

**ANTI-ANDROGEN ACTIVITY OF FLAVONOIDS**

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**Objectives/Design:** Breast and prostatic carcinomas are the second leading causes of cancer death in Canada. Many patients are searching for natural alternatives to drugs. These include flavonoids, found in plant foods. Here we assessed anti-androgen activity of 72 flavonoids and related compounds in the BT-474 human breast cancer cell line, containing androgen (AR), estrogen (ER) and progesterone (PR) receptors, and a PC-3 prostate cancer cell line, transfected with the AR gene, PC-3(AR)<sub>2</sub>. Quantification of prostate-specific antigen (PSA), an androgen-related protein, was the outcome measure.

**Methods:** BT-474 cells were incubated with a flavonoid or related compound at 10<sup>-5</sup> M and 10<sup>-7</sup> M with or without dihydrotestosterone (DHT) at 10<sup>-9</sup> M. DHT alone, determined maximum PSA production. Nilutamide (anti-androgen) was a positive control and ethanol, a negative control. After 7 days incubation, supernatants were harvested and analyzed for PSA. Compounds showing greater than 50% blocking were tested from 10<sup>-5</sup> to 10<sup>-8</sup> M in both cell lines. PSA was quantified with an ELISA-type immunofluorometric procedure.

**Results:** Twenty-two of the compounds showed anti-androgen activity in the BT-474 cell line at 10<sup>-5</sup> M. Several had dose-responsive activity, down to 10<sup>-7</sup> M. The estrogenic compounds showed diminished anti-androgen activity in the PC-3(AR)<sub>2</sub> cell line, while the non-estrogenic compounds maintained blocking.

**Conclusion:** Several flavonoids and related compounds possess anti-androgen activity. This activity may be exploited in nutraceutical and functional food forms for the prevention and/or management of prostate and breast cancers and other hormone-dependent diseases.