Synthesis and Cytotoxic Properties of Novel Triterpenoid-1,2,3-triazole Conjugates

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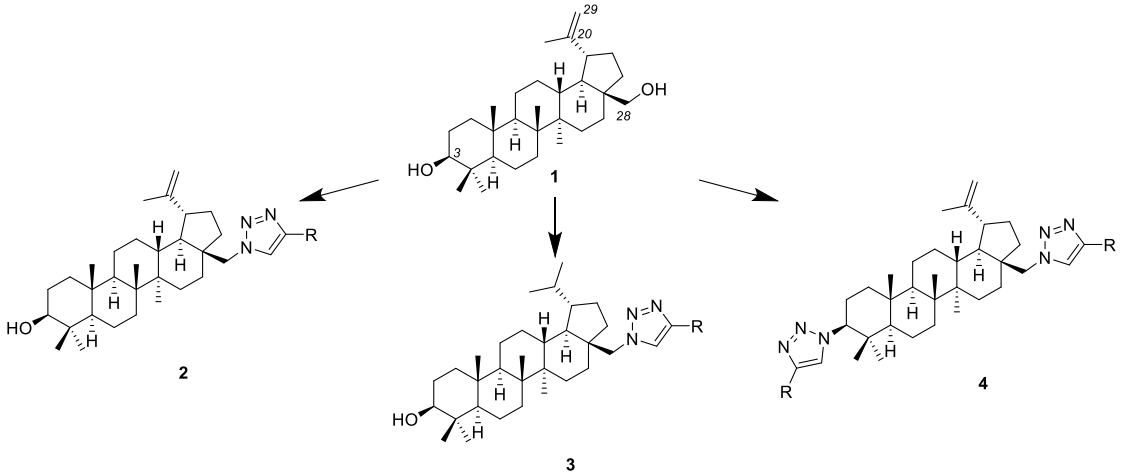
Betulin is an abundant naturally occurring triterpene, most commonly found in birch bark. Research shows that betulin and its derivatives possess wide spectrum of biological activities such as anti-HIV, andiinflammatory and anticancer [1,2]. Use of betulin is limited by its low solubility in water. Therefore, to improve properties of betulin, structural modifications with new biological activity simultaneously improving solubility in water are being made [3].

In this work, triterpenoid-1,2,3-triazole conjugates were obtained in 5 step synthesis from betulin (**1**). To obtain betulin (**2**) and lupan-3β-ol (**3**) monoconjugates, primary alcohol group at C(28) was chemoselectively oxidised. Obtained aldehyde was threated with hydroxylamine hydrochloride to obtain corresponding oxyme. Following catalytic hydrogenation under certain conditions gave amines with or without reduced C(20)-C(29) double bond. From the obtained amines respective azides were synthesised in diazotransfer reactions using trifluoromethanesulfonic azide. The latter were employed in Cu(I) catalyzed 1,3-dipolar azide-alkyne cycloaddition reactions to obtain betulin and lupan-3β-ol conjugates.

To obtain betulin-1,2,3-triazole diconjugates (**4**), betulin was oxidised in Swern conditions to yield corresponding ketoaldehyde. The obtained ketoaldehyde was treated with hydroxylamine hydrochloride to provide respective dioxyme, that was used in reductive amination with $NaCNBH_3$ to obtain corresponding diamine. Similarly to monoazides, diazide was synthesized from diamine in diazotransfer reaction using trifluoromethanesulfonic azide. Diazide was employed in 1,3-dipolar azide-alkyne cycloaddition reaction to obtain betulin-1,2,3-triazole diconjugate.

Novel triterpene-1,2,3-triazole conjugates were tested on rare cancer cell lines and observed cytotoxicity will be reported.



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