THE PHARMACOLOGICAL STUDY OF GLUCOSAMINE AND ITS COMBINATIONS WITH NSAIDS AND FLAVONOIDS

Davishnia N. V., Vetrova K. V., Sakharova T. S., Shebeko S. K.
National University of Pharmacy, Kharkiv, Ukraine
clinpharm@nuph.edu.ua

Introduction: Today at the Department of Clinical Pharmacology and Clinical Pharmacy of National University of Pharmacy, under the guidance of professor Zupanets I. A., is developing research area for the pharmacological study of promising compounds in the ranges of derivatives of aminosugar glucosamine and its combinations with NSAIDs and natural bioflavonoids. Glucosamine relates to natural aminosugar, is composed of polysaccharides, glycosaminoglycans, glycoproteins, lipopolysaccharides in the structure of biological membranes, intercellular substance, matrix of articular cartilage and other connective tissue components of organisms, thus performing the plastic function. The exogenous glucosamine detects a wide range of pharmacological activity, which is based on protective properties to all organs and tissues of the human body. It has cardioprotective, hepatoprotective, gastroprotective, nefroprotective, chondroprotective, pulmoprotective, cerebroprotective, anti-inflammatory, analgesic, immunomodulatory, reparative, antithrombotic, gonadoprotective, anti-toxic activities.
This research area has high relevance as the focus on optimization of degenerative and inflammatory diseases therapy and the correction of toxic effects of anticancer therapy.

Purpose of the study: pharmacological studies of glucosamine combinations with NSAIDs and bioflavonoids to optimize the treatment of osteoarthritis and correction toxic effects of anticancer drugs.

Materials and methods: for realization of research were used the pharmacological, biological, biochemical, electrocardiographic, histomorphological, immunohistochemical and statistics methods.

Results: The pharmacological study of glucosamine hydrochloride with ketoprofen combination (2.5:1) in the form of cream-gel firstly was performed and proved experimentally expediency of its use in the treatment of degenerative, inflammatory and destructive joint disease.

The comparative study of analgesic and anti-inflammatory properties of different combinations glucosamine and ketoprofen in topical dosage forms proved that the optimal composition of glucosamine was 5% and ketoprofen 2% in the form of a cream-gel. At the advanced stages of the pharmacological study was established that chosen drug had distinct analgesic effect in conditions of inflammatory hyperalgesia and acute gonarthritis in rats. The high protective and antiexudative influence and moderate antiproliferative activity of the investigated combination has been proven, that a balanced allowing it to influence to inflammatory processes.

Chondroprotective properties of combination was studied in the model of systemic steroid arthritis in rats and proved a positive influence by the content of biochemical markers of connective tissue and histological structure and ultrastructure of articular cartilage tissue. The application of glucosamine derivatives and their combination with quercetin to optimize the approaches to the prevention and correction of the toxic effects of anticancer drugs is a topical issue too.

It have been demonstrated the ability of glucosamine derivatives and their combination with quercetin to reduce general toxic effect of anticancer antibiotic doxorubicin in screening studies in mice. It have been proved that glucosamine derivatives and their combination with quercetin do not have cytotoxic effect on rat's intact cells of bone marrow and enhance their viability under the destabilizing influence of doxorubicin in the experiments «in vitro». At the advanced stages of the pharmacological study it have been found the corrective influence of glucosamine hydrochloride and combination of glucosamine hydrochloride and N-acetylglucosamine with quercetin on the cytostatic-induced toxicity (under the influence of doxorubicin, cyclophosphamide, methotrexate) in experiments on rats. Under the influence of the objects it have been observed the inhibition of the process of lipid peroxidation and displays of cytolysis, reduced inflammation and dystrophy, a significant decrease of the animals mortality (model of intoxication with doxorubicin), decrease of the immunosuppression (model of intoxication with cyclophosphamide). It have been proved the regulating effect on the process of doxorubicin-induced cell death by the investigated objects mediated with the interference in the bcl-2-dependent mechanisms of the apoptosis controls. Based on the complex of the pharmacological studies it have been selected the perspective object – the combination of glucosamine hydrochloride and N-acetylglucosamine with quercetin. Thus, the combination of glucosamine derivatives with quercetin can influence the pathogenesis of many of the toxic effects of anticancer drugs with different mechanisms of action (antibiotic doxorubicin, alkylating cytostatics cyclophosphamide, antimetabolite methotrexate). The effectiveness of combinations of glucosamine hydrochloride and N-acetylglucosamine of quercetin is caused by the presence of various components in the mechanism of action, such as antioxidant, antycytolitic, membrane stabilizing, anabolic, immunotropic, antiapoptotic and anti-inflammatory.

Conclusions: The results of studies justify advisability of further clinical study of combination with glucosamine and ketoprofen in the form of a cream-gel with the aim of implementation as new combined chondroprotective drug. The combination of glucosamine hydrochloride and N-acetylglucosamine with quercetin is a promising object for future to pre-clinical, clinical study and implementation of practical medicine as modifier of toxic effects of anticancer drugs.