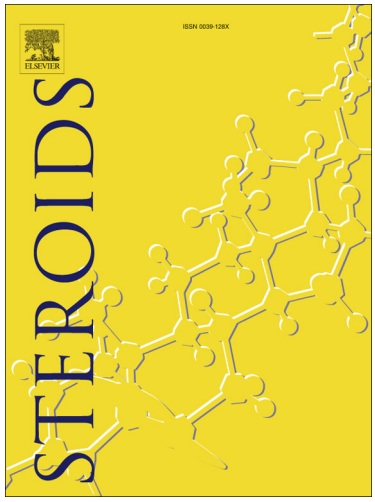

Clickable Conjugates of Bile acids and Nucleosides: Synthesis, Characterization, *in vitro* anticancer and antituberculosis studies

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Clickable Conjugates of Bile acids and Nucleosides: Synthesis, Characterization, *in vitro* anticancer and antituberculosis studies

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Abstract

A series of clickable bile acid-nucleosides conjugates linked directly or *via* amino acid linker were synthesized, and characterized by spectroscopic techniques such as ^{1}H NMR, ^{13}C NMR, FT-IR, HRMS and HPLC. The synthesized compounds **6a-p** were screened for their *in vitro* anticancer property against a panel of three cancer cell lines (PC-3, MCF-7, IMR-32). In addition, the synthesized derivatives were also tested for their antimycobacterial activity against *Mycobacterium tuberculosis* H_{37}Rv (ATCC 27294 strain). Among the screened compounds, cholic acid-uridine clicked conjugate (**6c**), and cholic acid-uridine clicked conjugate liked *via* phenylalanine moiety (**6m**) were found to be most active against MCF-7 and IMR-32 exhibiting an IC_{50} value of 8.084 and 8.71 µM, respectively. The antimycobacterial study of the synthesized conjugates revealed all the conjugates to be active with MIC values in the range of 4.09-15.41 µM. Deoxycholic acid-adenosine clicked conjugate (**6b**) showed most promising antituberculosis property with MIC value of 4.09 µM. Most of the synthesized conjugates were found to be safe at 50 µM against normal human embryonic kidney (HEK 293T) cell line.

Keywords: Bile acid, nucleosides, triazoles, anticancer, antimycobacterial.

1. Introduction

Cancer has been recognized worldwide as one of the deadly diseases. Studies have estimated about 8.2 million cancer-related deaths worldwide in 2012, and an expected increase of cancer patients to 22 million within the next two decades [1]. In spite of an incremental improvement in cancer treatment procedures including surgery, hormone therapy, radiation therapy, immunotherapy and combination chemotherapy, a continuous growth in the mortality has been observed [2]. In particular, the usage of chemotherapeutic agents *via* combination chemotherapy