Chemical Modification of Glycyrrhizic Acid in Relation to the Biological Activities

Lidiya A. Baltina,[a] Genrikh A. Tolstikov[b]

[a]*Institute of Organic Chemistry Ufa Research Centre of RAS, prospect Oktyabrya 71, Ufa, 450054, Russia; Fax: +7 (3472) 356066; E-mail: root@chemorg.ufanet.ru*

[b]*Novosibirsk Institute of Organic Chemistry, acad. Lavrentjev Avenue 9, Novosibirsk , 630090, Russia; Fax: +7 (3832) 344752*

Glycyrrhizic acid (GA) is the major saponin of licorice roots (*Glycyrrhiza glabra L., Gl. uralensis F.*) possessing different kinds of biological activities (antiinflammatory, antiulcerate, antiviral, antitumor, immunomodulate, etc.). Recently GA was shown to be effective against human immunodeficiency and Marburg viruses. Thus GA is noteworthy drugs among phytotherapeutics, while the licorice root itself has long been used in traditional or folk medicine of the East.

For the past years we studied the chemical transformations of GA to design new biologically active compounds for medicine. We developed new methods of preparation pure GA (90-95%) from commercial raw materials (the licorice extract and glycyram) to be tested successfully on the experimental equipment. New low toxic salts and esters of GA were produced to be effective as antiinflammatory and antiulcerate agents.

New bioactive amides of GA with antibiotices, pyrimidines, chinolines and pyridines were prepared using N,N'-dicyclohexylcarbodiimide. Triterpene glycopeptides - GA derivatives were synthesised including glycyrrhizyl-analogs of the known immunostimulator N-acetylmuramoyldipeptide (MDP) to be perspective as immunoregulators with the variety of useful for medicine properties. The synthesis of GA analogs with modified carbohydrate chain and aglycone was developed including 2-desoxy-, 2- and 6-amino- and nitro-glycosides.

The selective reduction of COOH groups of the carbohydrate part and C(11)=O group of the aglycon was made using $NaBH_4$ and β-D-Glcp-(1-2)-β-D-Glcp-olean-9(11),12-dien derivatives of GA were obtained in good yields.

Some GA related compounds were shown more pronounced antiinflammatory, antiulcerate and hepatoprotective activities in mice and rats as compared with natural glycoside. Some of the GA derivatives are effective as HIV-1 and HIV-2 inhibitors in vitro. Preparation niglizin was recommended for the clinical study as the HIV inhibitor and hepatoprotector.