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ОБЗОРЫ ПО КЛИНИЧЕСКОЙ ФАРМАКОЛОГИИ И ЛЕКАРСТВЕННОЙ ТЕРАПИИ

REVIEWS ON CLINICAL PHARMACOLOGY AND DRUG THERAPY

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The content of phloroglucinols (hyperforin, adhyperforin) was found in H. perforatum 27.9 mg/g DW.

Conclusions:

The results of the comparative chemical analysis showed an interspecific diversity in the chemical composition of the studied plants, which confirmed the advisibility of subsequent study of the *H. elegans* and *H. tetrapterum* plant raw materials as sources of biologically active compounds, particularly anthracene derivatives and flavonoids.

References:

[1] Casian I, et. al. Analele științifice ale USMF,, Nicolae Testemițanu", 1(10): 327-332 (2009).

NATURAL PRODUCTS: STRATEGIES TO CROSS BIOLOGICAL BARRIERS

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Natural products (NPs) are fascinating molecules not exclusively for their exciting structure variability but also for their ability to interact with diverse targets. In spite of these advantages, in many cases, the impressive *in vitro* activity to less or not significant *in vivo* efficacy is generally due to drug poor water solubility, low lipophilicity and inappropriate molecular size resulting in reduced absorption due to difficulties to cross biological barriers. In the gastrointestinal tract, a variety of physiological and morphological barriers such as gastric pH, proteolytic enzymes, colonic microflora and mucus layer can severely affect NPs bioavailability. Skin is a further physiological barrier, which essentially consists of four layers, and the stratum corneous, the outer layer of the skin (nonviable epidermis) represents the rate-controlling barrier for diffusion for almost all compounds. Small lipophilic NPs such a mono- and sesquiterpens have high permeation properties and largely used as penetration enhancers, but they can also need of specific formulations because usually thermolabile and susceptible to volatilization and degradation, mainly by oxidation and isomerization. Other important barriers are the pulmonary and nasal mucosae where NPs bioavailability is often limited by rapid degradation and/or clearance by the mucociliary system and alveolar macrophages. Additionally, blood retinal barrier and blood-brain barrier (BBB) are among the most challenging, ensuring proper homeostasis, mainly due to very selective and restrictive bidirectional transport of endogenous and exogenous compounds. Absorption through each pathway is dependent on different physical characteristics, such as molecular weight, hydrophobicity, ionization constants, and stability of absorbing molecules as well as biological barriers. Different approaches can be used to increase barrier-crossing properties of NPs, based on chemical permeation enhancement using small lipophilic NPs, polysaccharides, dendrimers, cyclodextrins, and the design and production of appropriate drug delivery systems, in particular those of a nanosize which is the most attractive to enhance the permeation through paracellular, transcellular, carrier-mediated, and receptor-mediated transport. Some properties such as mucoadhesion and retention to the mucosa can also be used to increase the cross biological barriers to achieve optimal pharmacological action at pathological sites.

References:

[1] Bilia et al. Curr Med Chem. 1, (2018).
[2] Bilia et al. Planta Med, 83(5):366-381 (2017).
[3] Bilia et al. Evid Based Complement Alternat Med. 651593, (2014).
[4] Bilia et al. Journal of Drug Delivery Science and Technology, 32, 241-255 (2016).
[5] Bilia et al. Food Nutr Sci. 5, 1212-1227 (2014).
[6] Bilia et al. NPC, 13, 1157-1160 (2018).

PROGNOSTICALLY RELEVANT TUMOUR INFILTRATING LYMPHOCYTES PROFILE IN CBA MICE UNDER MULTIPHYTOADAPTOGENE COMPLEX DRY POWDER PREVENTIVE ADMINISTRATION

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Aim of the Study:

To define the tumour infiltrating lymphocytes (TILs) profile in high-cancer CBA mice under multiphytoadaptogene complex dry powder (DMPAC) preventive administration in early ontogenesis and to evaluate the association with the clinicopathological characteristics.

Materials and Methods:

Control male mice CBA/LacY (n = 90) received water, experienced mice (n = 170) – 0,3% DMPAC water solution during the first month of life (preventive administration). DMPAC was produced by a special desiccation technology of forty medical herbs water-ethanol extracts mixture (multyphytoadaptogene complex, MPAC, including adaptogenes *Panax ginseng, Eleutherococcus senticosus, Aralia elata, Rhodiola rosea, Schisandra chinensis Echinopanax elatum*, etc.). The TILs were examined immunohistochemically using the avidin-biotin peroxidase complex method. The number of positively stained CD8+ CD11a+ CD11b+ lymphocytes was counted in 10 fields of view. The average number of cells was determined.

Results and Discussion:

TILs were observed rarely (2.3 ± 0.2 cells/field of view) in the control mice hepatocarcinomas. The number of TILs was 118.6 ± 11.0 cells/field of view in the DMPAC-exposed mice tumours. It was detected that hepatocarcinomas of experimental mice were infiltrated with CD8+ cytotoxic lymphocytes expressing LFA-1 (CD11a) and Mac-1 (CD11b) leukocyte integrins. Hepatocarcinomas lymphocyte infiltration was significantly associated with tumour destruction, increased expression of these antigens on peripheral blood cells and testosterone serum level as well as with a decrease of interleukin 6, 10 and corticosterone levels in the serum. At the same time in the DMPAC-exposed mice the tumours occurred with lower frequency (by 31%), the total hepatomas mass per one animal were lower (by 66%) than in the control animals. Moreovere mice with CD8+ CD11a+ CD11b+ TILs had a better average lifespan and survival median (by 18 and 19% respectively) as well as somatic status including motor activity.

Conclusions:

Hepatocarcinomas infiltration with CD8+ cytotoxic lymphocytes expressing LFA-1 and Mac-1 leukocyte integrins when exposed to DMPAC administration may be significant for reducing incidence of spontaneous tumours as well as for increasing the survival and quality of life in CBA mice.

NONTOXIC PLANT IMMUNOMODIFIER UNDER PREVENTIVE ADMINISTRATION EXTENDS LONGEVITY AND HEALTHSPAN IN CBA MICE

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Aim of the Study:

To determine the influence of multiphytoadaptogene complex dry powder (DMPAC) preventive administration on longevity and healthspan in CBA/LacY male mice with spontaneous hepatomas.

Materials and Methods:

Control mice (n = 90) received water, CBA/LacY mice (n = 170) – 0,3% DMPAC water-solution during the first month of life. DMPAC was produced by a special desiccation technology of forty medical herbs water-ethanol extracts mixture (multyphytoadaptogene complex, MPAC, including adaptogenes *Panax ginseng, Eleutherococcus senticosus, Aralia elata, Rhodiola rosea, Schisandra chinensis Echinopanax elatum*, etc.). The average lifespan and median survival (by Kaplan-Meyer method), body weight and coat state of mice were determined.

Results and Discussion:

The average lifespan and median lifespan of experienced mice was increased by 17% and 23% respectively compared to controls ($p \leq 0,015$). The body weight of the mice in both groups did not differ at the age of 4 and 8 months. At the age of 22 months, the control mice showed cachexia syndrome with a decrease in body weight from 32,0 ± 0,6 g to 28,0 ± 0,4 g (p = 0,0003). At the same time the body weight (34.0 ± 0.3 g) and motor activity of DMPAC-administered mice corresponded to the state of eight months' age. The coat state of experienced mice at the age of 22 months was normal in contrast to the control mice, which showed signs of alopecia in 20% of cases. The improved longevity and healthspan in DMPAC-administered mice was significantly associated with magnification of LFA-1 and Mac-1 leukocyte integrins expression on peripheral blood cells, tumours infiltration with cytotoxic CD8+ CD11a+ CD11b+ lymphocytes, with a decrease of interleukins 6 and 10 as well as catabolic stress-hormone corticosterone levels in the serum, with an increase of anabolic hormone testosterone. These results were accompanied by a lower tumour formation frequency and hepatocarcinomas size. It should be also noted that the effects obtained when exposed to DMPAC are similar to those for MPAC [1].

Conclusions: So, data obtained demonstrate that DMPAC nontoxic immunomodifier probably adjust the antitumor reactions which promote the longevity and healthspan in high-cancer animals.

References:

[1] Bocharov, E. et al. Billetin of Experimental Biology and Medicine, Vol 163(6), 789-92 (2017).