ANTIMICROBIAL ACTIVITY OF B-LACTAM–BILE ACID CONJUGATES

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β-Lactams are a large class of antibiotics characterized by the presence of an azetidine-2-one ring, which is the core of biological activity. The azetidine-2-one (β - lactam) ring system is a common structural feature of a number of broad spectrum β - lactam antibiotics, like penicillins, cephalosporins, carbapenems, nocardicins and monobactams, which have been widely used as chemotherapeutic agents for treating microbial diseases. It also shows many other interesting biological properties, such as cholesterol absorption inhibitors, human cytomegalovirus protease inhibitors, thrombin inhibitors, antihyperglycemic, anti-tumour, anti-HIV, antiinflammatory, analgesic activities9 and serine-dependent enzyme inhibitors. However, microorganisms have built up resistance against the most traditional b-lactam antibiotics due to the wide-spread overuse of antibiotics. Therefore, the phenomenon of bacterial resistance forces the continuous modification of structure of known active compounds and the development of new ones. Azoles are the largest class of antifungal agents in clinical use. 1,2,3-Triazole moieties are attractive connecting units, as they are stable to metabolic degradation and capable of hydrogen bonding, which can be favorable in binding of biomolecular targets and solubility.

Target molecules were synthesized using 1,3-dipolar cycloaddition reaction of β-lactams containing azide and bile acids containing terminal alkyne, in the presence of Cu(I) catalyst (click chemistry). The cycloaddition reaction of propargyl esters and with azido β-lactams in the presence of Cu(I) catalyst (click chemistry) under microwave irradiation furnished diastereomeric mixture of novel conjugates in excellent yields (85-97%). All the newly synthesized azido β-lactams, steroidalalkynes and 1,2,3-triazole-linked β-lactam–bile acid conjugates were tested in vitro for antifungal and antibacterial activity.

The antifungal activity was tested using isolate fungal strains *Candida albicans*, the antibacterial activity was evaluated against *Escheirchia coli* and *Staphylococcus aureus*. The MIC and IC50 values were determined using standard broth microdilution technique described by NCCLS. In comparison with the antimicrobial activity, amphotericin B and fluconazole were used as the reference antifungal agents, while tetracycline and ampicillin were used as the reference antibacterial agents. From the biological data, it was observed that azido β-lactams and steroidal alkynes were almost inactive against all the tested strains. The MIC value for all these compounds was >128 mcg/mL. The activity of compounds conjugates was higher or comparable to that of fluconazole against *C.albicans* with MIC value of 16–32 mcg/ml. Furthermore, those compounds showed good antibacterial activity against *E. coli* having MIC value of 16 mcg/ml. The compounds derived from cholic acid having 7-hydroxy group showed moderate antibacterial activity against *S. aureus*. However, the compounds derived from deoxycholic acid in the absence of 7-hydroxy were less active against *S. aureus* with MIC value of >128 mcg/ml. From the overall activity results, it was observed that the ester or amide linkage and chloro substituent on phenyl ring of β-lactam part did not affect the activity of the compounds.