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Taxifolin suppresses rat and human testicular androgen biosynthetic enzymes

Fei Ge [a, 1], Erpo Tian [b, 1], Li Wang [b, 1], Xiaoheng Li [a], Qiqi Zhu [a], Yiyan Wang [a], Ying Zhong [b] ✉, Ren-Shan Ge [a] ✉

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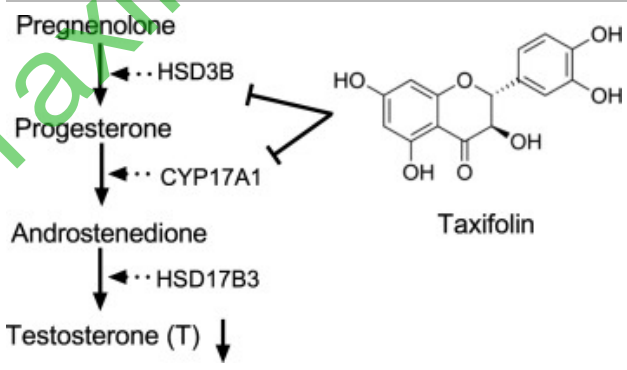
Abstract

Taxifolin is a flavonoid. It has been used as a chemopreventive agent and supplement. It may have some beneficial effects to treat prostate cancer by suppressing androgen production in Leydig cells. The objective of the present study was to study the effects of taxifolin on androgen production of rat Leydig cells isolated from immature testis and some rat and human testosterone biosynthetic enzyme activities. Rat Leydig cells were incubated with 100 μM taxifolin without (basal) or with 10 ng/ml luteinizing hormone (LH), 10 mM 8-bromoadenosine 3′,5′-cyclic monophosphate (8BR), and steroid enzyme substrates (20 μM): 22R-hydroxychloesterol, pregnenolone, progesterone, and androstenedione. The medium concentrations of 5α-androstane-3α, 17β-diol (DIOL) and testosterone were measured. Taxifolin significantly suppressed basal, LH-stimulated, 8BR-stimulated, pregnenolone-mediated, and progesterone-mediated androgen production by Leydig cells. Further study demonstrated that taxifolin inhibited rat 3β-hydroxysteroid dehydrogenase and 17α-hydroxylase/17, 20-lyase with IC_{50} values of 14.55 ± 0.013 and 16.75 ± 0.011 μM, respectively. Taxifolin also inhibited these two enzyme activities in human testis with IC_{50} value of about 100 μM. Taxifolin was a competitive inhibitor for these two enzymes when steroid substrates were used. In conclusion, taxifolin may have benefits for the treatment of prostate cancer.

Graphical abstract



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Abbreviations

8BR, 8-bromoadenosine 3′,5′-cyclic monophosphate; HSD3B, 3β-hydroxysteroid dehydrogenase; HSD17B3, 17β-hydroxysteroid dehydrogenase 3; 22R, 22R-hydroxycholesterol; CYP17A1, 17α-hydroxylase/17,20-lyase; D4, androstenedione; DIOL, 5α-Androstane-3α,17β-diol; DHT, dihydrotestosterone; LH, luteinizing hormone; P4, progesterone; P5, pregnenolone; TAX, taxifolin; T, testosterone

Keywords

Taxifolin; 3β-hydroxysteroid dehydrogenase; 17α-hydroxylase/17,20-lyase; Steroidogenesis; Leydig cells

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[1] These authors contribute to the work equally.