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Wild bee venom peptides

https://www.iocbtech.cz/project/wild-bee-venom-peptides-2-2/

NOVEL ANTIMICROBIAL AND ANTIFUNGAL COMPOUNDS

Scientists

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CHALLENGE

Increasing resistance of microbial, yeast and fungal strains to antibiotic and antifungal treatment is dangerous trend of last decade. Decreasing efficiency of common treatments poses a serious health and economical problem worldwide. Recently, we have isolated and characterized remarkable antimicrobial peptides (AMPs) from the venom reservoirs of wild bees which mechanism of action promises robust solution preventing further development of resistance.

TECHNOLOGY

AMPs from bee venom and its synthetic analogues are cationic peptides containing circa 10 – 20 amino acids. Amphipathic nature of AMPs is standing behind disruption of bacterial and fungal membrane resulting in eradication of pathogens. AMPs were preliminary tested for cell toxicity (mammalian cell cultures), hemolysis and rabbit eye irritation test without significant negative results, which indicated suitability of AMPs to be used in human medicine, dermatology, beauty industry, intimate hygiene or surface disinfection. Moreover, a stability of synthetic AMPs analogues has been increased to prevent hydrolysis of peptides by peptidases present on site or produced by pathogens. Efficacy of AMPs has been tested in using bacterial, fungal and yeast strains including common antibiotics or fluconazole resistant strains such as Staphylococcus aureus or Candida species. Despite peptide nature of compounds limits per oral application of compound in human medicine, topic application or use of compounds in dermatology or intimate hygiene should be beneficial mainly because of treatment efficacy and decreased exposure of patients to common antibiotics

RESULT PREVIEW

Peptide	Antimicrobial activity MIC (μM)						Hemolytic activity LC50 (μM)
	M.l.	*B.s.*	*S.a.*	*E.c.*	*P.a.*	*C.a.*	
A	1	1	8	2	10	10	>200
B	2	1.1	80	20	>100	>100	>100
C	1.1	1.3	65	5.5	80	>100	>100
D	1	1.1	93	7.8	93	>100	>100

M.l. Micrococcus luteus, B.s. Bacillus subtilis, S.a. Staphylococcus aureus, E.c. Escherichia coli, P.a.Pseudomonas aeruginosa, C.a. Candida albicans

	MIC, LL-III/12 [μM]				MIC, LL-III/A [μM]			
	A	10A	100A	1000A	A	10A	100A	1000A
Candida albicans	5	5	7.5 ± 2.5	32 ± 20	4.5 ± 0.5	6 ± 1	9 ± 4	28 ± 22
Candida glabrata	15 ± 5	10	10	30 ± 10	15 ± 4	15 ± 4	15	30 ± 8
Candida krusei	11 ± 2	10	10	47 ± 25	15 ± 8	15 ± 4	22.5 ± 7.5	47 ± 25
Candida parapsilosis	9 ± 6	15 ± 5	20	53 ± 34	14 ± 11	25 ± 5	45 ± 15	68 ± 23
Candida tropicalis	7.5 ± 2.5	5	5	36 ± 20	7 ± 2	6 ± 1	9 ± 1	26 ± 14

Antimicrobial activity represented by Minimum inhibitory concentration (MIC) has been studied for AMPs using various species of bacteria or yeast and compared with hemolytic activity of peptides. Several candidate AMPs were identified as compounds effective against broad range of pathogens while hemolytic activity has not been observed (see peptide A; Table 1). MIC values of peptides LL-III/2 and LL-III/A for different Candida species and for different number of cells in suspensions (A = circa 0.5-2.5×104 cells per mL) were measured. Peptides were found to be effective antifungal agent even for fluconazole resistant Candida strains (Table 2).

COMMERCIAL OPPORTUNITY

The project is offered for co-development and licensing.

DEVELOPMENT STATUS

Efficacy of various AMPs has been confirmed using various bacterial, fungal and yeast strains in vitro. Simultaneously, AMPs were tested for mammalian cell toxicity and hemolysis. Pilot experiments showed very low irritation using rabbit eye test. Testing of novel peptides and their analogues is under way aiming optimization of efficacy and stability. Tests of skin or mucous membranes irritation are planned.

PATENT SITUATION

AMPs from wild bee venom are protected by European patents EP 2265631 and EP 2396020. Newly isolated peptides and most promising synthetic analogues will be patented during spring 2014. This is opportunity for future industry partner to select areas

of interest which should be covered by patent.

IP OWNERS

Institute of Organic Chemistry and Biochemistry AS CR, v.v.i.
Veterinary Research Institute v.v.i.
Palacký University Olomouc

FURTHER READING

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