Peptoid Inhibition of Bacterial Growth

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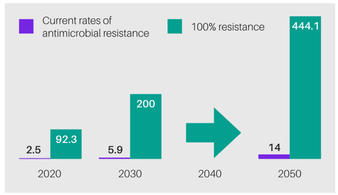
Introduction

- There has been an increase in antibiotic resistance in microorganisms over the past decade.[1]
- Peptoids have been proposed as a viable solution.
- Peptoids or poly-N-substituted glycines are structural analogs of peptides (short chains of two to fifty amino acids).[1]
- The N-substituted amide makes it resistant to proteolytic degradation which is its advantage over peptides.[2]
- The objective of this project is to analyze existing literature for structural characteristics of effective peptoids.



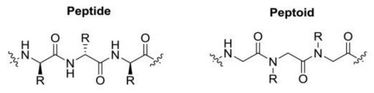
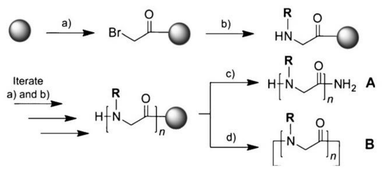
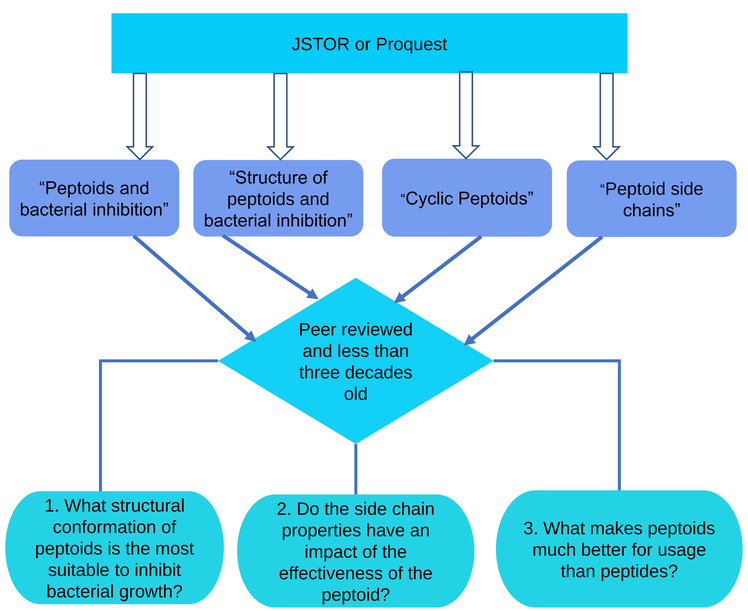


Figure 1: Typical peptide vs peptoid.[1]



Scheme 1: Solid phase synthesis of N-acetylated linear (A) and cyclic peptoids (B) where n = 6, 8 or 10.[2]

Methods



Results

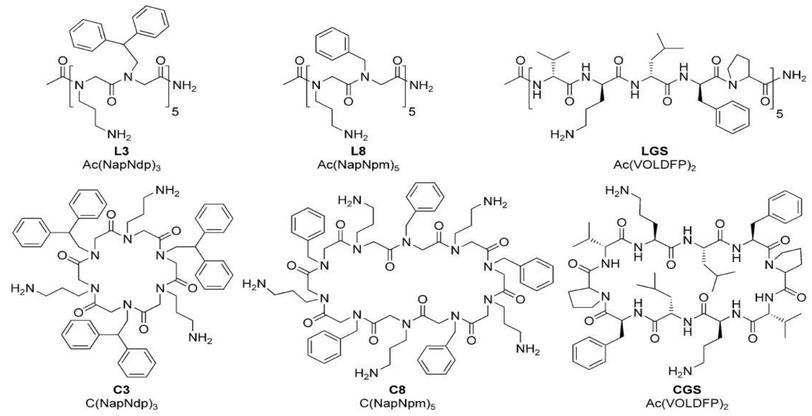


Figure 3: Structure of linear (L) and cyclic peptide and peptoids (C) utilized in the study. Cyclic decapeptide gramicidin S (CGS) and its N-acetylated linear counterpart LGS are peptides utilized as positive control. [2]

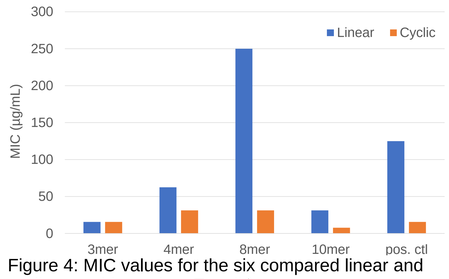


Figure 4: MIC values for the six compared linear and cyclic peptoids against *E. coli*.[2]

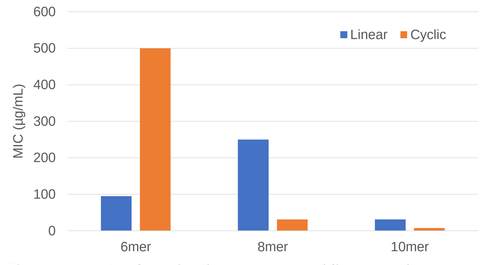


Figure 5: MIC values for three compared linear and cyclic peptoids against E coli comparing length where C6 & L6 are 6mers, C7 and L7 are 8mers and C8 and L8 are 10mers.[2]

Table 1: MIC values of fluorinated peptoids against SA = *S. aureus* [ATCC 29213], *MRSP = methicillin-resistant isolate of S. pseudintermedius, PA = P. aeruginosa, EC = E. coli*.[3]

		MIC (μg/mL)				
Compound	# of residues	SA	MRSP	PA	EC	# of Fluorines present
1	12	32	2	16	8	0
2	12	2	1	4	4	3
3	10	4	1	16	8	2
4	8	32	4	>32	>32	2
5	6	>32	>32	>32	>32	1
6	12	2	2	4	4	6
7	10	2	1	8	8	5
8	8	8	2	>32	32	4
9	6	>32	32	>32	>32	3

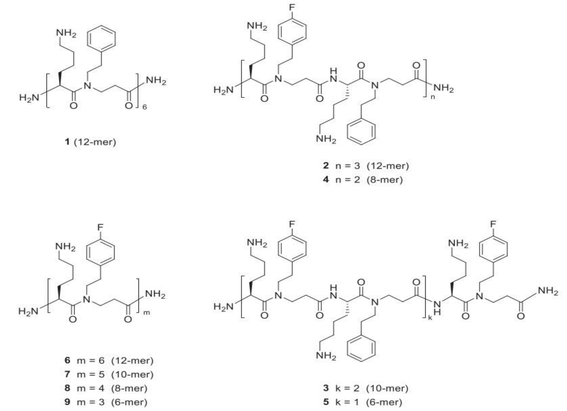


Figure 6: Structures of fluorinated and non-fluorinated peptoids used in the study.[3]

- Cyclic peptoids have been shown to have improved antibacterial activity in comparison to their linear counterparts. Lengthening the cyclic side chains will also help to boost activity.
- Adding fluorine to the side chain increases antibacterial activity.
- Compound 2 is most effective at inhibiting the growth of the four bacterial strains.

Discussion/Conclusion

- Cyclization enforces conformational rigidity that increases specificity.[4]
- Cyclic peptoids have improved cell penetration and enhanced antimicrobial activity compared to their linear precursors.[5]
- Fluorine increases the hydrophobicity and antimicrobial activity until saturation.[6]
- Sidechains between 6 to 12 residues increase antimicrobial activity.[7]
- A combination of fluorination and elongated hydrophobic side chains constitute the most optimal design.[1, 4]

References

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Acknowledgements

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