Combined OSMAC and metabolomics approaches for production of bioactive secondary metabolites of marine *Kocuria marina*

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Marine bacterial microorganisms are a prolific source of bioactive natural products and produce structurally diverse secondary metabolites (SMs). "One strain many compounds" (OSMAC) is an efficient technique to activate the silent genes of microorganisms; as they are likely to cessation of production of SMs over a time period. Metabolomics is an OMIC technique which studies the metabolite profile present in a biological sample. The re-isolation of known compounds is a major drawback in natural product research. Therefore, our study aims to identify the suitable fermentation media for the production of new bacterial SMs which show promising biological activities. In this study, marine actinobacterium *K. marina* was inoculated into five different media and extracted with methanol after 7 days of incubation period. The crude extracts were analyzed using HRESIMS. The data were processed using Xcalibur software. While metabolomics studies were done using MzMine and XCMS online database. AntiMarine and AntiBase databases were used for the dereplication process. From the dereplication analysis, a high number of SMs were identified and categorized mainly into: phenolic, nitrogen-containing metabolites including cyclic peptides and terpenoids. Production of significant amounts of phenolics and cyclic peptides were observed from Media 1 and 5 respectively. The total crude extracts from five media were tested against cervix HeLa, human breast and human adrenocortical carcinoma cell lines and DPPH radical scavenging activity. Media 1 showed more than 75% inhibitory activity for the anticancer (50 µg/mL) and 95% inhibitory activity for DPPH radical scavenging assay (1 mg/mL). This could be due to the presence of cyclic peptides and phenolic dimers as they are reported to have good anticancer and antioxidant activities. Further, the large-scale fermentation and isolation of bioactive compounds from the best suitable media identified from this study is in progress.

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