In silico prediction of ADME and pharmacokinetics

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Abstract

The computational approach is one of the newest and fastest developing techniques in pharmacokinetics, ADME (absorption, distribution, metabolism, excretion) evaluation, drug discovery and toxicity. However, to date, the software packages devoted to ADME prediction, especially of metabolism, have not yet been adequately validated and still require improvements to be effective. Most are ‘open’ systems, under constant evolution and able to incorporate rapidly, and often easily, new information from user or developer databases. Quantitative in silico predictions are now possible for several pharmacokinetic (PK) parameters, particularly absorption and distribution. The emerging consensus is that the predictions are no worse than those made using in vitro tests, with the decisive advantage that much less investment in technology, resources and time is needed. In addition, and of critical importance, it is possible to screen virtual compounds. Some packages are able to handle thousands of molecules in a few hours. However, common experience shows that, in part at least for essentially irrational reasons, there is currently a lack of confidence in these approaches. An effort should be made by the software producers towards more transparency, in order to improve the confidence of their consumers. It seems highly probable that in silico approaches will evolve rapidly, as did in vitro methods during the last decade. Past experience with the latter should be helpful in avoiding repetition of similar errors and in taking the necessary steps to ensure effective implementation. A general concern is the lack of access to the large amounts of data on compounds no longer in development, but still kept secret by the pharmaceutical industry. Controlled access to these data could be particularly helpful in validating new in silico approaches.

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