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Sugar-based biopolymers: Poly[3-(3,4-Dihydroxyphenyl)¬Glyceric acid] — The paradigm of a multifunctional biopolyether with applications in prostate cancer prevention and treatment

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Sugar-based biopolymer poly[oxy-1-carboxy-2-(3,4-dihydroxy¬phe¬nyl)¬ethylene] that is poly[3-¬¬(3,4-¬di¬¬hyd¬¬roxy¬¬phe¬nyl)¬glyceric acid] (PDPGA) was found to be the main chemical constit¬uent of high molecular (>1000 kDa) water-soluble preparations from Symphytum asperum, S. caucasicum, S. officinale, S. grandiflorum, Anchusa italica, Cynoglossum officinale and Borago officinalis (Boraginaceae). The structur elucidation of PDPGA was carried out according to data of liquid-state 1H, 13C NMR, APT, 1D NOE, 2D 1H/13C HSQC, 2D DOSY and solid-state 13C NMR spectra. The polyoxyethylene chain is the backbone of this regular polymer molecule with a residue of 3-(3,4-dihydroxyphenyl)glyceric acid as the repeating unit. PDPGA belongs to a class of poly(sugar acids) as well. Poly(2,3-glyceric acid ether) chain is the backbone of this polymer molecule and 3,4-dihydroxyphenyl groups are regular substituents at carbon atoms in the chain. The monomer of PDPGA 3-(3,4-dihydroxy-phe¬nyl)glyceric acid was synthesized via Sharpless asymmetric dihydroxylation of trans-caffeic acid using a potassium osmate catalyst. Methylated derivative of PDPGA was synthesized via ring opening polymerization (ROP) of 2-methoxycarbonyl-3-(3,4-dimethoxyphenyl)oxirane using a cationic initiator $BF_3 \cdot OEt_2$. Oligomers of PDPGA was synthesized by “green” chemistry enzymatic ROP of methyl 3-(3,4-dibenzyloxyphenyl)glycidate using lipase from Candida rugosa and further deprotection. PDPGA possesses the ability to inhibit the enzymatic activity of Hyal-1 completely. Consequently, PDPGA exhibited anti-inflammatory efficacy. PDPGA and synthetic monomer exerted anticancer activity in vitro and in vivo against prostate cancer (PCA) cells via targeting androgen receptor, cell cycle arrest and apoptosis without any toxicity, together with a strong decrease in prostate specific antigen level in plasma. Thus, PDPGA was identified as a potent agent against PCA.

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 anti-cancer agents. Besides, he has interested in obtaining of synthetic analogues of natural polyethers. He has completed his Ph.D and D.Sci. in 1978 and 1999. 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.