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BIOPOLYETHER FROM MEDICINAL PLANTS: AS ANTICANCER AGENT

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Within the field of pharmacologically active biopolymers the area of stable polyethers seems rather new and attractive. A new series of linear and regular caffeic acid derived polyether, namely poly[oxy-1-carboxy-2-(3,4-dihydroxyphenyl)ethylene] or poly[3-(3,4-dihydroxyphenyl)glyceric acid] (PDPGA) was isolated and identified in the water-soluble, high molecular weight fractions obtained from *Symphytum asperum, S.caucasicum, S.officinale, S.grandiflorum and Anchusa italica* (Boraginaceae). According to data of ^{13}C, ^{1}H NMR, 2D $^{1}H/^{13}C$ HSQC experiments, the polyoxyethylene chain is the backbone of the polymer molecule. 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. Most of the carboxylic groups of PDPGA from *A. italica and S.grandiflorum* unlike the *polymer of S.asperum, S.caucasicum and S.officinale* are methylated. The 2D DOSY experiment gave the similar diffusion coefficient for the methylated and non-methylated signals of *A. italica* PDPGA. Both sets of signals fell in the same horizontal. This would imply a similar molecular weight for methylated and non-methylated polymers. PDPGA is endowed with intriguing pharmacological properties as anticomplementary, antioxidant, anti-inflammatory, burn and wound healing effect. The synthesis of racemic monomer of PDPGA, 2,3-dihydroxy-3-(3,4-dihydroxyphenyl)propionic acid (DDPPA) and its enantiomers (+)-(2R,3S)-DDPPA and (−)-(2S,3R)-DDPPA was carried out via sharpless asymmetric dihydroxylation of *trans*-caffeic acid derivatives using a potassium osmiate catalyst and cinchona alkaloid derivatives (DHQ)2-PHAL and (DHQD)2-PHAL as chiral auxiliaries. PDPGA and DDPPA exerted anti-cancer efficacy *in vitro and in vivo* against 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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