

PHARMAEXPERT: ESTIMATING DRUG-DRUG INTERACTIONS AND FINDING COMPOUNDS WITH MULTIPLE MECHANISMS OF ACTION

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On the basis of structural formula of chemical compound, computer program PASS predicts ~2800 kinds of biological activity including ~370 pharmacotherapeutic effects, ~2300 mechanisms of action, ~40 toxic/side effects and ~110 metabolic terms with average accuracy ~93% (<http://www.ibmc.msk.ru/PASS>). PharmaExpert is the program, which interprets PASS predictions taking into consideration known mechanism-effect(s) and effect-mechanism(s) relationships, and provides a flexible mechanism for selection of compounds with desirable but without unwanted kinds of biological activity in libraries of chemical compounds. Knowledgebase of the current version of PharmaExpert (March 2007) contains information about 6003 names of biological activity, 9101 their synonyms, 5108 mechanisms of action, 634 pharmacotherapeutic effects, 61 adverse effects/toxicities, 227 metabolic terms, and 4998 relationships between these terms. Since PASS predictions contain a plethora of information about probable biological actions of chemical compounds, using PharmaExpert it is possible to select compounds with the required multiple mechanisms of action. Also, analyzing PASS predictions it is possible to estimate the probable drug-drug interactions, when a combination of compounds might lead to additive, synergistic or antagonistic effects. The last option may be particularly important in application to herbal medicines contained the mixtures of natural compounds. With PASS and PharmaExpert, most probable specific effects of separate substances can be analyzed as well as interactions between them. Application of PASS and PharmaExpert will be presented on example of finding of antihypertensive substances with combined mechanisms of action and dual COX/LOX inhibitors. Possibilities to find agents with multiple mechanisms of action in databases of commercially available samples will be analyzed.

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The text of the abstract should be within 2000 letters in length without blanks, no indentations. This example (see above) contains 1755 letters.