

SYNERGISM?

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In defending the lack of evidence for the activity of medicinal plants often synergy and prodrugs are mentioned as the reason why the common bioassay guided fractionation failed to find any biological active compound. It is easy to make such a statement, but how to prove this. First of all one should consider what synergism means. A definition of synergism is: "Two or more agents working together to produce a result not obtainable by any of the agents independently". Considering this for biological activity there are two types of synergism:

- Pharmacodynamic [PD] synergy results from two drugs directed at a similar target or physiological system;
- Pharmacokinetic [PK] synergy results from the process of drug absorption, distribution, biotransformation, or elimination. The consequence of this is that only in a living system one may prove synergism, and in fact for the pharmacokinetic synergy, only in humans

this can be measured, due to the species specific metabolism of drugs. With the complex mixtures of compounds present in plants it is impossible to test all possible combinations of single compounds, so only by a systemic approach one may find that a certain combination of compounds is needed for having an activity. That means a systems biology approach with metabolomics as the major tool is the only way to prove synergism.

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ANALYSIS OF EXPERTISE RESULTS OF ADVANTAGE/POSSIBLE HAZARD RATE OF HERBAL MEDICINAL PREPARATIONS SUBMITTED FOR STATE REGISTRATION IN RUSSIA

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The analysis of the results of safety monitoring (advantage/possible hazard rate) for 20 herbal medicinal preparations (HMP) submitted for approving of state registration in Russian Federation according to decrees of Ministry of health and social development № 749n dated 26.08.2010 and № 757n dated 26.08.2010 was done. Sixty percent of results of safety monitoring (75% domestic and 25% of foreign HMP) have passed expertise. For 40% of results of safety monitoring (12,5% domestic and 87,5% of foreign HMP) some comments were done. Main experts comments were: results of safety monitoring have covered not full registration period (p. 1.7.); difference in application of HPM in Russia and foreign countries are not marked; not all countries are indicate in which HMP is marketed; the date of HMP registration in some country is not indicated; not all countries listed in the periodical report about safety

are indicated (p. 2.1.); number of batches which were sold in Russia only is indicated (but HMP is marketed in other countries as well). Information about number of packages supplied by manufacturer and received by patients is not correct (pp. 2.5. and 2.6.). Pos. 2.4. was not completed; p. 2.16. was completed to according to rules; the job position, name and signature of responsible for results of safety monitoring of HMP were not indicated (p. 1.9.); date of submission of results of safety monitoring was not indicated (p. 1.8.); number of HMP registration certificate was wrong (p. 1.2.); date of HMP registration was wrong (p. 1.3.); the formulation of HMP was not correct (p. 1.5.); some information in the tables of document is not presented. Compliance of all rules of normative documents for pharmacovigilance and monitoring of safety of HMP after registration is very important.