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Solid-Phase Synthesis of Cyclic Peptide-Phakellistatin 18 and 21

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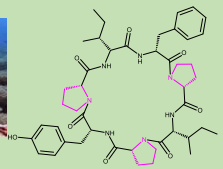
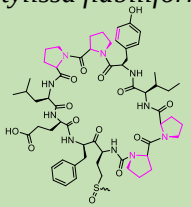
INTRODUCTION:

Marine organisims are powerful source of proline rich cyclic peptides. Peptides of phakellistatin family are reported to have significant biological activities. So far, twenty two members of phakellistatin class have been reported. Proline rich compounds are very often reported as mixture of proline rotamers.

Phakellistatin 18 and 21-proline-containing cyclic were isolated from marine sponge *Phakellia fusca* and *stylissa flablliformis* respectively.





Phakellistatin 21

To develope SAR studies of synthesized compounds ← **OBJECTIVE** → **To study the conformational changes of compound**

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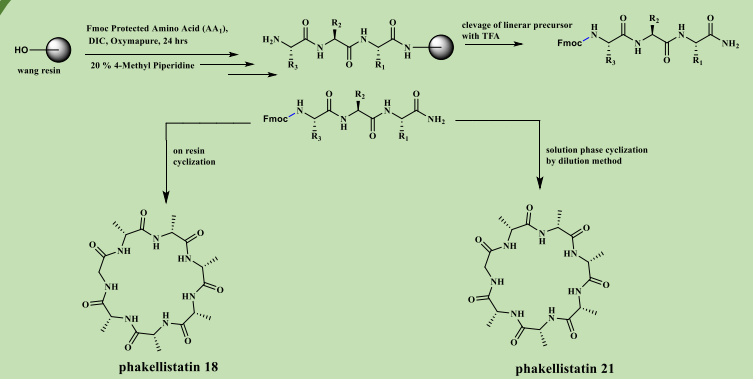
To evaluate biological activities of compound

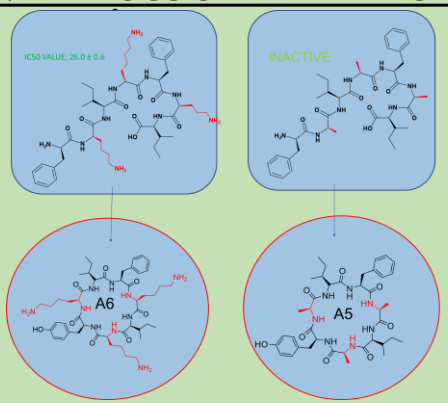
SYNTHETIC SCHEME



RESULT AND DISSCUSSION

- Natural product phakellistatin 21 was synthesized *via* on resin cylization, phakellistatin 18 and its analogs were synthesized by solid and solution phase methodology. Linear precursor of phakellistatin 18 were synthesized by loading Fmoc-protected Ile on Wang resin, followed by coupling of all remaining residues using Fmoc-synthesis protocol.
- The cleavage of peptide from the resin was performed by TFA coaktail to achieve linear precursor in crude form. The crude linear peptide was purified by RP-HPLC and subjected to cyclization by using dilution method.
- New analogs were prepared by using same strategy of synthesis in which proline was substituted by alanine and lysine..

NEW ANALOGS OF PHAKELLISTATIN 18



CONCLUSION

- New analogs of phakellistatin 18 were synthesized by using solid and solution phase synthesis while phakellistatin 21 *via* on resin cyclization.
- Linear analogs which contain lysine residue was found to be active against MCF-7.
- Structures of peptides were confirmed by using various spectroscopic technique

REFERENCE

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- Meli, A., Tedesco, C., Della Sala, G., Schettini, R., Albericio, F., De Riccardis, F., & Izzo, I. (2017). Phakellistatins: an underwater unsolved puzzle. Marine drugs, 15(3), 78.