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Title : ANTIMICROBIAL ACTIVITIES AND ENHANCERS OF DNA GYRASE INHIBITORS FROM MANURE COMPOST ACTINOMYCETES

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Actinomycetes are invaluable sources of bioactive microbial compounds and have been the central of novel drug research as they continuously contribute to the pharmaceutical industry. The traditional perception of actinomycetes being soil bound has currently changed with evidence demonstrating their colonization in unique microenvironment. Through evolution and environmental adaptation, development of unusual metabolic activities has resulted in a variety of anti-infective agents from these bacteria. Nevertheless, the discovery of actinomycetes and its bioactive secondary metabolites from manure compost materials remained understudied. This research was therefore undertaken with the aim of isolating and characterizing the diversity of actinomycetes from manure composts, identifying morphologically distinct isolates, screening isolates for potential antimicrobial activities and bioactive compounds which act as enhancers for DNA gyrase inhibitor as well as elucidating compound(s) responsible for these activities. A collection of 191 actinomycete isolates were recovered from five types of manure composts collected around Selangor, Malaysia. The highest recovery was observed on SCNA medium at 30ºC. The combination of micromorphological characteristics and 16S rRNA sequence analysis revealed considerable actinomycete diversity which covers 12 genera within nine families. It was also found that due to maturity and proper composting techniques, goat manure compost had the most diversified actinomycete community compared to other samples. *Streptomyces spp*. dominated the culture collection (79.1%) while the rest belonged to the non-*Streptomyces* group (20.9%), including an unusual isolate from the genus *Verrucosispora*. The assessment of antimicrobial activities demonstrated that 21.5% of the isolates exhibited antagonistic effect with strong inhibition observed against fungal strains compared to pathogenic bacteria. A modified resazurin-based assay however displayed higher inhibitory activity (40.0%) compared to the disc diffusion assay (26.0%) and was shown to be a better approach in preliminary screening of large numbers of microbial extracts. A new rapid assay was subsequently established to screen for bioactive compounds that enhance the activities of DNA gyrase inhibitor antibiotics using resazurin microtiter plate format. The assay resulted in 3.7% of the ethyl acetate extracts able to enhance nalidixic acid activity while none was able to restore the activity of novobiocin when applied to test organisms known to be resistant to both these antibiotics. The extract of *Streptomyces cheonanensis* (isolate G2B2) showed stable nalidixic acid enhancing potential and antimicrobial activities. Bioassay-guided fractionation was performed and yielded an antimicrobial active compound, 2-hydroxybenzoic acid. Unfortunately, due to limited amount of sample, the active enhancer compound (GB11B) was unable to be elucidated. Nevertheless, this study is the first to describe enhancer activities from *Streptomyces cheonanensis* using a newly developed assay and successfully isolated bioactive antimicrobial compound from this strain which has not been reported previously.