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PROSTATE CANCER

Resveratrol inhibits the AR

The natural phenol and phytoalexin resveratrol (*trans*-3,5,4′-trihydroxystilbene) and its analogues can inhibit wild-type and mutant forms of the androgen receptor (AR), according to newly published data.

Resveratrol is thought to be beneficial for health; however, any potential effect of resveratrol is limited by poor bioavailability. Researchers have sought to overcome this hurdle by synthesizing acetylated and methylated analogues of resveratrol and its metabolite piceatannol , which have longer half-lives and greater volumes of distribution.

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Previous studies have described the anticancer properties of resveratrol, and both resveratrol and its analogues have been shown to inhibit the activity of CYP17A1, a key enzyme in androgen synthesis. Furthermore, resveratrol has been shown to inhibit AR activation in LNCaP prostate cancer cells, which express a mutated AR. Thus, Lundqvist and colleagues sought to investigate the effect of resveratrol, piceatannol, and its analogues on the mutated AR expressed in LNCaP cells and on a wild-type AR in RWPE prostate cancer cells.

Cultured LNCaP and RWPE cells were exposed to the test compounds at concentrations ranging from 1 to 50 μM, after which they were tested for AR activity by transient transfection with a luciferase plasmid, with luciferase expression controlled by a regulatory element sensitive to ligand-activated AR. All studied compounds inhibited AR activation in both cell lines. The ability of all compounds to inhibit dihydrotestosterone-induced AR activity was dose dependent, although in general RWPE cells were less responsive to resveratrol and analogues than LNCaP cells. Levels of PSA, the expression of which is regulated by ligand-activated AR, were significantly reduced after exposure to resveratrol and all analogues at concentrations ≥10 μM.

The authors conclude that these compounds should be further developed as potential drugs for prostate cancer treatment and chemoprevention.

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