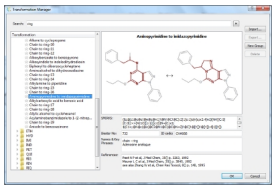
This review article has just been accepted by Expert Opinion in Drug Discovery and discusses recent developments in the methods and opinions in multi-parameter optimisation, focusing on applications to *de novo* drug design and illustrated with published examples.



Abstract

Introduction

A high quality drug must achieve a balance of physicochemical and ADME properties, safety and potency against its therapeutic target(s). Multi-parameter optimisation (MPO) methods guide the simultaneous optimisation of multiple factors to quickly target compounds with the highest chance of downstream success. MPO can be combined with 'de novo design' methods to automatically generate and assess a large number of diverse structures and identify strategies to optimise a compound's overall balance of properties.

Areas Covered

We will review MPO methods and recent developments in the methods and opinions in the field. We will describe advances in de novo design that improve the relevance of automatically generated compound structures and integrate MPO. Finally we will discuss a recent case study of the automatic design of ligands to polypharmacological profiles.

Expert Opinion

Recent developments have reduced the generation of chemically infeasible structures and improved the quality of compounds generated by de novo design methods.

There are concerns about the ability of simple drug-like properties and ligand efficiency indices effectively to guide the detailed optimisation of compounds.

De novo design methods cannot identify a perfect compound for synthesis, but can identify high quality ideas for detailed consideration by an expert scientist.

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