New artemisinin-cholic acid hybrids containing 1,2,3-triazole linkers

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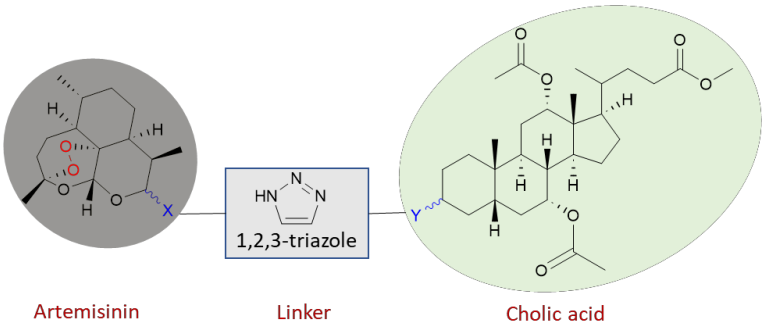
Artemisinin (ART) is a sesquiterpene lactone bearing a 1,2,4-trioxane ring (endoperoxide bridge) as a pharmacophore moiety. ART and its semisynthetic derivatives have shown not only antimalarial, but also anticancer properties via ferroptosis, cell cycle arrest and angiogenesis inhibition.[1] Interestingly, ART alters the expression of the androgen receptor (AR) via induced 26S proteasome-mediated degradation of the receptor protein and disrupts the androgen responsiveness in the prostate cancer cell lines PC-3 and LNCaP.[2]

Bile acids play an important role in the hepatobiliary circulation by regulating lipid absorption of vitamins and lipophilic drugs. Bile acid hybrid molecules have been designed to increase the cytotoxicity, cytoselectivity and cellular uptake of known chemotherapeutics.[3] Notably, artemisinin-bile acid hybrids have shown promising *in vitro* anticancer activities against various cancer cell lines.[4]



In the present study, a series of artemisinin-cholic acid hybrids incorporating a 1,2,3-triazole linker were designed and synthesized. 1,2,3-Triazole, as a structural feature of many pharmacologically active compounds possessing antiviral, antimalarial and anticancer properties,[5] is expected to confer on the chemical stability and anticancer activity of the new hybrids. Selected new hybrid compounds were evaluated *in vitro* in PC-3 prostate cancer cells, showing enhanced antiproliferative and cell migration inhibitory activity when compared with previously synthesized by our group hybrids with an ester type linkage between the ART and cholic acid moiety. Furthermore, all the tested hybrids showed no toxicity in the NIH-3T3 fibroblast cell line. Herein, the results of our synthetic efforts towards the new ART-cholic acid hybrids and the evaluation of their biological activity will be presented.

References:

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