

Novel polysaccharide – phenolic derivative of poly (glyceric acid ether) from different species of Boraginaceae family and its anticancer efficacy

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Abstract

The Boraginaceae family comprises a group of plants that are important for medicine and pharmaceuticals. The therapeutic effect of these plants is related to the content of many biologically active compounds. However, these plants are also rich in hepatotoxic pyrrolizidine alkaloids. The 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) were investigated. The fractionation of aforementioned preparations by means of ultrafiltration on membrane filter with cut off value of 1000 kDa permitted completely remove toxic pyrrolizidine alkaloids. Consequently the use of above mentioned plants does not rise any objection. The main chemical constituent of high molecular preparations was found to be poly[oxy-1-carboxy-2-(3,4-dihydroxyphenyl)ethylene] or poly[3-(3,4-dihydroxyphenyl)glyceric acid] (PDPGA)(1) (Fig. 1) according to data of liquid-state ^1H , ^{13}C NMR, 2D $^1\text{H}/^{13}\text{C}$ HSQC, 2D DOSY and solid-state ^{13}C NMR spectra. The polyoxyethylene chain is the backbone of this polymer molecule with a residue of 3-(3,4-dihydroxyphenyl)glyceric acid (2) (Fig. 2.) as the repeating unit. PDPGA as a phenolic derivative of poly(glyceric acid ether) belongs to a class of an acidic polysaccharides [poly(sugar acids)]. PDPGA exhibited anticomplementary, antioxidant, antiinflammatory, burn and wound healing and anticancer activities (Fig. 3). Human Hyaluronidase (Hyal-1) degrades high molecular Hyaluronic acid into smaller fragments which have pro-inflammatory effects. PDPGA possessed the ability to inhibit the enzymatic activity of Hyal-1 completely. Consequently PDPGA exhibited anti-inflammatory efficacy. Besides, PDPGA exerted anticancer activity in vitro and in vivo against androgen-dependent (LNCaP) and – independent (22Rv1) human prostate cancer (PCA) cells with comparatively lesser cytotoxicity towards non-neoplastic human prostate epithelial cells PWR-1E. PDPGA induced apoptotic death by activating caspases, and also strongly decreased androgen receptor and prostate specific antigen expression by 87%. Overall, this study identifies PDPGA as a potent agent against PCA without any toxicity, and supports its clinical application.



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. 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 Pharmacochimistry. 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.



Speaker Publications:

1. Gogilashvili L, Amiranashvili L, Merlani M, Salgado A, Chankvetadze B, Barbakadze V (2020) Poly[3-(3,4-dihydroxy-phenyl)glyceric acid] from *Cynoglossum officinale* L. (Boraginaceae). Bull. Georg. Natl. Acad. Sci. 14:108-113. <http://science.org.ge/bnas/vol-14-1.html>.
2. Merlani M, Song Z, Wang Y, Yuan Y, Luo J, Barbakadze V, Chankvetadze B, Nakano T (2019) Polymerization of bulky of oxirane monomers leading to polyethers exhibiting intramolecular charge transfer interactions. Macromol. Chem. Phys.1900331. <https://onlinelibrary.wiley.com/doi/10.1002/macp.201900331>.

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