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A rare class of poly (sugar acids): Poly [3-(3, 4-dihydroxyphenyl) glyceric acid] from medicinal plants of boraginaceae family and its anticancer efficacy

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Abstract

Natural polysaccharides have long been studied and widely used in medicine and pharmaceutics. Besides, within the field of pharmacologically active biopolymers the area of stable polyethers seems rather new and attractive. The main chemical constituent of high molecular (>1000 kDa) water-soluble preparations from medicinal plants of *Symphytum asperum, S.caucasicum, S.officinale, S.grandiflorum, Anchusa italica, Cynoglossum officinale* and *Borago officinalis* (Boraginaceae) according to data of liquid-state 1H, 13C NMR, 2D 1H/13C HSQC, 2D DOSY and solid-state 13C NMR spectra was found to be poly[oxy-1-carboxy-2-(3,4-dihydroxyphenyl) ethylene] or poly[3-(3,4-dihydroxyphenyl)glyceric acid] (PDPGA). The polyoxyethylene chain is the backbone of this biopolymer. 3, 4-Dihydroxyphenyl and carboxyl groups are regular substituents at two carbon atoms in the chain. The repeating unit of this regular polyether is 3-(3, 4-dihydroxyphenyl) glyceric acid residue. PDPGA as a 3,4-dihydroxyphenyl derivative of poly(2,3-glyceric acid ether) belongs to a rare class of poly(sugar acids) as well. Its basic monomeric moiety glyceric acid is oxidative form of aldotriose glyceraldehyde. In this case poly (2, 3-glyceric acid ether) chain is the backbone of this polymer molecule and 3,4-dihydroxyphenyl groups are regular substituents at 3C carbon atoms in the chain. Every repeating structural unit of a unique PDPGA contains two phenolic hydroxyl groups in ortho-position and one carboxyl group. Multifunctionality of PDPGA should be a reason of its wide spectrum of biological activities. Oligomers of PDPGA was synthesized by "green" chemistry enzymatic ring opening polymerisation of methyl 3-(3, 4-dibenzyloxyphenyl) glycidate using lipase from Candida rugosa and further deprotections. Enzymatically obtained oligomers cause interest for diverse biological tests. PDPGA exerted anticancer activity in vitro and in vivo against androgen-dependent and -independent human prostate cancer (PCA) cells via targeting androgen receptor, cell cycle arrest and apoptosis without any toxicity, together with a strong decrease (87%) in prostate specific antigen level in plasma. Thus, PDPGA was identified as a potent agent against PCA without any toxicity.

Biography

Barbakadze V has his expertise in isolation and structure elucidation of a new series of plant polyethers, which are endowed with pharmacological properties as anti-cancer agents. Besides, he interested in enantioselective synthesis and biological activities of basic monomeric moiety of these biopolyethers, synthesis of enantiomerically pure epoxides as chiral building blocks for the production of synthetic analogues of natural polyethers. He has completed his Ph.D and D.Sci. in 1978 and 1999, respectively. He is the head of Department of Plant Biopolymers and Chemical Modification of Natural Compounds at the Tbilisi State Medical University I.Kutateladze Institute of Pharmacochemistry. In 1996 and 2002 he has been a visiting scientist at Utrecht University, The Netherlands, by University Scholarship and The Netherlands organization for scientific research (NWO) Scholarship Scientific Program, respectively. He has published more than 100 papers in reputed journals. In 2004 he was Georgian State Prize Winner in Science and Technology.

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