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Abstract

The Boraginaceae family comprises a group of plants that are important for medicine and pharmaceutics. The main chemical constit¬uent 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 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 repeating unit of PDPGA 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 class of acidic polysaccharides [poly(sugar acids)]. Its basic monomeric moiety glyceric acid is a three-carbon sugar acid. The monomer of PDPGA 3-(3,4-dihydroxyphenyl)glyceric acid was synthesized via Sharpless 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 (ROP) of 2-methoxycarbonyl-3-(3,4-dimethoxyphenyl)-oxirane using BF3•OEt2. Oligomers of PDPGA was synthesized by “green” chemistry ROP enzymatic polymerization of methyl 3-(3,4-dibenzyloxyphenyl)glycidate using lipase from Candida rugosa and further deprotection. 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 suppressed the growth and induced death in androgendependent and -independent human prostate cancer (PCA) cells, with comparatively lesser cytotoxicity towards non-neoplastic human prostate epithelial cells. PDPGA induced apoptotic death by activating caspases, and also strongly decreased androgen receptor and prostate specific antigen (PSA) expression. Plasma analyses revealed that PDPGA administration of male athymic nude mice with 22Rv1 xenografts caused a strong dose-dependent decrease in PSA levels by 87%. Methylated PDPGA did not show any activity against PCA. Thus, PDPGA was identified 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 polyethers, which are endowed with pharmacological properties as anticancer 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. In 1978 and 1999 he has completed his Ph.D and D.Sci., respectively. In 2006 up to date he is the Head of Department of Plant biopolymers and Chemical Modification at 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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