EFFECT OF SEVERAL EPILOBIUM SPECIES ON THE PROLIFERATION OF HUMAN PROSTATE CELLS

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The use of plant extracts for the treatment of lower urinary tract symptoms associated with benign prostatic hyperplasia is very common in Europe and USA [1]. The plant extracts most commonly used are from *Serenoa repens*, *Urtica dioica* and *e1040Pygeum africanum.* Recently, extracts of *Epilobium* (*E.*), that consist of over 200 species and have been used to improve healing of wounds, and for menstrual disorders, have received attention in folk medicine for treatment of prostatic disease.
Purpose of this study was to evaluate whether the use of *E.* in prostatic adenoma could be supported by a specific biological action of these extracts on prostate cells. The effects of five different *E.* species (*spicatum* or *angustifolium, rosmarinifolium, hirsutum, palustre, tetragonum*) on the proliferation of the human prostatic epithelial cell line PZ-HPV-7 [2] were initially assessed by MTT assay and by [methyl-^{3}H] thymidine incorporation [3-4]. Three concentrations of each compound were tested (1-0.1-0.01 mg/ml of ethanolic extract) and the results showed that all species inhibited cell proliferation in a concentration-dependent manner, with *E. rosmarinifolium* and *E. tetragonum* being the more potent. While the high concentrations of all extracts caused significant cytotoxicity, as determined by the trypan blue exclusion test, significant inhibition of DNA synthesis was also observed at concentrations that caused minimal or no cytotoxicity. Flow cytometric analysis [5], carried out with *E. tetragonum*, *E. rosmarinifolium* and *E. spicatum*, indicated that these extracts were capable of inhibiting the $G_0/G_1 \rightarrow S$ cell cycle progression. These results indicate the ability of different *E.* species in inhibiting proliferation on human epithelial prostate cells.
The selectivity of the antiproliferative effect was evaluated using the [methyl-^{3}H] thymidine incorporation assay in three different human cell lines (LNCaP prostate cancer cells, HMEC normal mammary cells and 1321N1 astrocytoma cells). *E.* extracts had similar growth inhibitory effects in all cells, except in 1321N1 cells, which were somewhat less sensitive than the two prostate and the mammary cell lines.
The antiproliferative action of *E.* may be ascribed to flavonoids, macrocyclic ellagitannins or sterols which has been found in these extracts [6]. Such hypothesis is supported by the finding that inhibition of DNA synthesis was mostly due to the non polar fraction of the extracts, which is expected to contain these compounds. Polar fractions were devoid of any effect with the exception of *E. rosmarinifolium.*
Among the ellagitannins, oenothein B has been isolated from different *E.* species and was therefore tested for its ability to inhibit DNA synthesis. Oenothein B inhibited DNA synthesis in all four cell lines tested, and similarly to the *E.* extracts, was less potent toward astrocytoma cells.
The amount of active principle extracted from the plants could vary in function of the extraction processes, genetic differences between species, part of the plants and climatic and soil differences. Therefore, the effect of an *3E. angustifolium* extract supplied from

another company was investigated. Both extracts were obtained from the same part of the plant, by the same extraction process, but one derived from plants grown in Europe while the other from plants grown in Canada. The Canadian extract was ten times more potent than the European one in inhibiting DNA synthesis in PZ-HPV-7 cells.
In summary, these studies indicate that *0E.* species extracts inhibit proliferation of prostate cells, however this effect is not prostate-specific. They also suggest that oenothein B may play a role in the inhibition of DNA synthesis and suggest that determination and standardization of the active ingredients is extremely important to meaningfully compare the effects of different extracts.

References

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