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Novel (+)-decursin derivatives as inhibitors of the Wnt/β-catenin pathway

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The Wnt/β-catenin signaling pathway is associated with the development of embryos and regulates the proliferation and differentiation of cells. Abnormal activity of this pathway and the growth of β-catenin-dependant transcription induce various tumors development including colon and prostate cancer. In this study, it were synthesized the (+)-decursin derivatives originating from decursin, isolated from Angelica gigas, and screened in a cell-based assay for detection of relative Luciferase reporter activity. As a result, decursin derivative (8b), introduced substituent of 3-acetoxy cinnamoyl group, showed the most potent inhibitory activity (97.0%) for Wnt/β-catenin pathway. In structure activity relationship (SAR), it shows that double bond, included in cinnamoyl group of decursin derivatives, is necessary for of Wnt/β-catenin pathway. Also inhibitory activities are most effective, when functional groups locate ortho- or meta-positions, substituted on benzene ring of cinnamoyl group. In HEK293 reporter cells, it was revealed that 8b inhibited dose-dependently CRT induced by Wnt3a (IC50 = 9.85 mM) and decreased of intracellular β-catenin's protein level. Also, 8b decreased dose-dependently cytosolic β-catenin's protein level in PC3 prostate cancer cell. And it acted as promoter of the degradation of β-catenin and suppressed the expression of Cyclin D1 and c-myc, which are downstream target genes of β-catenin. As shown these results, compound 8b may lead to candidate of new anti-tumor agents for prostate cancer.

Biography

Gyu-Yong Song has completed his PhD from Chungnam National University and Postdoctoral studies from the Univiersity of Georgia. He is a Professor at College of Pharmacy, Chungnam National University and the Leader of Chungnam National University's LINC (Leaders in INdustry-university Cooperation) project group. He has published more than 30 papers in reputed journals and has registered more than 20 patents. He has performed a development of DMNQ derivatives, decursin derivatives, carbazole derivatives and flavon derivatives, related to Wnt signaling pathway, platelet aggregation, anti-aging and so on. He has carried out the processing of ginseng, such as black ginseng.

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