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BOOK OF ABSTRACTS

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T3-P-2 Cytotoxic prenylated phenols of false indigo-bush (*Amorpha fruticosa L.*)

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KEYWORDS: Amorpha fruticosa; 5,7-dihydroxy-8-geranylflavanone; 2-carboxy-3,5-dihydroxy-4-geranylbibenzyl; amorfrutin A; cytotoxic activity

INTRODUCTION:

False indigo-bush (*Amorpha fruticosa L.*, Fabaceae) is an invasive shrub native to central and eastern North America. In Serbia, it can be found along roads, railways, and riverbeds, where it spreads easily. Previous studies have shown that *A. fruticosa* contains several classes of secondary metabolites (e.g. rotenoids, isoflavonoids, prenylflavanones, chalcones, and stilbenoids) and exhibits various biological activities (e.g. antioxidant, anti-inflammatory, antidiabetic, insecticidal).

OBJECTIVES:

This study aimed to examine the *in vitro* cytotoxic activity of prenylated phenolic constituents of false indigo-bush.

METHOD / DESIGN:

An aliquot (0.82 g) of ethanol-soluble part of n-hexane fruit extract (1:10, m/V) was loaded onto silica gel column (3 × 43 cm) and eluted with mixtures of n-hexane and ethyl acetate (100:0 _ 0:100, V/V). 96 Fractions were collected, analyzed by silica gel TLC and combined based on chemical composition similarity. Compound 1 (6.9 mg) precipitated as the white powder during solvent removal from the united fractions 59–69. The pooled fractions 89–92 (80.6 mg) and 95–96 (59.6 mg) gave compounds 2 (29.8 mg, Rf = 0.5) and 3 (5.8 mg, Rf = 0.53), respectively, after separation by preparative silica gel TLC in a solvent system consisting of n-hexane, ethyl acetate and formic acid (80:20:1, V/V/V). The structure determination of the isolated prenylated phenols were based on their UV, MS, and ^{1}H and ^{13}C NMR spectra. MTT assay was employed to assess their cytotoxicity against human tumor cell lines (HeLa, HT^{-29}, HCT^{-116}, LS174) derived from the cervix adenocarcinoma and colorectal carcinomas, as well as human fetal lung fibroblasts (MRC-5). cis-Diamminedichloroplatinum (CDDP) was used as a control substance. The activity is expressed as the IC_{50} value, i.e. the concentration of the tested substance that led to 50% inhibition of survival, compared to the vehicle-treated control group. The statistical analysis was performed using the Student's *t*-test.

RESULTS:

Based on a comparison of recorded spectral data and literature data, compound 1 was identified as 5,7-dihydroxy-8-geranylflavanone, compound 2 as 2-carboxy-3,5-dihydroxy-4-geranylbibenzyl, and compound 3 as 2-carboxy-3-hydroxy-4-prenyl-5-metoxybibenzyl (amorfrutin A). All tested constituents showed cytotoxicity with the IC_{50} values in the range 10.55–166.11 μg/mL. The non-selectivity of compounds 2 and 3 could be observed. On the other hand, compound 1 was selective and exhibited pronounced activity against the HeLa cell line (IC_{50} = 10.55 μg/mL). HT-29 (IC_{50} = 122.28 μg/mL) and HCT-116 (IC_{50} = 147.09 μg/mL) cancer cell lines, as well as normal cell line MRC-5 (IC50 = 166.11 μg/mL), were less susceptible to the

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action of compound 1, whereas the survival of LS174 cell line was not affected at all by compound 1 in the tested concentration range. The effectiveness of the control substance CDDP in reducing the survival of the HeLa cancer cell line was the highest (IC_{50} = 5.20 μg/mL). It should be emphasized that CDDP, among tested substances, was also the most toxic against the MRC-5 cell line (IC_{50} = 8.28 μg/mL). IC_{50} values ranges of compounds 2 and 3 were 31.97–56.29 μg/mL and 35.67–53.21 μg/mL, respectively.

CONCLUSIONS:
5,7-Dihydroxy-8-geranylflavanone, the constituent of false indigo-bush fruit, exhibited strong and selective activity against the human cervix adenocarcinoma cell line in the MTT assay, therefore, its cytotoxic potential can be considered significant. Further studies are needed to fully assess the demonstrated effect.

T3-P-3 Excipients with potential to cause adverse drug reactions in approved hormonal medicines for systemic use

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KEY WORDS: excipients with known effect; side effects; pharmacovigilance

INTRODUCTION: In addition to the active pharmaceutical ingredient (API), the composition of the medicines also includes excipients which are only ideally completely pharmacologically inactive. It has been shown that excipients can cause effects opposite to the pharmacological effect of the medicine. Therefore, it is very important to talk about excipients with known effect (EKE), which are excipients that have been proven to cause adverse drug reactions (ADRs) when they are in the composition of medicines.

OBJECTIVES: The aim of the study was to identify potentially harmful excipients in hormonal medicines for systemic use approved in the Republic of Serbia.

METHOD: The study was conducted during August 2021 and included the analysis of medicines that received a marketing authorization from the Medicines and Medical Devices Agency of Serbia (ALIMS). Qualitative compositions of hormonal medicines for systemic use (ATC group H) available in SmPC documents on the ALIMS's official website were observed. Excipients considered potentially harmful if they are recognized as excipients with known effect (EKE) in European regulation, Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use', available from European Medicines Agency's official website.

RESULTS: We analyzed 92 hormonal medicines for systemic use that are approved in Serbia. In their composition we found 70 different excipients. By comparing detected excipients with appropriate European regulation we identified 21 excipients from examined preparations that represent potential causes of ADRs: phosphate buffers (8 different buffers), mannitol, benzyl alcohol, benzalkonium-chloride, lactose-monohydrate, sodium, ethanol, glycerol, propylene-glycol, glucose, sodium-lau-

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