COMPUTER-AIDED DRUG REPURPOSING: NEW USES FOR OLD DRUGS OR FILLING GAPS IN BIOMEDICAL KNOWLEDGE?

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Motivation and Aim: Biological activity is one of the most important properties of organic substances, which provides the possibility of their use as medicines. The current dimensionality of chemical-biological space for available chemical compounds and known pharmacological targets is about 10^{10}, while for virtual compounds and potential targets it is about 10^{16}. Thus, experimental study of the interaction of all drug-like structures with each known pharmacological target could not be accomplished from both economical and practical point of view, and all existing information about biologically active compounds is incomplete. Bio- and Chemoinformatics shed light on a hidden pharmacological potential of launched drugs that may provide the reasons for their repurposing. Due to the current knowledge about pharmacodynamics and pharmacokinetics of the launched drugs, their repurposing may significantly reduce the time & financial expenses and risks of the development.
Methods and Algorithms: We will present an overview of the currently existing target-based and ligand-based methods of computer-aided drug repurposing with particular highlighting of our software PASS and PharmaExpert [1, 2].
Results: Published in 2001 PASS predictions of novel pharmacotherapeutic actions for eight from the list of Top200 drugs have been further confirmed either by the experimental or by clinical studies for Sertraline (Cocaine dependency treatment), Amlodipine (Antineoplastic enhancer), Oxaprozin (Interleukin 1 antagonist), Ramipril (Antiarthritic). Later we anticipated the nootropic action of some antihypertensive drugs (Perindopril, Ramipril, Quinapril, etc.) that has been confirmed by the experiment [3] and in clinical trials [4].
Conclusions: The considered examples undoubtedly demonstrate the potential of computer-aided methods in drug repurposing. Moreover, computer-aided approaches leads to the filling the gaps in the existing biomedical knowledge due to the extraction of novel "drug – target – effect – disease" associations.
References:
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