

CHEMICAL COMPOSITION, ANTI-INFLAMMATORY EFFECT AND ANTITUMOR ACTIVITY OF CURLY DOCK FRUIT (*RUMEX CRISPUS L.*, POLYGONACEAE)

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Curly dock (*Rumex crispus L.*) is a perennial herbaceous plant that is traditionally used in the treatment of gastrointestinal ailments, infections and skin diseases. The aim of this study was to examine the chemical composition, *ex vivo* anti-inflammatory effect and *in vivo* antiproliferative activity of water extract of curly dock fruit. The polyphenolic profile was analyzed by LC-DAD-ESI-MS technique. The effect on the production of arachidonic acid metabolites was examined in human platelets. Antitumor activity of orally administered extract (concentration: 5% w/v; doses: 1, 2 and 5 mL/kg of body weight/day; treatment length: 7 days) to Ehrlich ascites tumor and hepatocellular carcinoma was assessed in an animal experiment. Ascites volume, viable cell percentage and antioxidant enzyme levels were determined. The presence of phenolic acids (gallic and protocatechuic acids), proanthocyanidins (monomers, dimers and trimers), flavonoid glycosides and anthraquinone emodin was revealed in the water extract of *R. crispus* fruit. The content of the quantitatively dominant compound miquelianin was 2.4%. The investigated preparation concentration-dependently inhibited the synthesis of 12(S)-hydroxy-(5Z,8E,10E)-heptadecatrienoic acid ($IC_{50} = 4.96$ mg/mL) and 12(S)-hydroxy-(5Z,8Z,10E,14Z)-eicosatetraenoic acid ($IC_{50} = 2.06$ mg/mL). The antitumor effect in animals was dose-dependent and manifested as suppression of tumor growth and induction of cell death of malignantly transformed cells. Values of biochemical parameters suggested that oxidative stress was induced in cancer cells, and it can be assumed that this mechanism was at least partly responsible for the activity. Water extract of *R. crispus* fruit has significant pharmacological potential that justifies further research.

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HEMIJSKI SASTAV, ANTIINFLAMATORNI EFEKAT I ANTITUMORSKA AKTIVNOST PLODA ŠTAVELJA (*RUMEX CRISPUS* L., POLYGONACEAE)

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Štavelj (*Rumex crispus* L.) je višegodišnja zeljasta biljka koja se tradicionalno koristi u tretmanu gastrointestinalnih tegoba, infekcija i kožnih oboljenja. Cilj ove studije je bio da se ispita hemijski sastav, *ex vivo* antiinflamatorni efekat i *in vivo* antiproliferativna aktivnost vodenog ekstrakta ploda štavelja. Polifenolni profil je analiziran *LC-DAD-ESI-MS* tehnikom. Uticaj na produkциju metabolita arahidonske kiseline je ispitana u humanim trombocitima. Antitumorska aktivnost oralno primjenjenog ekstrakta (koncentracija: 5% m/V; doze: 1, 2 i 5 mL/kg telesne težine/dan; dužina tretmana: 7 dana) prema *Ehrlich*-ovom ascitnom tumoru i hepatocelularnom karcinomu procenjena je u eksperimentu na životnjama. Određeni su zapremina ascitesa, procenat vijabilnih ćelija i nivoi antioksidanata enzima. U vodenom ekstraktu ploda *R. crispus* je utvrđeno prisustvo fenolnih kiselina (galna i protokatehinska kiselina), proantocijanidina (monomeri, dimeri i trimeri), flavonoidnih heterozida i antrahinona emodina. Sadržaj kvantitativno dominantnog jedinjenja mikvelijanina je iznosio 2,4%. Ispitivani preparat je koncentraciono-zavisno inhibirao sintezu 12(S)-hidroksi-(5Z,8E,10E)-heptadekatrienske kiseline ($IC_{50} = 4,96$ mg/mL) i 12(S)-hidroksi-(5Z,8Z,10E,14Z)-eikozatetraenske kiseline ($IC_{50} = 2,06$ mg/mL). Antitumorski efekat u životinja je bio dozno-zavisan i ispoljio se kao suprimiranje rasta tumora i indukcija ćelijske smrti maligno transformisanih ćelija. Vrednosti biohemičkih parametara su sugerisale da je u ćelijama karcinoma došlo do indukovanja oksidativnog stresa, te se može prepostaviti da je ovaj mehanizam bio barem delom zaslužan za aktivnost. Vodeni ekstrakt ploda *R. crispus* poseduje značajan farmakološki potencijal koji opravdava dalje istraživanje.

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