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Novel representative of poly(sugar acids): A poly[3-(3,4-dihydroxyphenyl) glyceric acid ether] its synthetic analogues and their comparative anticancer efficacy

Vakhtang Barbakadze
University of Catania, Italy

The main chemical constit¬uent of water-soluble crude polysaccharides from medicinal plants 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 one and the same high molecular (>1000 kDa) glyceric acid-derived polyether: 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 PDPGA. Dihydroxyphenyl and carboxyl groups are regular substituents at two carbon atoms in the chain. The repeating unit of PDPGA is 3-(3,4-dihydroxyphenyl) glyceric acid residue. PDPGA as derivative of poly(glyceric acid ether) belongs to a class of acidic polysaccharides [poly(sugar acids)]. Its basic monomeric moiety glyceric acid is a three-carbon sugar acid which is oxidative form of aldotriose glyceraldehyde. The monomer of PDPGA 3-(3,4-dihydroxyphenyl)glyceric acid was synthesized via Sharp less asymmetric dihydroxylation of trans-caffeic acid using a potassium osmate catalyst which is new findings in sugar acids. Methylated derivative of PDPGA was synthesized via ring opening polymerization of 2-methoxycarbonyl-3-(3,4-dimethoxyphenyl)oxirane using BF3•OEt2. Human Hyaluronidase (Hyal-1) degrades high molecular mass Hyaluronic Acid (HA) into smaller fragments which have pro-inflammatory effects. PDPGA possesses the ability to inhibit the enzymatic activity of Hyal-1 completely. Consequently PDPGA exhibited anti-inflammatory efficacy. PDPGA and its synthetic monomer exerted anticancer activity in vitro and in vivo against androgen-dependent and-independent human Prostate Cancer (PCA) cells with lesser cytotoxicity towards non-neoplastic human prostate epithelial cells PWR-1E. PDPGA exhibited anticancer efficacy against PCA via targeting androgen receptor, cell cycle arrest and apoptosis together with a strong decrease in prostate specific antigen level (87%) in plasma. The anticancer efficacy of PDPGA against PCA cells is more compared to its synthetic monomer. Methylated PDPGA did not show any activity against PCA. Overall, this study identifies PDPGA as a potent agent against PCA without any toxicity.

Biography

Vakhtang Barbakadze has his expertise in isolation and structure elucidation of a new series of plant polysaccharides, 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 biopolymers. He has completed his PhD 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 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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