Indian Journal of Experimental Biology
Vol. 63, March 2025, pp. 229-238
DOI: 10.56042/ijeb.v63i03.13585

Genomic analysis of *Streptomyces amritsarensis* MTCC 11845 and characterization of novel lanthipeptide 2A

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Received 07 September 2024; revised 23 January 2025

Antibiotic resistance in pathogenic bacteria is on the rise, and regrettably, existing antibiotics are becoming less effective against these resilient pathogens. Genus *Streptomyces* members are potent producers of antibiotics and other bioactive secondary metabolites. In the current study, genome of *Streptomyces amritsarensis* (MTCC 11845) was analyzed to identify biosynthetic gene clusters responsible for encoding potent antimicrobial compounds based on its *in vitro* antimicrobial activity. Analysis with antiSMASH database showed presence of biosynthetic gene clusters encoding secondary metabolites. Average nucleotide identity (ANI) of the *S. amritsarensis* 2A whole genome sequence showed 99.04–83.31% identity, with type strains of all closely related species. Whole-genome analysis revealed the presence of multiple peptide synthetase, Non-ribosomal peptide synthetase (NRPS) and polyketide synthase (PKS) biosynthetic gene clusters producing various antimicrobials. The active antimicrobial compound produced by *S. amritsarensis* 2A, purified and characterized using chromatographic techniques. MALDI-TOF data revealed that the active novel peptide has molecular mass of 1341.7 Da, and exhibiting 37–60% similarity with other lanthipeptide sequences available in database. AntiSMASH data reveals that peptide has 14 amino acids and it belongs to the Class III lanthipeptides. Lanthipeptide 2A was stable at high temperatures and *p*H ranging from 4.0–10.0. It exhibits potent antimicrobial activity against various test strains, with MIC values ranging from 2.2 to 30.8 µg/mL. It is non-haemolytic even at 5× MIC concentration and effectively reduces bacterial load after 2 h of incubation. Lanthipeptide 2A, with its broad antimicrobial activity, stability, and non-haemolytic characteristics, emerges as a promising candidate for therapeutic applications.

Keywords: Lanthipeptide 2A, Antimicrobial, Therapeutic agent