СЕКЦІЯ 18
ФАРМАКОЛОГІЧНА ДІЯ ТА ФАРМАКОКІНЕТИКА ЛІКАРСЬКИХ ЗАСОБІВ

Basaraba R. Yu.

PHARMACOGNOSTIC INVESTIGATION OF *ANTENNARIA DIOICA*

Department of Pharmacy
Higher State Educational Establishment of Ukraine
«Bukovinian State Medical University»

For the first time, a comprehensive pharmacognostic research of Antennaria dioica (L.) Gaertn.), from Asteraceae family, a valuable medicinal herb, is conducted. A qualitative composition, the content of amino acids, polysaccharides, organic acids including ascorbic one, lipophilic compounds (chlorophylls and keratinoids, fatty acids), volatile compounds, the substances of phenol nature (hydroxycinnamic acids, flavonoids, tannins and polyphenols), macro-elements and trace elements are determined.

A qualitative composition of free organic and ascorbic acids are determined in the examined herb – (1,94±0,12) % and (0,32±0,01) % respectively. By means of high-performance liquid chromatography (HPLC) method a qualitative composition of individual organic acids is determined in Antennaria dioica herb, namely, tartaric, pyruvic, citric, isocitric, succinic and malic acids. Malic acid is found in the biggest amount (11663,85 mcg/gr).

The content of phenol nature substances in Antennaria dioica herb was detected by means of spectrophotometric method: amount of phenol compounds – (6,89±0,01) %, amount of hydroxycinnamic acids – (7,99±0,11) %), amount of flavonoids – (2,09±0,01) %), tannins – (3,04±0,05) %), polyphenols – (5,85±0,01) %). By means of HPLC method a qualitative composition and quantitative content of individual phenol nature compounds are found in Antennaria dioica herb: hydroxycinnamic acids (chlorogenic acid and its isomers – 0,79 % and 1,14 % respectively, rosemary acid – 0,94 %, caffeic acid – 0,06 %, п-coumaric acid – 0,03 %, ferulic acid – 0,07 %); flavonoids (quercetin – 0,01 %, isoquercetin – 0,16 %, luteolin – 0,12 %, apigenin and hyperoside – 0,03 % each, rutin – 0,05 %); catechines (epigallocatechin – 0,15 %, gallocatechin – 0,21 %, catechine and epicatechine – 0,04 % each), free acids including gallic (0,01 %) and ellagic (0,04 %). Rosemary, chlorogenic acids and their isomers prevail in the examined herb. Among tannin agents gallocatechin is found to be in the biggest amount, and among flavonoids – isoquercetin.

Polysaccharide complex of Antennaria dioica herb is investigated, fractions of water-soluble polysaccharides (WSPS) and pectin substances are isolated, which quantitative content is the following: WSPS – (14,27±0,25) %, pectin substances – (8,41±0,33) %. By means of gas chromatography/Mass spectrometry (GC/MS) method 14 sugars are found in Antennaria dioica herb. The main of them are D-fructose (10,79 mg/kg), D-glucose (7,16 mg/kg) and sucrose (6,72 mg/kg).

Amino acid content in Antennaria dioica herb is determined. 17 combined and 16 free amino acids are found. Proline prevails among free amino acids (3,06 mcg/mg). Cysteine is not found. Analysis of the combined amino acids showed that Antennaria dioica herb contains great amounts of glutamic acid (7,38 mkg/mg) and aspartic acid (5,38 mkg/mg), lysine (3,31 mkg / mg) and cysteine (3 29 mkg / mg).

Lipophilic fraction from Antennaria dioica herb is obtained yielding (5,26 ± 0,07)%. By means of thin layer chromatography (TLC) method a quantitative content of chlorophylls and keratinoids was determined – (0,09 ± 0,003)% and (0,03 ± 0,001)%, respectively.

Among fatty acids in Antennaria dioica herb unsaturated acids prevail over saturated ones – 29,09 mg/kg and 20,60 mg/kg respectively. Linolenic and linoleic acids dominate among fatty unsaturated acids of the examined material –14,50 mg/kg and 14,59 mg/kg, respectively.For the first time, a systemic morphological-anatomical study of Antennaria dioica herb is conducted, the major macro– and micro-diagnostic signs are determined.

An optimal technology to receive the substance – a dry extract of the examined herb – is developed. Examination of acute toxicity found that a dry extract of Antennaria dioica herb can be

referred to VI class of toxicity according to K.K. Sydorov classification, that is, relatively harmless substances, LD50>5000 mg/kg. Bile-expelling and hepatoprotective activity of a dry extract of Antennaria dioica herb is determined in the dose of 50 mg/kg.

Drachuk V.M.

NEPHROPROTECTIVE ACTIVITY OF THE ADEMETIONINE AND GLUTATHIONE IN ISCHEMIA-REPERFUSION ACUTE KIDNEY INJURY

Department of Pharmacology
Higher State Educational Establishment of Ukraine
«Bukovinian State Medical University»

Today, due to significant advances in drug treatment and the improvement of renal substitution therapy, the mortality rate from acute kidney injury (AKI) remains high and is about 40-65%. There is no exception for the ischemic-reperfusion form of the AKI with its multifactorial pathogenetic development and rapid progressive course, the cause of which is usually injury, sepsis, kidneytransplantation, and the effects of toxic substances. Aim of research – to study a nephroprotective potential of ademetionine and glutathione in in ischemia-reperfusion acute kidney injury in rats.

Experiments were conducted on 21 sexually active non-linear white rats weighing 130-180 g. Animals were divided into 3 groups (n=7): group I – control (pseudo-operated animals), group II – Ischemia/Reperfusion modeling (I/P), group III animals received intramuscular injection of ademetionine 20 mg/kg (Heptral, «Abbott SpA», Italy) intradermally during the three days prior to I/P simulation, animals of the IV group received glutathione 30 mg/kg (TAD 600, «Biomedica Foscama», Italy). Doses of drugs are determined by reverse extrapolation. Ischemia was modeled according to aseptic conditions under general anesthesia (aethaminalum sodium, 40 mg/kg): they performed mid-laparotomy, isolated each kidney, impositioning on the renal leg of the clamp for the purpose of crossing the artery, veins and ureter for 60 minutes, followed by sealing the abdominal cavity. After removing the clamp, the abdominal cavity was stained with subsequent 24-hour reperfusion and a grading of the kidneys. Statistical processing of the results was performed using SPSS Statistics 17.0. The reliability of the difference between the scores was evaluated using the parametric t-criterion of Student (in normal distribution) and non-parametric Mann-Whitney U-criterion (in case of mismatch with normal distribution). The critical value level was adopted for $p<0.05$.

In animals, after the pathology modelling were significant changes in the excretory function of the kidneys, which manifested in a decrease of diuresis by 84%, a decrease in GFR in 3.1 times, and a significant reduction in water reabsorption, indicating the development of renal hypophiltration, and, accordingly, the oliguric stage of the AKI. Significant decrease in glomerular filtration led to the development of retention azotemia: the concentration of creatinine in the blood plasma increased by 2.6 times, compared with the group of pseudo-controlled animals. Instead, the administration of the investigational drugs led to increased urinary excretion in the treated animals, preventing the development of oliguria: when using ademetionine, diuresis increased by 53.8 %, glutathione – by 81.1 %, compared with those of the animals in the group of pathology. Accordingly, there was a resumption of glomerular filtration (with the use of ademetionine GFR increased 1.7 times glutathione - 2.7 times) with a significant restoration of water retention and reduction of retention azotemia: the concentration of creatinine in blood plasma decreased by 1.4 times and in 2 , 1 time in comparison with animals of the group of pathology. Due to the injury of the filtration apparatus of the nephron in animals of the model pathology group, there was a significant proteinuria: the concentration of protein in the urine increased 3.1 times, and its excretion – 4.8 times, compared with the group of intact animals. The use of the investigational drugs led to a significant reduction in proteinuria: ademetionine reduced the concentration of protein in urine by 1.5 times, glutathione – by 2.2 times, with excretion decreasing 1.7 times in the group of ademetionine and 3.2 times in the glutathione group, which indicates a decrease in the degree of damage to the nephrocytes.