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In Silico Screening of Bioactive Surfactant obtained from Indian Marine Sources for the Development of Pharmaceutical Formulations

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Abstract

Bioactive surfactants are the best surfactants that can be used in different pharmaceutical formulations. In this work bioactive surfactant obtained from marine sources were analyzed on the basis of Physiochemical Properties, ADME properties, skin sensitivity and Drug likeliness properties of Fengycin, Surfactin, Ituridinet D, Rhamnolipid1 and Pumilacidin. Fengycin which exhibited characteristic of Ampiphilicity from Physciochemical properties calculated. Rhamnolipid 1exhibited least molecular weight 650.80 g/mol. Skin permeability score of surfactin is good as compare to all the other biosurfactants even Maximum Recommended Therapeutic Dose 213 mg/day was also revealed by the surfactin. The acceptable properties of this marine source of surfactants make Surfactin a better surfactant.

Keywords: Marine, Surfactants, Surfactin, Fengycin, biosurfactants.

Introduction

Biosurfactants are majorly biological surface-active compounds, which possess environment friendly properties like less toxicity and more biodegradability. They are green and smart biocides[1]. It has been observed that huge and wide source of natural compounds can be retrieved from the marine environment. Marine microorganisms shows unique metabolic and physiological capabilities,[2] they do have ability to survive in extreme odd conditions and produce novel metabolites, Hence, the marine environment have treasure of novel and potential compounds including antibiotics, enzymes, vitamins, drugs and biosurfactants.

A marine Bacillus species mainly produce biosurfactant. B. circulans producing extracellular biosurfactants was isolated and identified from Andaman and Nicobar Islands, India. Bacillus species have been widely reported as producers of extracellular biosurfactants, mostly lipopeptide Bacillus circulans marine, Andaman Nicobar Islands, India, To purify the biosurfactant produced by a marine Bacillus circulans strain and evaluate the improvement in surface and antimicrobial activities Surfactin,[3] Bacillus licheniformis NIOT-06 has surfactin

.its obtain in South Andaman and also producing biosurfactants. A sponge from North Bay and South Andaman Bacillus Licheniformis also produces Biosurfactants.[4]

Bacillus megaterium, from seawater, Andaman Nicobar Islands, India is also reported to produce bio surfactant. *Pseudomonas aeruginosa*, coastal sediment, Odisha, India, *Bacillus pumilus* pumilacidin, seawater. Biosurfactant Production by *Pseudomonas aeruginosa* from Renewable Resources[6,7] Biosurfactant are economically cheaper Satisfactory emulsifiers. In this work an attempt is made to determine the potential of Marine surfactant by analyzing their toxicity, ADME sar study and sensitivity[8,9]. Surfactant have been widely used in the pharmaceutical formulations like Emulgel, Emulsions, Suspensions, Multiple emulsions and Micro to nanoparticulate formulation formation[10,11].

Material and Method

following studies were conducted using online open accessible softwares. The software used for the insilico study was mainly coded in Python 2.7 The process of screening of surfactant adopted on the basis of Favorable properties of Surfactant molecules on the basis of *in-silico* physiochemical properties, ADME study and toxicological studies .

Result and Discussion

The surfactant molecule subjected for in silico prediction for HLB and Log P indicated that all the biosurfactants can be easily used use to prepare oil in water sort of emulsion since they all have HLB Value more than 9 if we analyze the partition coefficient of the surfactant then it can be easily concluded that all the surfactants are potentially hydrophobic in nature excluding Fengycin which exhibited characteristic of Ampiphilicity From Physciochemical properties calculated Rhamnolipid 1exhibited least molecular weight 650.80 g/mol. Total PSA of all the biosurfactant are more than 140 angstroms square.[12] None of the biosuractant is completely or freely soluble in water as all of them are potentially hydrophobic in nature .

Pharmacokinetic Properties of Biosurfactants reveals that all the surfactant have low absorption from the GI Track and the most desirable property is none of them permeate through blood brain barrier[14]. and the consequences of their permeation by BBB do not observe. Skin permeability score of surfactin is good as compare to all the other biosurfactants[15] which shows its good skin permeability and ultimately this surfactant can be used in the formulation which could help to increase the permeability of drug using this surfactant.

All the biosurfactants exhibited violation from drug likeliness properties the best bioavailability score is shown by Ituridint D.[16]

Toxicity study of the Biosurfactants

It has been observed through the in-silico toxicity study that all the biosurfactant are free from liver toxicity .None of these Surfactant exhibited affinity for memberane transport protein like Pgp inhibitor and Pgp Substrate and neither though Blood brain barrier. Maximum Recommended Therapeutic Dose 213 mg/day in case of surfactin .33 mg/day in case of Pumilacidin and the least in the case of Iturin D that is 7.9mg/day. Which exhibit Surfactin can be used up to the specified higher concentration in the formulation. Inturin D and Fengycin showed mitochondrial dysfunction which implicated in cancer, diabetes, neurodegenerative disorders, and cardiovascular diseases. In-silico sensitivity study of Bioactive surfactant from marine sources revealed that all the surfactant were non sensitive for the skin.

(Table 1, 2, 3 and 4 end of the paper)

Conclusion

From this insilico study it could be concluded that Skin permeability score exhibited by surfactin was good as compare other biosurfactants of Marine sources which makes it a better surfactant since it promotes penetration of the formulation apart from its pharmaceutical attributes as an excipients even Maximum Recommended concentration 213 mg/day was also revealed by it. The acceptable properties of this marine source of surfactants make Surfactin a better surfactant.

Acknowledgement

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Conflict of Interest

There is no conflict of interest.

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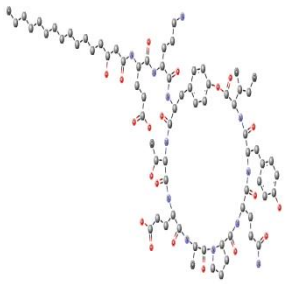
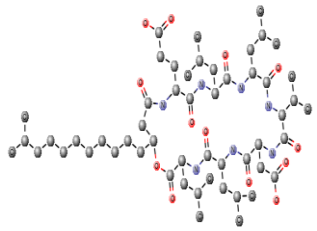
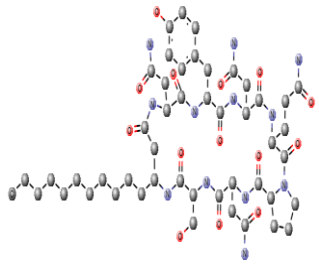
Table 1.Species, Structure, LogP, HLB value and Name of Biosurfactans.

Species	Chemical Structure	Surfactant	HLB and Log P	Name
Bacillus circulans		**Fengycins**	HLB = 11.38 Log P nonionic species =1.03	4-[(4-amino-1-{[4-(butan-2-yl)-10-(2-carbamoylethyl)-22-(2-carboxyethyl)-25-(1-hydroxyethyl)-7-[(4-hydroxyphenyl)methyl]-19-methyl-3,6,9,12,18,21,24,27-octaoxo-2-oxa-5,8,11,17,20,23,26-heptaazatricyclo[28.2.2.0^{13,17}]tetratriaconta-1(32),30,33-trien-28-yl]carbamoyl}butyl)carbamoyl]-4-(3-hydroxyhexadecanamido)butanoic acid
Bacillus licheniformis		**Surfactin**	Griffin HLB = 10.16 logp -6.24	3-[9-(carboxymethyl)-3,6,15,18-tetrakis(2-methylpropyl)-25-(10-methylundecyl)-2,5,8,11,14,17,20,23-octaoxo-12-(propan-2-yl)-1-oxa-4,7,10,13,16,19,22-heptaazacyclopentacosan-21-yl]propanoic acid
Bacillus megaterium		**Iturin D**	Griffin HLB = 12.88 logP-4.61	3-[3,13,19-tris(carbamoylmethyl)-6-(hydroxymethyl)-16-[(4-hydroxyphenyl)methyl]-1,4,7,11,14,17,20,23-octaoxo-9-undecyl-hexacosahydro-1H-pyrrolo[2,1-i]1,4,7,10,13,16,19,22-octaazacyclopentacosan-22-yl]propanamide

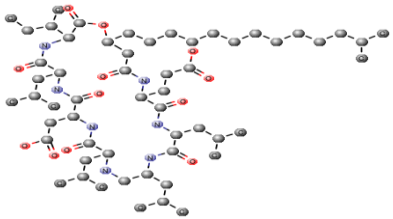
Bacillus pumilus		**Pumilacidin**	Griffin HLB = 9.63 log p of nonionic species is 8.16	3-[3-(butan-2-yl)-9-(carboxymethyl)-6,12,15,18-tetrakis(2-methylpropyl)-25-(12-methyltridecyl)-2,5,8,11,17,20,23-heptaoxo-1-oxa-4,7,10,13,16,19,22-heptaazacyclopentacosan-21-yl]propanoic acid

Table 2.Physiochemical Properties of Bioactive surfactants

S. no	PHYSICOCHEMICAL PROPERTIES	FENGYCINS	SURFACTIN.	ITURIN D	Pumilacidin	RHAMNOLIPID 1
1	Molecular weight	1463.71g/mol	1036.34g/mol	1043.17g/mol	1064.44g/mol	650.80 g/mol
2	Num. heavy atoms	104	73	74	75	45
3	Num. arom. Heavy atoms	12	0	6	0	0
4	Fraction Csp^3	0.64	0.81	0.62	0.84	0.94
5	Num. rotatable bonds	39	24	22	27	22
6	Num. H-acceptor	21	13	14	13	13
7	Num. H-donors	16	9	13	9	6
8	Molar refractivity	408.19	308.02	294.51	322.24	164.92
9	TPSA	512.91 A^2	304.60 A^2	436.83 A^2	287.53 A^2	201.67 A2
10	Class	Insoluble	Insoluble	Poorly soluble	Poorly soluble	Poorly soluble
	Pharmacokinetic Properties					
11	GI absorption	Low	Low	Low	Low	Low
12	BBB permeant	No	No	No	No	No
13	P-gp substrate	Yes	Yes	Yes	no	Yes
14	Log K_P (skin permeation)	-13.43 cm/s	-6.36 cm/s	-13.77 cm/s	-7.69 cm/s	-13.43 cm/s

Table 3.Drug likeness Properties of Bioactive surfactants

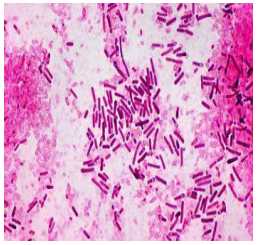
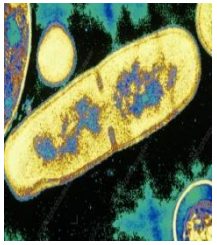
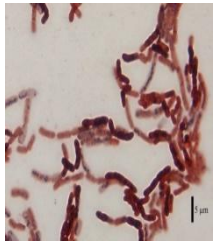
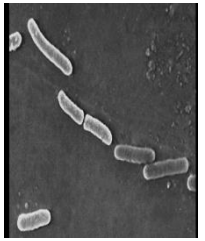
S. NO	**Drug likeness**	**FENGYCINS**	SURFACTIN.	ITURIN D	Pumilacidin	RHAMNOLIPID 1
1	Lipinski	No; 3 violations: MW> 500, NorO> 10, NHorOH>5	No; 3 violations: MW> 500, NorO> 10, NHorOH>5	No; 3 violations: MW> 500, NorO> 10, NHorOH>5	No; 3 violations: MW> 500, NorO> 10, NHorOH>5	No; 3 violations: MW> 500, NorO> 10, NHorOH>5
2	Veber	No; 2 violations: Rotors>10 TSPA> 140,	No; 2 violations: Rotors>10 TSPA> 140,	No; 2 violations: Rotors>10 TSPA> 140,	No; 2 violations: Rotors>10 TSPA> 140,	No; 2 violations: Rotors>10 TSPA> 140,
3	Egan	No; 1violations: TSPA> 131.6,	No; 1violations: TSPA> 131.6,	No; 1violations: TSPA> 131.6,	No; 1violations: TSPA> 131.6,	No; 1violations: TSPA> 131.6,
	Bioavailability score	0.11	0.11	0.17	0.11	0.11
6	Species					
		Bacillus circulans	Bacillus licheniformis	Bacillus megaterium	Pseudomonas aeruginosa	Bacillus pumilus

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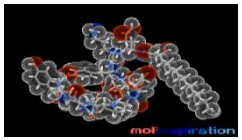
Table 4.Toxicity and sensitivity studies of bioactive surfactants

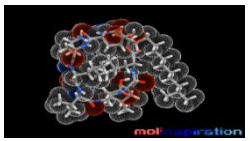
FENGYCINS



Query	Liver Toxicity		Metabolism						Membrane Transporters			Others			
			Cyp Inhibitors for												
	DILI	Cyto-toxicity	HLM	1A2	3A4	2D6	2C9	2C19	BBB	P-gp Inhibitor	P-gp Substrate	hERG Blocker	MMP	AMES	MRTD (mg/day)
	No	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	Yes	⊘	⊘

Non-sensitizer

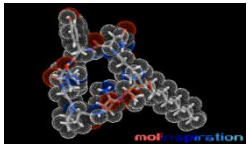
SURFACTIN.



Query	Liver Toxicity		Metabolism						Membrane Transporters			Others			
			Cyp Inhibitors for												
	DILI	Cyto-toxicity	HLM	1A2	3A4	2D6	2C9	2C19	BBB	P-gp Inhibitor	P-gp Substrate	hERG Blocker	MMP	AMES	MRTD (mg/day)
	⊘	⊘	⊘	No	No	No	No	No	⊘	⊘	⊘	⊘	⊘	⊘	213

Non-sensitizer

ITURIN D



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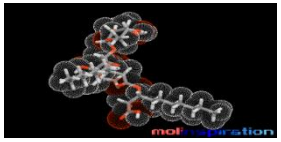
			Cyp Inhibitors for												
	DILI	Cyto-toxicity	HLM	1A2	3A4	2D6	2C9	2C19	BBB	P-gp Inhibitor	P-gp Substrate	hERG Blocker	MMP	AMES	MRTD (mg/day)
	No	⊘	⊘	⊘	Yes	Yes	No	⊘	⊘	⊘	⊘	⊘	Yes	⊘	7.9

Non-sensitizer

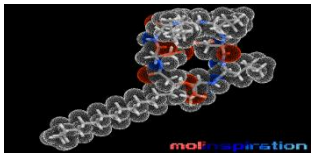
Pumilacidin



Query	Liver Toxicity		Metabolism						Membrane Transporters			Others			
			Cyp Inhibitors for												
	DILI	Cyto-toxicity	HLM	1A2	3A4	2D6	2C9	2C19	BBB	P-gp Inhibitor	P-gp Substrate	hERG Blocker	MMP	AMES	MRTD (mg/day)
	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	No	⊘	⊘	33

Non-sensitizer

RHAMNOLIPID 1



Query	Liver Toxicity		Metabolism						Membrane Transporters			Others			
			Cyp Inhibitors for												
	DILI	Cyto-toxicity	HLM	1A2	3A4	2D6	2C9	2C19	BBB	P-gp Inhibitor	P-gp Substrate	hERG Blocker	MMP	AMES	MRTD (mg/day)
	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘	⊘

Non-sensitizer

