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Biomacromolecule poly[3-(3,4-dihydroxyphenyl)glyceric acid] with potential therapeutic effect

The high molecular (>1000 kDa) water-soluble preparations from different species *(Symphytum asperum, S. caucasicum, S. officinale, S. grandiflorum* and *Anchusa italica)* of Boraginaceae family were isolated. According to ^{13}C, ^{1}H NMR, 2D heteronuclear $^{1}H/^{13}C$ HSQC spectral data and 1D NOE experiments their main chemical constit¬uent was found to be poly[oxy-1-carboxy-2-(3,4-dihydroxyphenyl)ethylene] or poly[3-(3,4-dihydroxyphenyl)glyceric acid] (p-DGA). The polyoxyethylene chain is the backbone of this polymer molecule and 3,4-dihydroxyphenyl and carboxyl groups are regular substituents at two carbon atoms in the chain. The repeating unit of this regular polymer is 3-(3,4-dihydroxyphenyl)glyceric acid residue. This compound is a first representative of a new class of natural polyethers. Then the racemic monomer 2,3-dihydroxy-3-(3,4-dihydroxyphenyl)propionic acid (DDPPA) and its virtually pure enantiomers (+)-(2R,3S)-2,3-dihydroxy-3-(3,4-dihydroxyphenyl) propionic acid and (:)-(2S,3R)-2,3-dihydroxy-3-(3,4-dihydroxyphenyl)propionic acid were synthesized for the first time via Sharpless asymmetric dihydroxylation of trans-caffeic acid derivatives using an osmium catalyst, a stoichiometric oxidant N-methylmorpholine-N-oxide and enantiocomplementary catalysts cinchona alkaloid derivatives $(DHQ)_2$-PHAL and $(DHQD)_2$-PHA as chiral auxiliaries. p-DGA has wide spectrum of biological activity: anticomplementary, antioxidant, anti-inflammatory properties, burn and wound healing effect. p-DGA and DDPPA exerted anti-cancer efficacy *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 in prostate specific antigen level in plasma. However, our results showed that anticancer efficacy of p-DGA is more effective compared to its synthetic monomer. Overall, this study identifies p-DGA as a potent agent against PCA without any toxicity, and supports its clinical application.

Biography

Vakhtang Barbakadze has completed his PhD and DSci in 1978 and 1999 from Zelinsky Instiute of Organic Chemistry, Moscow, Russia and Durmishidze Institute of Biochemistry and Biotechnology, Tbilisi, Georgia, respectively. From 2006, till to date he is the head of laboratory of plant biopolymers at the Tbilisi State Medical University Institute of Pharmacochemistry. In 1996 and 2002, he has been a visiting scientist at Utrecht University (faculty of pharmacy), The Netherlands, by University Scholarship and The Netherlands organization for scientific research (NWO) Scholarship Scientific Program, respectively. He has published more than 73 papers in reputed journals.

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