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Anti-Bacterial Activity Studies of Derivatives of 6β-Hydroxy Betunolic Acid against Selected Stains of Gram (+) and Gram (-) Bacteria

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Abstract : Multi-drug resistant microbial pathogens are a serious global health problem, and hence, there is an urgent necessity for discovering new drug therapeutics. However, finding alternatives is a one of the biggest challenges faced by the global drug industry due to the spiraling high cost and serious side effects associated with modern medicine. On the other hand, plants and their secondary metabolites can be considered as good sources of scaffolds to provide structurally diverse bioactive compounds as potential therapeutic agents. 6β-hydroxy betunolic acid is a triterpenoid isolated from bark of Schumacheria castaneifolia which is an endemic plant to Sri Lanka which has shown antibacterial activity against both Staphylococcus aureus (ATCC 29213) and methicillin-resistant S. aureus with Minimum Inhibition Concentration (MIC) of 16 µg/ml. The objective of this study was to determine the anti-bacterial activity for the derivatives of 6β- hydroxy betunolic acid against standard strains of Staphylococcus aureus (ATCC 29213 and ATCC 25923), Enterococcus faecalis (ATCC 29212), Escherichia coli (ATCC 35218 and ATCC 25922), Pseudomonas aeruginosa (ATCC 27853), carbepenemas produce Kebsiella pneumonia (ATCC BAA 1705) and carbepenemas non produce Kebsiella pneumonia (ATCC BAA 1706) and four stains of clinically isolated methicillin resistance S. aureus and Acinetobacter. Structural analogues of 6β-hydroxy betunolic acid were synthesized by modifying the carbonyl group at C-3 to obtain olefin and oxime, the hydroxyl group at C-6 position to a ketone, the carboxylic acid at C-17 to obtain amide and halo ester and the olefin group at C-20 position to obtain epoxide. Chemical structures of the synthesized analogues were confirmed with spectroscopic data and antibacterial activity was determined through broth micro dilution assay. Results revealed that 6β- hydroxy betunolic acid shows significant antibacterial activity only against the Gram positive strains and it was inactive against all the tested Gram negative strains for the tested concentration range. However, structural modifications into oxime and olefin at C-3, ketone at C-6 and epoxide at C-20 decreased its antibacterial activity against the gram positive organisms and it was totally lost with the both modifications at C-17 into amide and ester. These results concluded that the antibacterial activity of 6β- hydroxy betunolic acid and derivatives is predominantly depending on the cell wall difference of the bacteria and the presence of carboxylic acid at C-17 is highly important for the antibacterial activity against Gram positive organisms.

Keywords : antibacterial activity, 6β- hydroxy betunolic acid, broth micro dilution assay, structure activity relationship
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