Hypericum alpestre extract exhibits in vitro and in vivo anticancer properties by regulating the cellular antioxidant system and metabolic pathway of L-arginine

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Abstract

Conventional treatment methods are not effective enough to fight the rapid increase in cancer cases. The interest is increasing in the investigation of herbal sources for the development of new anticancer therapeutics. Particularly, much attention is given to finding combined phytochemical/chemotherapeutic treatment models to overcome drug resistance and decrease side effects. The aim was to investigate the antitumor capacity of *Hypericum alpestre* herb extract *in vitro* and *in vivo,* either alone or combined with the inhibitors of the L-arginine/polyamine/nitric oxide pathway and characterize its active phytochemicals using advanced chromatographic techniques. The antioxidant capacity of *H. alpestre* extract was assessed through chemical spectrophotometric tests (DPPH and ABTS) and in biological systems using Cellular Antioxidant Activity assay. The inhibitory effect of *H. alpestre* extract on the growth of human colorectal (HT29) and breast cancer (MCF-7) cell cultures was explored by the MTT test. The genotoxicity of the tested extract was studied using a comet assay. *In vivo,* the antitumor properties of *H. alpestre* and its combinations were explored in a rat mammary gland carcinogenesis model induced by subcutaneous injection of 7,12-dimethylbenz[a]anthracene. The polyphenolic substances present in *H. alpestre* extract have been characterized using the LC-Q-Orbitrap HRMS system. The *H. alpestre* extract expressed promising antiproliferative effects on MCF-7 and HT29 cells. The extract did not exhibit genotoxic activity nor possessed antigenotoxic properties. The *in vivo* rat mammary carcinogenesis model data showed that the *H. alpestre* extract stimulated the activity of antioxidant enzymes in the liver, brain, and tumors of rats in the experimental groups, demonstrating its antioxidant protective effects. The herb alone and in combination with N $^{\omega}$-OH-nor-L-arginine and N $^{\omega}$-nitro-L-arginine methyl ester exhibited pro-/antioxidant, antiproliferative, anti-angiogenic, and cytotoxic effects.

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