J Microb Biochem Technol 2018, Volume: 10
DOI: 10.4172/1948-5948-C2-041

12th World Congress on

Biotechnology and Microbiology

June 28-29, 2018 | Amsterdam, Netherlands

Phenothiazines and structurally related compounds: highly promising sources for novel antimicrobics

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The growing problem of multidrug resistances among pathogens has been studied extensively and became focus of many investigators. Although new antimicrobial agents are claimed speedy appearance of mutations and acquisition of drug resistance plasmids restrict their usage. Studies by several researchers revealed that drugs belonging to various pharmacological categories possess antimicrobial action. These are designated as 'non-antibiotics'. *In vitro* action was determined following international guidelines. Protective capacity of every compound was evaluated in a standard animal model. MIC of methdilazine, fluphenazine, diclofenac and dicyclomine varied from 5-25 µg/ml in most of the pathogens; MIC of remaining phenothiazines and other drugs ranged from 10-100 µg/ml. Most agents were bactericidal while few were bacteriostatic. Animal protective values were usually between 15 to 30 µg per mouse, trimeprazine could protect at 4 µg/mouse level. These agents could successfully eliminate viable bacteria from blood, liver and spleen. 'Non-antibiotics' exhibit properties that render them important for therapy of infections by multidrug resistant bacteria. Investigations on structure activity relationship of phenothiazines, containing tricyclic benzene rings, show that antimicrobial properties are possibly linked to methyl-thio substituent at position 10 and a halogen moiety at position two of basic phenothiazine structure. In other compounds there are two cyclic rings connected with different moieties in a manner that they often appear as incomplete tricyclic compounds. Moreover, presence of halogen moieties in these compounds has given them greater potentials for antimicrobial function. Thus, non-antibiotics are the most prospective solution for overcoming the enormous problem of infections by multidrug resistant bacteria.

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