DESIGN AND SYNTHESIS OF NOVEL ANTIVIRAL TRITERPENE DERIVATIVES FOR MEDICINE

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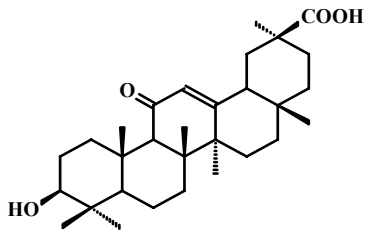
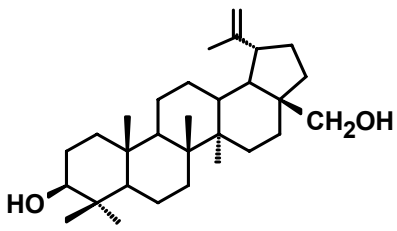
Triterpene compounds of natural origin, Glycyrrhetinic Acid (GLA) (1) to be the major triterpenoid of oleanene type isolated from licorice roots (Gl. uralensis Fisher) and Betulin (BL) (2), the main lupane group triterpenoid of the birch bark of Betula pendula, are of great interest for medicine due to wide range of biological and pharmacological activities (anti-inflammatory, anti-ulcerogenic, antibacterial, hypolipidemic, antitumor, antiviral, etc.) [1]. Using software PASS prediction of biological activity spectra on the basis of structure of compound quantity relations of "structure-antiviral activity" for BL, and related compounds were obtained and used for the chemical design of new bioactive derivatives for structure-antiviral activity relationships studies.

Selective chemical transformations of GLA, BL, allobetulin, betulinic, and betulonic acids were carried out by using simple protocols. Novel groups of nitrogen containing derivatives (amides, ureids, peptides, hydrazides etc.) of GLA and its related compounds (11-desoxo-GLA, 18,19-dehydro-GLA), betulonic and betulinic acids were synthesized. A-nor- and seco-derivatives of allobetulin and 11-deoxo-GLA were synthesized by using dehydrating agents and ozonolysis. Selective oxidative transformations of BL and its derivatives, GLA and related compounds have been studied by using ozone, peracids, dimethyldioxirane, and NaOCl. Lactones and lactames were synthesized on the basis of 3-oxo-derivatives. Structures of novel compounds were confirmed by high resolution NMR spectroscopy.

Among BL, betulonic acid and GLA derivatives produced potent inhibitors of influenza A, herpes simplex type 1, ECHO 6 enterovirus, HIV-1 inhibitors and anti-SARS corona virus active compounds were found.





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