Ursolic Acid Induces Apoptosis of Prostate Cancer Cells via the PI3K/Akt/mTOR Pathway.

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Abstract

Ursolic acid (UA), a pentacyclic triterpenoid, is known to exert antitumor activity in breast, lung, liver and colon cancers. Nonetheless, the underlying mechanism of ursolic acid in prostate cancer cells still remains unclear. In the present study, we report the chemotherapeutic effects of ursolic acid as assessed using in vitro and in vivo models. Treatment of human prostate cancer cells (LNCaP and PC-3) with UA inhibited the proliferation and induced apoptosis in both cell lines as characterized by the increased Annexin V-binding. The induction of apoptosis by UA was associated with a decrease in the levels of Bcl-2, Bcl-xl, survivin, and activated caspase-3. Treatment with UA also inhibited the expression of phosphatidylinositol-3-kinase (PI3K), phosphorylation of Akt and mTOR signaling proteins. Further, administration of UA significantly inhibited the growth of LNCaP prostate tumor xenografts in athymic nude mice, which was associated with inhibition of cell proliferation, induction of apoptosis of tumor cells and decreased expression of PI3K downstream factors, such as p-Akt and p-mTOR in tumor xenograft tissues. Our study demonstrates that UA not only inhibits cell growth but also induces apoptosis through modulation of the PI3K/Akt/mTOR pathway in human prostate cancer cells. We suggest that UA may be a new chemotherapeutic candidate against prostate cancer.

KEYWORDS:

Apoptosis; PI3K/Akt/mTOR Pathway; Prostate Cancer; Ursolic Acid

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