APPLICATION OF X-RAY CRYSTALLOGRAPHY IN THE RESEARCH AND DEVELOPMENT OF DRUGS

Autor(res)

Carolina Passarelli Gonçalves
Allan Blener Da Silva

Categoria do Trabalho

1

Instituição

UNIVERSIDADE ANHANGUERA DE OSASCO

Resumo

X-ray crystallography is the best microscopy technique for macro-molecules structures, being favoured for pharmaceutical companies by providing a detailed structural parameters, at atomic level resolution, which are prerequisites for rational drug design. This review aims to measure the application of this technique in the pharmaceutical field with evidences that proves the applicability of this method for research and development of drugs. This is a method for obtaining structural information about a macromolecule that consist of forming a crystalline precipitate by crystallization, in which we expose to an x-ray beam generating diffraction spots that can be used to calculate an electron density map and the structure of the macromolecule can be determined. This 'gold standard' detailed structural information provides a wealth of structural details that can be used to examine, at an experimental level, the interactions of small organic molecules with proteins and their protein-ligand as well as enzymatic mechanisms. Playing an important and widely recognized role in drug design the potential of X-ray crystallography was already evidenced as it allowed the unambiguous structure determination of penicillin and, as another notable example, inhibitors of HIV protease. Thus, we can affirm that structural information has paved the way for drug design by serving as the central source of experimental data used in the optimization and discovery of new drugs. As a reaction the use of structure-based design from Crystal structures provided by x-ray crystallography has become common in pharmaceutical research, resulting in several marketed drugs such as Captopril an antihypertensive, Agenerase and Viracept for HIV, dorzolamide to treat glaucoma, and Relenza for the treatment of influenza, and many others. Thereby, this rational drug design became na established discipline in most pharmaceutical companies. The impact of x-ray crystallography in the pharmaceutical field has extended from an improvement of the basic understanding of molecular biology to an improvement in human health by the generation and optimization of new drugs in the pharmaceutical industry. Leading to advancements and inspiring new hypotheses and experiments we can be sure that x-ray crystallography will continue to serve as the primary source of experimental structural data used in research and development of drugs.