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ОБЗОРЫ ПО КЛИНИЧЕСКОЙ ФАРМАКОЛОГИИ И ЛЕКАРСТВЕННОЙ ТЕРАПИИ

REVIEWS ON CLINICAL PHARMACOLOGY AND DRUG THERAPY

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CHAENOMELES MAULEI FRUIT JUICE ANTAGONIZES RESERPINE-INDUCED HYPOKINESIA IN RATS

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Introduction: Plants belonging to the *Chaenomeles* genus have been a subject to pharmacological investigations, but none of them has explored the biological activities of *Chaenomeles japonica var. maulei (Mast.) Lavall,e. Chaenomeles maulei* fruit juice (CMFJ) is extremely rich in polyphenolic substances. Dietary polyphenols have been demonstrated to possess important beneficial effects on central nervous system functions.

Aim of the Study: We assessed the effects of CMFJ on reserpine-induced hypokinesia in rats using the open field test.

Materials and Methods: The total content of phenolic compounds in CMFJ was 8900 mg/l as gallic acid equivalents measured by the Folin-Ciocalteu assay [1]. Male Wistar rats (200–250 g) were divided in 5 groups of 10 animals. Reserpine was administered as a single intraperitoneal dose of 6 mg/kg (0.3% solution in 5% DMSO, 2 ml/kg) to rats belonging to groups R, R + $CMFJ_{2.5}$, R + $CMFJ_5$ and R + $CMFJ_{10}$ while the Control group was injected intraperitoneally with 5% DMSO (2 ml/kg). CMFJ was applied orally through an orogastric cannula on the 0^{th}, 19^{th} and 23^{rd} hour after reserpine administration at doses of 2.5 ml/kg, 5 ml/kg and 10 ml/kg to groups R + $CMFJ_{2.5}$, R + $CMFJ_5$ and R + $CMFJ_{10}$, respectively. The groups Control and R received distilled water (10 ml/kg) at the same time points. The open field test was carried out 24 hours after reserpine administration. The indices for locomotor activity were: crossings (the number of lines crossed with the four paws) and rearings (the number of times the animal stood on its hind limbs). The time spent in the central area of the field was recorded as a measure of anxiety.

Results and Discussion: The number of crossings of rats belonging to group R (36.6 ± 8.0) were significantly lower ($p < 0.05$) than the corresponding number of the Control group (74.8 ± 11.5). Reserpine also induced a decrease in the number of rearings and the time spent in the central area of the open field but these effects were not significant. CMFJ antagonized the effects of reserpine on rat locomotor activity. The crossings of R + $CMFJ_{2.5}$, R + $CMFJ_5$ and R + $CMFJ_{10}$ groups were respectively 45.0 ± 10.5, 53.7 ± 14.1 and 74.1 ± 16.4. All the measured indices of rats treated with CMFJ at the three administered doses did not differ significantly from those of the Control group. Reserpine-induced hypokinesia in animals was probably due to the depletion of monoamines in the brain as a result of the irreversible block of the vesicular monoamine transporter. The effect of CMFJ was probably due to the modulation of monoaminergic neurotransmission by the polyphenolic constituents which had been proven to act as monoaminooxidase inhibitors [2].

Conclusions: *Chaenomeles maulei* fruit juice antagonized the reserpine-induced hypokinesia in rats probably due to the modulation of monoaminergic neurotransmission.

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GASTROPROTECTIVE EFFECTS OF *ARONIA MELANOCARPA* FRUIT JUICES AND *ARONIA MELANOCARPA*-BASED JUICES IN A RAT MODEL OF INDOMETHACIN-INDUCED ULCERS

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Introduction: *Aronia melanocarpa* fruit juice is extremely rich in phenolic substances. It has been demonstrated to exert a protective effect against indomethacin-induced gastric ulcers in rats [1].

Aim of the Study: The aim of the present study was to investigate the effects of two *Aronia melanocarpa* (Michx.) Elliott fruit juices and two *Aronia melanocarpa*-based fruit juices on indomethacin-induced gastric mucosal damage in rats.

Materials and Methods: The following fruit juices were used: AM1, AM2, AMRC and AMAV. AM1 and AM2 were produced from homogenized *Aronia melanocarpa* fruits at 20°C and 60°C, respectively. AMRC was a mixture of AM2 with *Rosa canina* fruit extract (70 : 30). To produce AMAV, the milled herb *Alchemilla vulgaris* (20 g) was added to 1 l of AM2, the mixture was incubated at 60°C and filtered. The total polyphenols (mg/l) in AM1, AM2, AMRC and AMAV were respectively 7722.7, 11237.4, 10802.1 and 15929.1. Male Wistar rats were divided in 6 groups (n = 12): Control, Indo, AM1+Indo, AM2+Indo, AMRC+Indo and AMAV+Indo. In the course of 10 days, groups Control and Indo were pretreated orally with distilled water (10 ml/kg) while the other groups were pretreated with the respective juice at a dose of 10 ml/kg. On the 10th day 1 h after the pretreatment, control rats received the vehicle for indomethacin and the rest of the groups were treated orally with indomethacin (30 mg/kg). After 4 hours, gastric ulcer formation was estimated morphometrically and histopathologically.

Results and Discussion: The pretreatment with the four juices reduced the number and area of indomethacin-induced gastric lesions but the effect was the highest by AMAV, less pronounced by AM2 and even lower by AM1 and AMRC. The ulcer indices of groups Indo, AM1+Indo, AM2+Indo, AMRC+Indo and AMAV+Indo were respectively 4.4, 3.2, 3.0, 3.8 and 1.4. The percentages of protection against gastric ulcers in groups AM1+Indo, AM2+Indo, AMRC+Indo and AMAV+Indo were respectively 28.12%, 31.97%, 14.97% and 68.25%. Histopathological examination of rat stomachs demonstrated that in Indo group the prevalent changes were heavy destructions of gastric glands and erosions. In the rats pretreated with the juices both gastric gland destruction and gastric erosions were reduced.

Conclusions: The protective effect of *Aronia melanocarpa* fruit juices and *Aronia melanocarpa*-based fruit juices against indomethacin-induced gastric lesions was in correlation with their polyphenolic contents.

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A NEW APPROACH FOR DETERMINATION OF FLAVONOID CONTENT IN HERBAL SAMPLES BY ^{1}H NMR SPECTROSCOPY

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Introduction: According to different Pharmacopoeia the identification and quantification of flavonoids and their glycosides are held by HPLC and spectrophotometry methods, which need rare and expensive standard samples unavailable for many flavonol glycosides.

Aim of the Study: The task of this work is to develop NMR ^{1}H spectroscopy method for identification and quantitative determination of flavonoids in drugs and dietary supplements based on ginkgo biloba leaf extract (*Ginkgo biloba L.*) that does not require standard samples.

Materials and Methods: Samples of drugs and dietary supplements based on the extract of ginkgo biloba in the form of capsules and tablets purchased in the Russian pharmaceutical market, as well as a commercially available extract from the leaves of ginkgo biloba were studied. The measurements were performed on a JNM ECA 600 NMR spectrometer (JEOL, Japan). DMSO-d6 was chosen as the solvent, the residual proton signal was used as a comparison signal in quantitative determination.

Results and Discussion: A new approach for determination of flavonol glycosides and their aglycones in herbal extracts by ^{1}H NMR spectroscopy method was worked out. This method is based on deshielded proton signals of hydroxyl group at position 5 (5-OH) of flavonoids, which make a strong intermolecular hydrogen bond with oxygen of neighboring carbonyl group. These protons are least shielded and for different groups of flavonol glycosides appear in a certain range from 11.8 to 13.5 ppm [1]. All flavonol glycosides of ginkgo biloba extracts contain 5-OH, and their main aglycons are quercetin (R = OH), kaempferol (R = H) and isoramnetin (R = OCH_3) [2]. The validation of the method was carried out according to the following indicators: accuracy, repeatability, linearity, selectivity, quantitation limit. The accuracy of the obtained results is estimated by comparison with the results of pharmacopoeia methods - spectrophotometry (State Pharmacopoeia of Russia) and HPLC-UV (USP, EurPharm). The linearity of the method is 0.9992. The limit of quantification – 0.1 mg/ml.