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Caffeic acid-derived polyether from medicinal plants, its synthetic monomer, methylated derivative of synthetic analogue and their comparative anticancer efficacy

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According to data of ^{13}C, ^{1}H NMR, 2D heteronuclear $^{1}H/^{13}C$ HSQC (heteronuclear single quantum coherence) and 2D diffusion-ordered spectroscopy (DOSY) experiments the main chemical constit¬uent of high molecular (>1000 kDa) water-soluble preparations from different species of two genera *Symphytum* and *Anchusa* (Boraginaceae family) was found to be polyether poly[oxy-1-carboxy-2-(3,4-dihydroxyphenyl)ethylene] or poly[3-(3,4-dihydroxyphenyl)glyceric acid] (PDPGA). 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. Then enantioselective synthesis was carried out via sharpless asymmetric dihydroxylation of *trans*-caffeic acid derivative using a potassium osmiate catalyst and enantiocomplementary catalysts cinchona alkaloid derivatives $(DHQ)_2$-PHAL and $(DHQD)_2$-PHA as chiral auxiliaries obtaining (+)-(2R,3S)-2,3-dihydroxy-3-(3,4-dihydroxy-phenyl)propionic acid and (-)-(2S,3R)-2,3-dihydroxy-3-(3,4-dihydroxyphenyl)propionic acid, respectively. Methylated derivative of PDPGA was synthesized via ring opening polymerization of 2-methoxycarbonyl-3-(3,4-dimethoxyphenyl)oxirane using a cationic initiator. 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 androgen-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 anticancer efficacy of PDPGA against human PCA cells is more compared to its synthetic monomer. Methylated synthetic analogue of PDPGA did not show any activity against PCA. Overall, this study identifies PDPGA as a potent agent against PCA without any toxicity, and supports its clinical application.

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