	0.25/0.50	0.062/0.125	0.25/0.25	0.5/0.5	Synergistic/ synergistic
	Ampicillin	2/4	0.5/1	0.25/0.25		
	Fucoïdan	0.25/0.25	0.062/0.125	0.25/0.5	0.5/0.75	Synergistic/ additive
	Ampicillin	0.25/1	0.0625/0.25	0.25/0.25		
	Fucoïdan	0.125/0.25	0.031/0.062	0.25/0.25	0.5/0.5	Synergistic/ synergistic
	Ampicillin	0.5/1.0	0.125/0.25	0.25/0.25		

ATCC, American type culture collection; KCTC, Korean collection for type cultures.

^a Fucoïdan: mg ml⁻¹, ampicillin: µg ml⁻¹.

^b The MIC and MBC of the fucoïdan with ampicillin.

^c The fractional inhibitory concentration index (FIC index)/the fractional bactericidal concentration index (FBC index).

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