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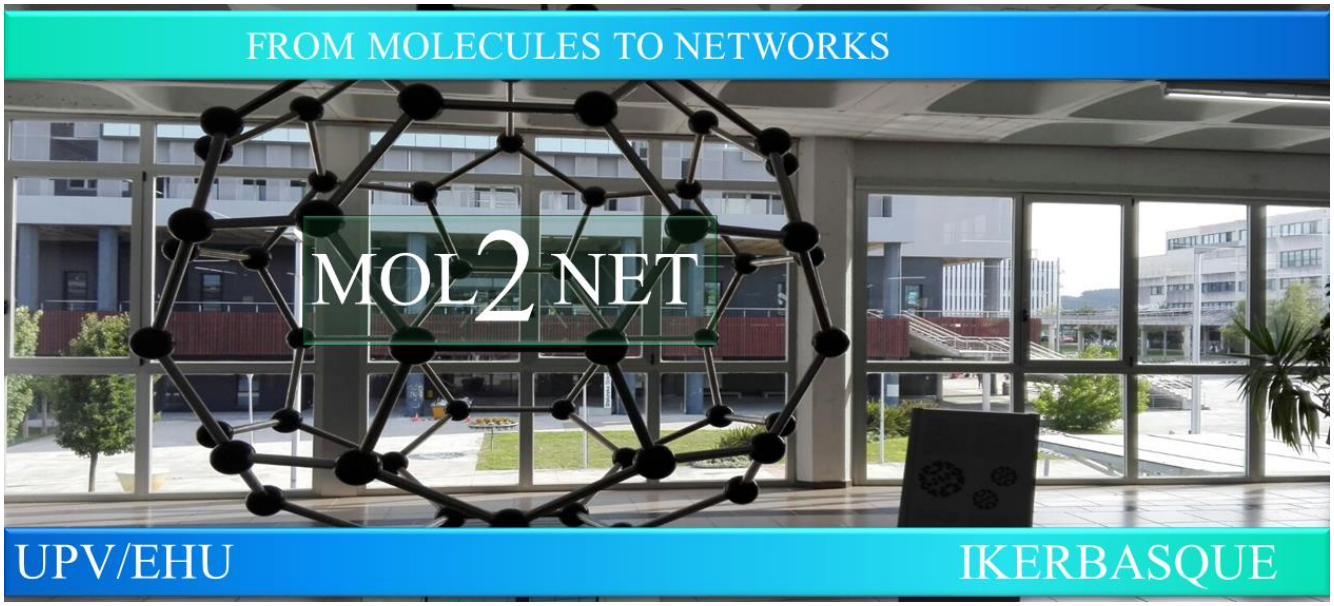

Application of information technology in optimization of combined metabolitotropic cardioprotection

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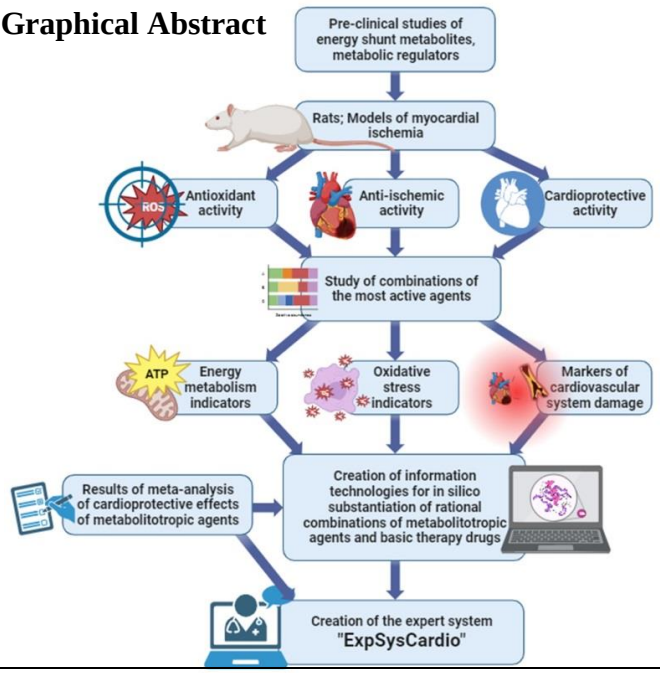
Graphical Abstract



Abstract.

Cardiovascular diseases are one of the most serious problems of modern medicine. Creation of combinations of metabolitotropic cardioprotectors selectively affecting individual target links of ischemic cascade of myocardial damage with the involvement of information technologies is a new promising approach. The aim of the study: to determine experimentally the approaches to the directed metabolic pharmacocorrection of ischemic myocardium and to develop the principles of combined prescription of metabolitotropic cardioprotectors on the basis of the created information technology of computer prediction. We have developed the basic theoretical concepts of a new scientific complex methodology with the involvement of information technologies for the selection and creation of drug

	combinations of metabolitotropic agents with improved pharmacological and toxicological properties for metabolitotropic cardioprotection. The obtained results were used in the development of an expert system for in silico substantiation of rational combinations of metabolitotropic drugs. The expert system was developed in the form of web application. The obtained data became theoretical and experimental substantiation for the creation of combined drugs based on L-arginine, glycine, tryptophan, L-lysine. The application of new information technology in the targeted development of rational combinations of metabolitotropic drugs will increase the efficiency of complex therapy of cardiovascular diseases of ischemic genesis.

Introduction. The beginning of this millennium was marked by a significant spread of cardiovascular diseases, which ranked 2-3 in the mortality structure of industrialized countries. The main goal in correcting myocardial ischemia is to eliminate (or reduce) the mismatch between myocardial oxygen demand and myocardial oxygen delivery. The criteria for successful treatment of angina pectoris are complete or almost complete elimination of anginal attacks (recommendations of the European Society of Cardiology and the American College of Cardiology, 1997). Achieving this goal significantly improves the quality of life of patients and reduces the risk of adverse disease outcomes. This direction may be the main content of metabolic therapy of ichemic heart disease (IHD). For pharmacocorrection of disorders of energy metabolism, oxidative stress, hyperlipidemia, nitric oxide synthesis in hypertension, IHD, chronic heart failure, cerebral vascular pathologies, metabolic and metabolitotropic drugs are used in complex therapy. Combination of means of metabolitotropic cardioprotection, directed at several target links at once or strengthening the effect on one target, can be a significant reserve for increasing the therapy of myocardial ischemia. The use of information technologies to predict the efficacy and safety of possible combinations of drugs, including metabolitotropic drugs, is considered promising. However, modern technologies for justification of drug combination focus only at detection of potential adverse reactions and include the use of automatic verification of drug prescriptions (in the form of so-called computerized decision support systems - DSS). All this makes extremely promising the development of information technology and a new complex methodology of approach to the creation of combinations of metabolitotropic cardioprotectors that selectively affect the individual target links of the ischemic cascade of myocardial damage - violations in the Krebs cycle, malate-aspartate shuttle mechanism, succinatoxidase mechanism, mitochondrial dysfunction, oxidative stress, deprivation of endogenous mechanisms of cardioprotection. There is a need to develop a computer program for wireless devices Medscape (for iPhone, iPad, as well as for other cell phones

and tablet computers), allowing to predict (on the basis of identified molecular and biochemical disorders in myocardial ischemia) rational combinations of metabolitotropic cardioprotectors "at the patient's bedside". The above has determined the relevance and perspective of this paper.

The aim of the study: to determine experimentally the approaches to the directed metabolic pharmacocorrection of ischemic myocardium and to develop the principles of combined prescription of metabolitotropic cardioprotectors on the basis of the created information technology of computer prediction.

Results and Discussion. For the first time we have formed a scientific direction to solve the fundamental problem of medical informatics and pharmacology, which consists in the development of information technology and a new complex methodology of approach to the creation of rational combinations of metabolitotropic drugs that selectively affect the individual target links of the ischemic cascade of myocardial damage, and exhibit cardioprotective, anti-ischemic, mitoprotective effect [1, 2]. Experimental data on the action of metabolitotropic agents (intermediates of energy metabolism, modulators of HSP70, modulators of glutathione system) and their combinations in myocardial ischemia were obtained for the first time [3, 4] (Figure 1).

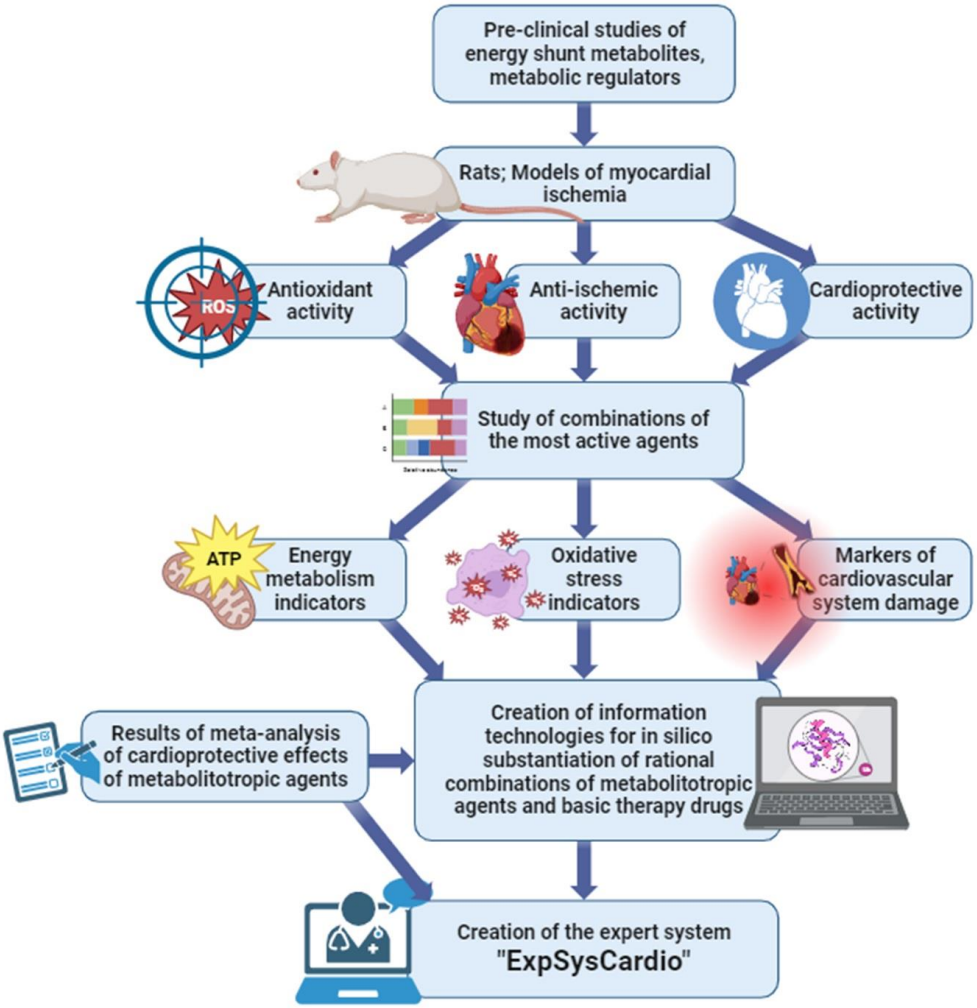


Figure 1. Study design. Development of an expert system for in silico substantiation of rational combinations of metabolitotropic drugs.

We have developed the basic theoretical concepts of a new scientific complex methodology, which is the basis for the creation of new approaches, methods, information technologies, computer systems for the selection and creation of drug combinations of metabolitotropic drugs with improved pharmacological and toxicological properties for metabolitotropic cardioprotection. The obtained data became a theoretical and experimental justification for the creation of combined drugs based on L-arginine, glycine, tryptophan, L-lysine.

The obtained results were used in the development of an expert system for in silico substantiation of rational combinations of metabolitotropic drugs [5]. The expert system is developed in the form of web-application of a computer program with a built-in database of obtained experimental data and the ability to update via the Internet. The computer program could be used for Medscape wireless devices (for iPhone, iPad, and other cell phones and tablets) and predict (by entering the molecular-biochemical parameters of a particular patient) rational combinations of metabolitotropic cardioprotective agents (Figure 2).

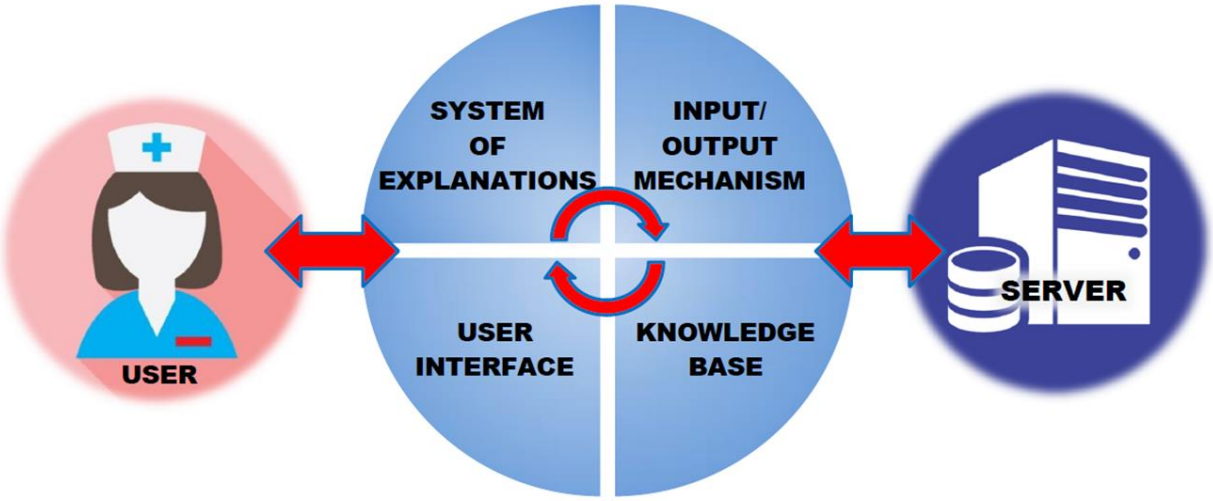


Figure 2. Scheme of the expert system.

Conclusions. Application of new information technology in the directed development of rational combinations of metabolitotropic drugs will increase the effectiveness of complex therapy of diseases of the cardiovascular system of ischemic genesis.

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