antibacterial drugs are alkaloids, including the antituberculosis medicine bedaquiline with its quinoline scaffold and the synthetic quinolones derived from quinine. Many alkaloids also fall well within the parameters for being considered drug-like by Lipinksi's Rule of Five, and they have more skeletal structural and functional group diversity than other chemical classes. Cordell et al. noted that only 702 out of 21 120 known alkaloids have been evaluated in more than five bioassays and that many new alkaloid skeletons could be discovered from plant families that are already studied for alkaloids. Alkaloids thus represent a promising source of antibacterial compounds, and further research should be performed while considering their potential toxicity at an early stage of the drug discovery process.

Mechanisms of the biological effects of phytoestrogens

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Introduction. Interest of both public and specialists in medicine and functional food production in the physiological role and practical application of plant bioactive compounds has increased dramatically over the last decade. Of particular interest in relation to human health are the class of compounds known as the phytoestrogens, which includes several groups of non-steroidal estrogens that are widely distributed within the plant kingdom. There is a growing body of evidence, that consumption of some these plants or their molecules could be an additive efficient tool to prevent and to treat several dysfunctions and diseases related to aging, mental processes, metabolism, malignant transformation, cardiovascular diseases and reproduction - breast and prostate cancers, menopausal symptoms, osteoporosis, atherosclerosis and stroke, and neurodegeneration.

The aim of the study. To analyze the literature data on biochemical mechanisms of biological and pharmacological effects.

Materials and methods. Scientific articles on experimental studies of biochemical studies of phytoestrogens on the processes that provide pharmacological activity have been used.

Results and their discussion. Phytoestrogens are strikingly similar in chemical structure to the mammalian estrogen, estradiol, and bind to estrogen receptors alpha and beta with a preference for the more recently described estrogen receptor beta. These receptors after binding with ligand are able to move from cytoplasm to the nucleus, bind and affect the transcription-control regions of DNA or small RNAs and therefore the expression of specific genes. Furthermore, steroids are able to bind to receptors of cell surface, promote formation of cytoplasmic cyclic nucleotides and related protein kinases, which in turn via transcription factors control the expression of target genes. Therefore, phytoestrogens can potentially affect all the processes regulated by estrogens including induction sex hormone binding globulin and inhibition aromatase. Estrogen receptors are present in different tissues – central nervous system (including hypothalamo–hypophysial axis), gonads, reproductive tract, placenta, mammary gland, bones, gastrointestinal tract, lung a.o. This suggests that phytoestrogens may exert tissue specific hormonal effects. The estrogen receptor-specific effects may occur too. For example, estrogen receptors alpha are considered as promoters of cell proliferation, whilst estrogen receptors beta are in charge for promoting mainly cellular apoptosis.

Phytoestrogens besides their ability to bind to estrogen receptors, have other biological effects, which

are not mediated with these receptors – activation of serotoninergic receptors, IGF-1 receptors, binding of free radicals, inducting DNA methylation, affecting tyrosine kinase, cAMP/protein kinase A, cGMP/NO, phosphatidylinositol-3 kinase/Akt and MAP kinases, transcription factors NF-kappaB and DNA topoisomerase activities, histone modification, RNA expression and other intracellular regulators of cell cycle and apoptosis. These abilities are probably responsible for antioxidant, antiproliferative, antimutagenic and antiangiogenic effects of phytoestrogens and their ability to promote human health and longevity. Nevertheless, the hormonal and non-hormonal mechanisms of phytoestrogen effect on particular processes listed below are sometimes difficult to discriminate due to multiple signaling pathways mediating phytoestrogen effects and the insufficient related knowledge. The current studies and related publications are focused more to clinical application, than to basic studies of the mechanisms of phytoestrogen effects.

Metabolic syndrome associated with obesity and type 2 diabetes is a serious public health problem worldwide. The mutual stimulating intrrelationships between obesity and type 2 diabetes have been demonstrated. The high levels of pro-inflammatory cytokines and leptin, secreted by the adipose tissue, contribute to the insulin resistance induction; for instance the high levels of free fatty acids leads to an overproduction of reactive oxygen species that participate in pancreatic β cells failure and apoptosis. These two dysfunctions are the fundamental defects that precede type 2 diabetes. An isoflavone genistein can exert the suppressive effect on obesity and type 2 diabetes via inhibition the adipocyte life-cycle, obesity-related low-grade inflammation, oxidative stress and protection of pancreatic beta cells. The stimulatory effect of genistein on beta-cell proliferation, which has not been mediated via estrogen receptor, but via protein kinase A and MAP/ERK1/2 kinase has been reported too. In addition, isoflavones can increase HDL and decrease LDL concentrations in human plasma, increase lean body mass and reduce fat accumulation. Therefore soy genistein has been proposed as a promising compound for the metabolism improvement and treatment of metabolic disorders. In contrast to soy, red clover isoflavones failed to influence women serum cholesterol level.

The ability of soy phytoestrogens to inhibit the intracellular signaling pathway related to NF-kappaB – transcription factor activating inflammation and immune response suggest potential influence of phytoestrogens on immune system. Genistein can suppresses antigen-specific immune response *in vivo* and lymphocyte proliferation response *in vitro*. However, genistein can enhance the cytotoxic response mediated by NK and cytotoxic T cells and the cytokine production from T cells. Thus, the effect of genistein on immunity is immune cell-dependent. Due to its effect on immune function, genistein has been used for the treatment of the immune diseases in animal models. It has been found that genistein inhibits allergic inflammatory responses. Several epidemiological studies suggest that consumption of traditional soy food containing isoflavones is associated with reduced prevalence of chronic health disorders. Nevertheless, the potential therapeutic action of isoflavones on human immuno-disfunctions require further validation. Malignant transformation of healthy cells and tumorgenesis can be associated with increased DNA mutagenesis, cell proliferation, tissue vascularization, decreased apoptosis, immune response and other processes whose can be under control of estrogens. These processes could be affected by phytoestrogens via estrogen receptor-dependent and -independent mechanisms. The antioxidant, antimutagenic, antiproliferative, antiangiogenic, pro-apoptotic and general anti-cancer effects of a number of phytoestrogens produced by friuts, vegetables, soy, green tea, rooibos, honey bush have been reported.

Traditional consumption of soy products is considered as a cause of lower incidence of breast and prostate

cancers in China and Japan versus United States and European countries. The ability of soy isoflavone genistein to inhibit carcinogenesis has been demonstrated in animal models. There are growing body of experimental evidence that shows the inhibition of human cancer cells by genistein through the modulation of genes that are related to the control of cell cycle and apoptosis. Moreover, it has been shown that genistein inhibits the activation of NF-kappa B and Akt signaling pathways, both of which are known to maintain a homeostatic balance between cell survival and apoptosis and affect immunodeletion of cancer cells. Furthermore, genistein has been found to have antioxidant property, and shown to be a potent inhibitor of angiogenesis and metastasis. Both *in vivo* and *in vitro* studies have shown that genistein could be a promising reagent for cancer chemoprevention and/or treatment. Some long-term studies showed reported potential benefit of soy isoflavones for prevention of colon, endometrial and ovarian cancer. On the contrary, the breast cancer studies generated conflicting and even negative evidence from epidemiological, intervention and experimental animal studies regarding the chemopreventing effects of soy isoflavones in breast cancer. Some studies did not show any association between phytoestrogen intake and breast cancer risk. Moreover, the estrogenic action of soy isoflawones may even promote breast cancer development. Therefore, some specialists donot recommend indisputably accept soy or red-clover as a source of isoflavones to prevent breast cancer. Men may benefit from the intake of soy isoflavones with regard to reducing the risk of prostate cancer. Meta-analyses of the two studies including men with identified risk of prostate cancer found a significant reduction in prostate cancer diagnosis following administration of soy/soy isoflavones. Lignans and their derivates – phytoestrogens and antioxydants enterodiol and enterolactone are produced in the colon by the action of bacteria on the plant precursors in the diet. It has been suggested that the high production of these antiestrogenic mammalian lignans in the gut may serve to protect against breast cancer in women and prostate cancer in men. *In vitro* experiments suggested that they can significantly suppress the growth of human colon tumor cells, and enterolactone can inhibit the estrogen-induced proliferation of breast cancer cells. There are evidence on high anticancerogenic activity of enterodiol and enterolactone arising from flaxseed lignans. The evidence-based biomedical researches on various models in experimental carcinogenesis, on the tumor cells *in vitro*, in clinical trials in patients with hormone-dependent tumors, and, finally, the epidemiological studies have proved the anticarcinogenic activity of the components of the flaxseed antioxidant and validity of recommendations for their both preventive and curative use in hormone-dependent tumors.

Conclusions. The available publications demonstrate the effect of phytoestrogens on a number of physiological and pathological processes related to reproduction, immune systems, metabolism and cancer via various targets and mechanisms.

In some cases phytoestrogens can support normal physiological processes (like female reproduction, bone formation etc.) or they can be safe and easy alternative to hormonal therapy, an efficient tool to prevent and/or to suppress cancerogenesis and some age-related disfunctions induced by estrogen deficit (menopausal syndrom, osteoporosis, neurodegenerative disorders, skin aging). Benefits of estrogens are proposed to be the cause of sex differences in vitality, longetivity and other phyiological characteristics. The first problem is to understand and distinguish the numerous mechanisms of action on phytoestrogens on physiological and pathological processes and their functional interrelationships. This problem is due to the multiple targets and mechanisms of phytoestrogens action, the multiple causes and mechanisms of disorders development and the complexity of interrelationships between various regulatory systems. For example, diseases can be induced by oxydative stress-induced apoptosis, mutagenesis, changes in cell

cycle, cholesterol and carbohydrate metabolism, local vascularization, intracellular protein kinases, transcription factors a.o., whilst each of this interlinked processes may be targeted by phytoestrogens. Understanding targets and mechanisms of phytoestrogen action can be important not only from theoretical, but also from practical viewpoints to predict and to avoid the negative side-effects of phytoestrogen application. The second major problem is the discrepancy between the results of experimental studies and the data from clinical trials. This is likely because the phytoestrogens clinical trials have been limited in many aspects including the number of participants enrolled, the clinical end points investigated, and the lack of long-term follow-up. The third problem is to find an adequate source of phytoestrogens for practical application. The majority of reported studies are focused on soy and red clover isoflavones. Other perspective phytoestrogens and plants (for example, the molecules of flaxseed origin) are studied much less despite their high therapeutic potential. In addition, the general plant-based approaches are associated with serious disadvantages: the production, isolation and application of plant phytoestrogens are time- and labour-consuming, whilst their specificity and reproducibility are sometimes insufficient. Phytoestrogen spectrum and content varies between the plant species, sort and origin, and even the same molecule arising from the different sources can exert various effect. It may not be excluded, that synthetic phytoestrogens with desirable structure and activity could be easier and safer alternative of the traditional plant product of variable origin, phytoestrogen content and activity.

Phytochemical study of the herba of *Cardaria draba* L.

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Introductions. An topical problem of modern pharmacy is the expansion of the nomenclature of herbal medicinal raw materials, the sources of which are plants of the domestic flora, as well as those that are cultivated. Medicinal plant raw materials have advantages over synthetic analogues: the absence or small number of side effects, a diverse range of therapeutic effects.

Cardaria draba is a species of plant from the genus *Cardaria* of the family *Brassicaceae*. The range covers southern Europe, the Mediterranean, Iran, North Africa, Western and Central Asia; in Northern Asia and North and South America, Australia, South Africa it is found as drifting. In Russia, it is widespread in the middle and southern regions of the European part, Crimea, the Caucasus, and southern Siberia. The tap root is long, strong; lateral roots are horizontal, branched; the root system deepens up to 6 m. The stem is straight, branched, short pubescent, 20-50 cm high. The leaves are alternate, from salad-green to gray-green due to the pressed short simple pubescence. The lower ones are petioled, whole, lyre-shaped or notched, with a wedge-shaped base, usually drying by the time of flowering; Stems and upper ones are sessile with a heart-shaped or slightly arrow-shaped base, oblong-ovate, often toothed and notched. Inflorescence on the top of the stem, thyroid, branched, with 2-4 lateral brushes. The flowers are small, 4-6(8) mm in diameter, fragrant, white, with petals up to 3 mm long. Sepals are bare, half as short as the petals, with a wide membranous margin. The fruit is a heart-shaped-oval, flattened, non-opening, double-nested, light yellow or yellowish-grey pod, 3-4 mm long and 3.5-5 mm wide, glabrous, with leathery flaps and a long column. The seeds are ovoid or obverse-ovoid, with a faintly