INOPTEP 2023 PTEP 2023

BOOK OF ABSTRACTS

VIII INTERNATIONAL CONFERENCE SUSTAINABLE POSTHARVEST AND FOOD TECHNOLOGIES **INOPTEP 2023**

and

XXXV SCIENTIFIC - PROFESSIONAL CONFERENCE PROCESSING AND ENERGY IN AGRICULTURE **PTEP 2023**

Subotica – Palić, hotel Elitte Palić,
23 – 28. april 2023.

Publisher / Izdavač
National Society of Processing and Energy in Agriculture, Novi Sad, Serbia
Nacionalno društvo za procesnu tehniku i energetiku u poljoprivredi, Novi Sad,
Trg Dositeja Obradovića 8
Co-publisher / Suizdavač
Faculty of Agriculture, Novi Sad, Serbia
Poljoprivredni fakultet, Novi Sad, Trg Dositeja Obradovića 8
Editor in Chief / Glavni i odgovorni urednik:
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For Publisher / Za izdavača:
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Dr. Milivoj Radojčin
Printed by / Štampa:
E-publishing PTEP Society
Edition / Tiraž: 200
ISBN: 978-86-7520-581-4
E-mail: ptep@ptep.org.rs
www.ptep.org.rs

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ANTIPROLIFERATIVE PROPERTIES OF HONEY TYPES FROM THE WESTERN BALKANS

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Honey is a natural sweetener used not only for food, but also for therapeutic purposes. It contains carbohydrates, primarily glucose and fructose (85–95%) but also contains about 200 substances present in small amounts (minerals, proteins, enzymes, amino acids, organic acids, vitamins, polyphenols and others).
The type of honey is characterized by the type of pollen, insect secretions, as well as climatic conditions and soil composition.
The health benefits of honey results from its antioxidant nature, antimicrobial and antiproliferative activity.
Several studies demonstrate the anticancer activity of honey, namely honey shows a chemopreventive effect against various cancer cell lines and tissues in in vitro and in vivo studies. This activity can be explained by different mechanisms including cell cycle arrest, induction of apoptosis, modulation of oxidative stress and immuno-modulation. Therefore, honey can be applied in alternative medical treatment of human tumors.
With the aim to assess the antiproliferative properties of different types of honey characteristic for The Western Balkans, nineteen samples (acacia, linden, heather, sunflower, phacelia, basil, anise, sage, chestnut, hawthorn, buckwheat, lavender and meadow) were collected from different locations in the mentioned region and examined. The quality of honey samples was also tested to ensure that they meet the requirements defined by the national and international legislation.
All tested honey samples were in accordance with the regulations of national and EU regulations.
The antiproliferative activity of honey samples was evaluated using human tumor cell lines HeLa (cervcal carcinoma), MCF7 (breast epithelial adenocarcinoma), HT-29 (colon adenocarcinoma) and MRC-5 (normal fetal lung fibroblasts).
The most active samples were linden honey sample from Fruška gora (IC_{50}^{MCF7} = 7.46 ± 1.18 mg/mL and IC_{50}^{HeLa} = 12.4 ± 2.00 mg/mL) and meadow sample 2 (IC_{50}^{MCF7} = 12.0 ± 0.57 mg/mL, IC_{50}^{HeLa} = 16.9 ± 1.54 mg/mL and IC_{50}^{HT-29} = 23.7 ± 1.33 mg/mL) towards breast (MCF7), cervix (HeLa), and colon (HT-29) cancer cells. The most active samples, linden and meadow 2 also affected the growth of MRC-5 cells derived from healthy lung tissue with IC_{50}^{MRC-5} = 9.93 ± 0.68 mg/mL and IC_{50}^{MRC-5} = 12.9 ± 0.34 mg/mL, respectively. Colon carcinoma cell line HT-29 was the least sensitive to the evaluated samples. Standard (glucose) had lower and uniform cell growth effect with IC_{50} values ranging from 33–40 mg/mL towards all evaluated cell lines, indicating that active components in samples other than sugars contributed to cell growth activity. These compounds are probably polyphenols. Polyphenolic profile investigation will be needed to correlate antiproliferative activities and polyphenol contents for evidences of the mechanisms of their action.
Key words: *honey, antiproliferative properties*

Acknowledgment: This work was financially supported by the Ministry of Science, Technological Development and Innovation, Republic of Serbia (Contract No. 451-03-47/2023-01/200222).

ANTIPROLIFERATIVNA SVOJSTVA MEDA SA ZAPADNOG BALKANA

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Med je prirodni zaslađivač koji se koristi ne samo u ishrani, već i u terapeutske svrhe. Sadrži ugljene hidrate, pre svega glukozu i fruktozu (85–95%), ali i oko 200 supstanci prisutnih u malim količinama
(minerali, proteini, enzimi, aminokiseline, organske kiseline, vitamini, polifenoli i dr.).
Vrstu meda karakteriše vrsta polena, izlučevine insekata, kao i klimatski uslovi i sastav zemljišta.
Zdravstvene dobrobiti meda proizilaze iz njegove antioksidativne prirode, antimikrobne i antiproliferativne aktivnosti.
Nekoliko studija ukazuje na antikancerogenu aktivnost meda, odnosno med ispoljava hemopreventivni efekat protiv različitih ćelijskih linija i tkiva raka u in vitro i in vivo studijama. Ova aktivnost se može objasniti različitim mehanizmima uključujući zaustavljanje ćelijskog ciklusa, indukciju apoptoze, modulaciju oksidativnog stresa i imuno-modulaciju. Stoga se med može primeniti u alternativnom medicinskom lečenju tumora kod ljudi.
U cilju procene antiproliferativnih svojstava različitih vrsta meda karakterističnih za Zapadni Balkan, prikupljeno je i ispitano devetnaest uzoraka meda (bagrem, lipa, vres, suncokret, facelija, bosiljak, anis, žalfija, kesten, glog, heljda, lavanda i livada) sa različitih lokacija pomenutog regiona. Uzorci meda su ispitani i u pogledu kvaliteta kako bi se osiguralo da ispunjavaju uslove definisane nacionalnom i međunarodnom regulativom.
Svi ispitani uzorci meda bili su u skladu sa propisima nacionalne i EU regulative.
Za procenu antiproliferativne aktivnosti meda korišćene su humane tumorske linije HeLa (karcinom grlića materice), MCF7 (adenokarcinom epitela dojke), HT-29 (adenokarcinom debelog creva) i MRC-5 (normalni fetalni fibroblasti pluća).
Najaktivniji uzorci bili su uzorak lipovog meda sa Fruške gore (IC_{50}^{MCF7} = 7,46 ± 1,18 mg/ml i IC_{50}^{HeLa} = 12,4 ± 2,00 mg/ml) i uzorak livadskog meda 2 (IC_{50}^{MCF7} = 12,0 ± 0,57 mg/ml IC_{50}^{HeLa} = 16,9 ± 1,54 mg/ml /mL i IC_{50}^{HT-29} = 23,7 ± 1,33 mg/ml) prema ćelijama raka dojke (MCF7), grlića materice (HeLa) i debelog creva (HT-29). Antiproliferativno najpotentniji uzorci, uzorak lipovog meda sa Fruške gore i uzorak livadskog meda 2, uticali su, takođe, na rast MRC-5 ćelija fibroblasta pluća sa vrednostima IC_{50}^{MRC-5} = 9,93 ± 0,68 mg/ml i IC_{50}^{MRC-5} = 12,9 ± 0,34 mg/ml, respektivno. Ćelijska linija karcinoma debelog creva HT-29 bila je najmanje osetljiva na ispitivane uzorke. Standard (glukoza) je imao niži i ujednačen uticaj na rast ćelija sa vrednostima IC_{50} u rasponu od 33–40 mg/ml u slučaju svih ćelijskih linija, što ukazuje da su aktivne komponente u uzorcima meda primarno obezbedile antiproliferativnu aktivnost, pre nego šećer. Neophodno je ispitivanje polifenolnog profila da bi se uspostavila korelacija antiproliferativnih aktivnosti i sadržaja polifenola za dobijanje dokaza o mehanizmima njihovog delovanja.
Ključne reči: *med, antiproliferativna aktivnost*

Zahvalnica: Ovaj rad je rezultat istraživanja koje je finansirano od strane Ministarstva nauke, tehnološkog razvoja i inovacija Republike Srbije (ugovor broj 451-03-47/2023-01/200222).