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Novel biopolymer with anticancer activity

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Tithin the field of pharmacologically active biopolymers the area of stable polyethers seems rather attractive. The highmolecular fractions from the several species of two genera Symphytum and Anchusa were isolated by ultrafiltration of water-soluble crude polysaccharides on the membrane filter with cut-off value of 1000 kDa. According to IR, ¹³C and ¹H NMR, 1D NOE, 2D heteronuclear ¹H/¹³C HSQC and 2D DOSY experiments the main structural element of these preparations was found to be a new regular polymeric molecule. The polyoxyethylene chain is the backbone of this biopolymer. 3,4-Dihydroxyphenyl and carboxyl groups are regular substituents at two carbon atoms in the chain. The repeating unit of this regular caffeic acidderived polyether, is 3-(3,4-dihydroxyphenyl) glyceric acid residue. Thus, the structure of natural polymer under study was found to be poly[oxy-1-carboxy-2-(3,4-dihydroxyphenyl)ethylene] or poly[3-(3,4-dihydroxyphenyl)glyceric acid] (PDPGA). Such caffeic acid-derived biopolymer to our knowledge has not been known and has been identified for the first time. This compound represents a new class of natural polyethers. Then the racemic monomer and its pure enantiomers (+)-(2R,3S)-2,3-dihydroxy-3-(3,4-dihydroxy-phenyl)-propionic acid [(2R,3S)-DDPPA] and (-)-(2S,3R)-2,3-dihydroxy-3-(3,4-d phenyl)-propionic acid [(2S,3R)-DDPPA] were synthesized for the first time via Sharpless asymmetric dihydroxylation of trans-caffeic acid derivatives using an osmium catalyst and (DHQ)2-PHAL and (DHQD)2-PHAL as chiral auxiliaries. PDPGA is endowed with intriguing pharmacological activities as anticomplementary, antioxidant, anti-inflammatory, burn and wound healing and anticancer properties. PDPGA and its synthetic monomer exerted anticancer activity 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 PDPGA is more effective compared to its synthetic monomer. Overall, this study identifies PDPGA as a potent agent against PCA without any toxicity and supports its clinical application.

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