Plumbagin, A Medicinal Plant-Derived Naphthoquinone, Is A Novel Inhibitor Of The Growth And Invasion Of Hormone-Refractory Prostate Cancer

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UroToday.com - Dr. Moammir Aziz and colleagues from the University of Wisconsin reported in the November 1, 2008 issue of Cancer Research that plumbagin, a medicinal plant derived naphthoquinone, inhibits castration-resistant prostate cancer (CaP) growth and invasion. Plumbagin was isolated from the roots of Plumbago zeylanica L. (Chitrak), which has been used in Indian medicine for thousands of years.

Numerous benign and malignant CaP cell lines were studied in vitro. In a collagen-based cell invasion assay, both 5 and 20 μmol/L of plumbagin (PL) significantly inhibited CaP cell invasion. PL induced apoptosis in the malignant CaP cell lines irrespective of androgen responsiveness and p53 status with modulation of cellular redox status and generation of reactive oxygen species. Apoptosis was not induced in benign prostate cells.

In athymic nude mice, PL at 2mg/kg body weight was given intra-peritoneal 3 days after implantation of castration-resistant Du145 cells. PL administration delayed tumor growth by 3 weeks and significantly reduced both the tumor weight and volume throughout the experimental period. Discontinuation of PL in PL-treated mice for as long as 4 weeks did not result in an increase in tumor growth. PL significantly inhibited expression of signaling molecules Stat3 and PKC, as well as VEGF and MMP-9. The PL treated mice gained weight and did not exhibit toxicity. Also, the PI3K and AKT pathway was inhibited, with decreased phosphorylation (activation) of AKT. PL inhibited the DNA binding of transcriptional factors NF-κB, AP-1 and Stat3. These signaling and transcriptional molecules are well known for their role in the growth, invasion and metastatic properties of prostate cancer.

Plumbagin holds translational promise for treatment of castration-resistant prostate cancer.

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