Bioorganic & Medicinal Chemistry Letters 27 (2017) 2579–2582

Contents lists available at ScienceDirect

Bioorganic & Medicinal Chemistry Letters

journal homepage: www.elsevier.com/locate/bmcl

Novel bioactive molecules from *Lentzea violacea* strain AS 08 using one strain-many compounds (OSMAC) approach

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ARTICLE INFO

Article history:
Received 16 January 2017
Revised 1 March 2017
Accepted 24 March 2017
Available online 25 March 2017

Keywords:
Actinomycetes
Lentzea violacea
Bioactive compounds
Antitumor and antimicrobial activity

ABSTRACT

A new eudesmane sesquiterpenoid (**1**), and a new homologue of virginiae butanolide E (**2**) along with butyl isobutyl phthalate (**3**) were isolated from, actinomycete-*Lentzea violacea* strain AS08 isolated from north western Himalayas by stressing on modified one strain-many compounds (OSMAC) method. The structures of the new compounds were elucidated by extensive spectroscopic analyses including 1D, 2D NMR along with HR-ESI-MS and FT-IR data. Herein, a distinctive method was added for inspecting secretory profile of the strain by quantification of extract value of cell free supernatant in different types of culture media fallowed by HPLC profiling of respective extracts, which revealed a highly altered metabolic profile of the strain and formed the base for the selection of media. The compounds **1** and **2** showed moderate activity against Gram negative (MIC ~32–64 μg ml^{-1}) in comparison to Gram positive bacterial pathogens. Compound **1** exhibited significant activity in human cancerous cell lines (IC_{50} ~19.2 μM).

Actinomycete genera represent the microbial factories for production of wide range of metabolites with extensive biological activities.[1] Around the globe a small portion of the existing ecosystems have been systematically searched for isolation of actinomycetes for discovery of novel chemical scaffolds.[2,3] During isolation of actinomycetes from soils of untapped Himalayan ecosystems for their chemical diversity and screening in drug discovery paradigms, as part of our programme, we encountered a rare actinomycete strain, characterised as *Lentzea violacea* strain AS08**.** Preliminarily activity of crude extract and no report on molecules from this strain became inspiration for further investigation. The discouragements owing to re-isolation of previously isolated molecules it became imperative to adopt new dereplication methods for production of novel bioactive secondary metabolites.[4,5] So for dereplication, we modified one strain-many compounds **(**OSMAC) method for estimation of secondary metabolites, wherein mass of organic extracts obtained with respect to different growth media was quantified and correlated with their HPLC chromatograms for the chemical diversity. The selective fermentation conditions were set for large scale culture to gain mass of extract for isolation of molecules. The study describes the isolation, structural elucidation, anti-bacterial and anti-tumor activities of compounds **1**–**3** (Fig. 1). The bioactive actinomycete strain, AS08, was isolated and selected during screening of soil samples from high altitude, cold regions of Thajiwas glacier located in north western Himalayas. The strain displayed whitish vegetative and yellowish aerial mycelial colours and also produced green soluble pigment on incubation after 15 days in CYPS media. 16S rRNA gene sequence (1419 bp) revealed that the strain belongs to genus *Lentzea* and species *violacea* as evident from the high similarity to 16S rRNA gene sequences from *Lentzea violacea* (Accession No. FJ486311.1) and *Lentzea violacea* strain F173540 (Accession No. EU593726.1).

Taking together the physical characteristics and the nucleotide sequence of the corresponding 16S rRNA, the actinomycete was identified as *Lentzea violacea* strain AS08. The nucleotide sequence of rRNA gene sequences of the isolate-*Lentzea violacea* was submitted to NCBI under gene bank accession number KX444628.1, and phylogenetic analysis was carried out (Supplementary Fig. S16).

As the strain was isolated from cold climate areas, duplicate cultures of strain were grown in CYPS broth at different

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http://dx.doi.org/10.1016/j.bmcl.2017.03.075
0960-894X/