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A Review: In Silico Study and Characterization Bioactive Compound by Using Lcms Techniques from Plant Extract

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ABSTRACT:

An in silico study is one performed via simulation on a computer. In silico simulations are frequently used to predict how a compound will react with proteins in the body or with pathogens. Bacterial sequencing techniques represent a group of in silico methods that are used to identify bacteria. These techniques sequence bacterial DNA and RNA. Polymerase chain reaction (PCR) is the most commonly used technique, a method that has become more widely known due to its use in testing for COVID-19. Another popular in silico method of molecular modeling, a technique capable of showing how therapeutic molecules interact with the nuclear receptors of cells. Natural products, such as plants extract, either as pure compounds or as standardized extracts, provide unlimited opportunities for new drug discoveries because of the unmatched availability of chemical diversity. According to the World Health Organization (WHO), nearly 20,000 medicinal plants exist in 91 countries including 12 mega biodiversity countries.

Keywords: In silico, RNA, Polymerase chain, bacteria, Natural products

INTRODUCTION:
IN SILICO STUDY

The term ‘in silico’ has not been around in the scientific community for many years. It is a relatively new term used to describe an emerging area of study. In silico originally meant “performed on computer or via computer simulation”, in modern science it refers to experimental techniques performed by computers and is related to the more established terms of in vivo and in vitro studies.An in silico study is one performed via simulation on a computer. In silico simulations are frequently used to predict how a compound will react with proteins in the body or with pathogens.

History and evolution of in silico approaches

Drug design and related disciplines in drug discovery did not wait for the advent of informatics to be born and to grow as sciences. As masterfully summarised by Albert (1971, 1985), the earliest intuitions

and insights in structure–activity relations can be traced to the nineteenth century. A relation between activity and a physicochemical property was firmly established by Meyer (1899) and Overton (1901), who proposed a 'Lipoid theory of cellular depression' such that the higher the partition coefficient between a lipid solvent and water, the greater the depressant action. Such papers paved the way for the recognition of lipophilicity and electronic properties as major determinants of PD and PK responses, as best illustrated by the epoch-making and still ongoing work of Corwin Hansch (Hansch and Fujita, 1964; Hansch, 1972), a founding father of drug design.

Other pioneers (for example, Crum Brown and Fraser; reviewed by (Albert, 1971)) saw that chemical structure (that is, the nature and connectivity of atoms in a molecule, in fact the two-dimensional structure (2D) of compounds) also played an essential role in pharmacological activity. The conceptual jump from 2D to three-dimensional (3D) structure owes much to the work of Cushny (1926), whose book summarises a life dedicated to relations between enantiomerism and bioactivity. This vision was expanded in the mid-twentieth century by the discovery of conformational effects on bioactivity (Burgen, 1981).

In parallel with our growing understanding of the concept of molecular structure, a few visionary investigators in the late nineteenth and early twentieth centuries (for example, John Langley, Paul Ehrlich and Alfred Clark; reviewed by (Arïens, 1979; Parascandola, 1980) developed the concept of receptors, namely the targets of drug action. The analogies between receptors and enzymes were outlined by Albert (1971).

The converging lines of progress in chemistry and biology generated a flood of information and knowledge which went beyond the usual capacity of 'in cerebro' data handling and was a driving force in the emergence and development of computer sciences. Hansch was among the very first in the 1950s to use calculators and statistics to arrive at quantitative relations between structure (in fact, parameters and descriptors) and activity. Such was the birth of quantitative structure–activity relationships (QSARs), followed in the 1980s and 1990s by computer graphics and molecular modelling. However, computer sciences rapidly ceased to be a simple tool in drug discovery and pharmacology and became a major contributor to progress. The chemistry–biology–informatics triad has now evolved into a life of its own and is bringing pharmacology to new heights, as this review will briefly attempt to illustrate.

THE DEVELOPMENT OF IN SILICO TECHNIQUES IN PHARMACOLOGY

While in silico studies are a relatively new method of investigating hypotheses, the number of research projects that have begun to rely on For example, in silico methods (software emulations) were used in a 2009 study that predicted how certain already-approved drugs could be used to treat numerous drug-resistant strains of tuberculosis. Using conventional methods, such an investigation would have taken considerable more time and resources. These methods is rapidly growing. Often, they are being used to explore how novel therapeutics interact with certain molecules in the body, biological tissues, and pathogens. These studies have already produced findings that have made waves in the medical sector.For example, in silico methods (software emulations) were used in a 2009 study that predicted how certain already-approved drugs could be used to treat numerous drug-resistant strains of tuberculosis. Using conventional methods, such an investigation would have taken considerable more time and resources.

Bacterial sequencing techniques represent a group of in silico methods that are used to identify bacteria. These techniques sequence bacterial DNA and RNA. Polymerase chain reaction (PCR) is the most commonly used technique, a method that has become more widely known due to its use in testing for COVID-19. PCR works by duplicating a single or several pieces of DNA, creating millions of copies of the sequence. As a result, it is a highly sensitive method of detecting bacteria and viruses that underlie serious diseases.

Another popular in silico method of molecular modeling, a technique capable of showing how therapeutic molecules interact with the nuclear receptors of cells. One molecular modeling study of particular note is that of Trevor Marshall, who used computer-based emulations to reveal that a particular metabolite of vitamin D, 25-D, along with a substance generated by bacteria, Capnine, is able to turn off the vitamin D receptor.

Common applications for in silico studies include

-Drug candidate screening (molecular docking studies)

-Prediction of adverse drug reactions

-Whole cell simulations

-Sequencing (in silico PCR)

LCMS:

A brief history of mass spectrometry may be found in LIQUID CHROMATOGRAPHY-MASS SPECTROMETRY. J.J. Thomson of Manchester, England, is credited with developing modern mass spectrometry through cathode-ray tube experiments in 1897.
-Wolfgang Paul won the physics Nobel Prize in 1953 for developing the quadrupole and quadrupole ion trap.
-Malcolm Dole created electrospray ionisation in 1968. (ESI).
-Horning invented atmospheric pressure chemical ionisation (APCI) in 1974.
-The thermospray technique was created in 1983 thanks to Vestal and Blakely's work with heating a liquid stream.
The idea of mass spectrometry was first presented by the English physicist Sir J.J. Thomson, who discovered the electron in 1887. He received the 1906 Physics Nobel Prize. A technique for decomposing a complicated mixture into its constituent parts is called LC-MS. The combination of these two techniques is known as LC-MS. • High sensitivity of mass spectroscopy offers the information for identification of compounds or structural elucidation of compounds. • The metabolites enter the mass detector as they emerge from the column's end, where the solvent is drained away and the metabolites are ionised. A method known as LC-MS combines the mass analysis skills of mass spectrometry with the physical separation capabilities of liquid chromatography• It is a technique that combines the mass spectrometry detection power with the HPLC separation power. • In LC-MS, the detector is taken out of

the LC column and fitted to the MS interface. • Ionization sources are typically employed as the LC-MS interface.

INTERFACES

A device for introducing samples (like an HPLC), an interface for connecting such a device, an ion source that ionises samples, an electrostatic lens that effectively introduces the created ions, a mass analyzer unit that separates ions based on their mass-to-charge (m/z) ratio, and a detector unit that detects the separated ions. • However, if the LC unit is simply connected to the MS unit in an LC-MS system, the liquid mobile phase would evaporate and significant amounts of gas would be delivered into the MS unit, lowering the vacuum level and preventing the target ions from reaching the detector. Interfaces should therefore be used.

TYPES OF INTERFACES

It is difficult to interface a liquid chromatography to a massspectrometer cause of the necessity to remove the solvent. The commonly used interfaces are

1. Electrospray ionization (ESI)
2. Thermospray ionization (TSI)
3. Atmospheric pressure chemical ionization (APCI)
4. Atmospheric pressure photoionization(APPI)

Applications of LC-MS - Pharmaceutical Applications:

1. Rapid chromatography of benzodiazepines
2. Identification of bile acid metabolite

Biochemical Applications:

Rapid protein identification using capillary LC/MS/MS and database searching.

Clinical Applications:

1. High-sensitivity detection of trimipramine and thioridazine

Applications of LC-MS Food Applications:

1. Identification of aflatoxins in food
2. vitamin D3 in poultry feed supplements

Environmental Applications:

1. Detection of phenylurea herbicides
2. Detection of low levels of carbaryl in food

Forensic Applications:

1. Illegal substances, toxic agents
2. Explosives

3. Drugs of abuse

BIOACTIVE COMPOUND:

Natural products, such as plants extract, either as pure compounds or as standardized extracts, provide unlimited opportunities for new drug discoveries because of the unmatched availability of chemical diversity (Cos et al., 2006). According to the World Health Organization (WHO), more than 80% of the world's population relies on traditional medicine for their primary healthcare needs. The use of herbal medicines in Asia represents a long history of human interactions with the environment. Plants used for traditional medicine contain a wide range of substances that can be used to treat chronic as well as infectious diseases (Duraipandiyan et al., 2006). Due to the development of adverse effects and microbial resistance to the chemically synthesized drugs, men turned to ethnopharmacognosy. They found literally thousands of phytochemicals from plants as safe and broadly effective alternatives with less adverse effect. Many beneficial biological activity such as anticancer, antimicrobial, antioxidant, antidiarrheal, analgesic and wound healing activity were reported. In many cases the people claim the good benefit of certain natural or herbal products. However, clinical trials are necessary to demonstrate the effectiveness of a bioactive compound to verify this traditional claim. Clinical trials directed towards understanding the pharmacokinetics, bioavailability, efficacy, safety and drug interactions of newly developed bioactive compounds and their formulations (extracts) require a careful evaluation. Clinical trials are carefully planned to safeguard the health of the participants as well as answer specific research questions by evaluating for both immediate and long-term side effects and their outcomes are measured before the drug is widely applied to patients.
According to the World Health Organization (WHO), nearly 20,000 medicinal plants exist in 91 countries including 12 mega biodiversity countries. The premier steps to utilize the biologically active compound from plant resources are extraction, pharmacological screening, isolation and characterization of bioactive compound, toxicological evaluation and clinical evaluation. A brief summary of the general approaches in extraction, isolation and characterization of bioactive compound from plants extract.

List of Bioactive compound

Alkaloids
Terpenoids
Coumarins
Flavonoids
Nitrogen-containing compounds
Organosulfur compounds Phenolics

Identification and Characterization

Due to the fact that plant extracts usually occur as a combination of various type of bioactive compounds or phytochemicals with different polarities, their separation still remains a big challenge for the process of identification and characterization of bioactive compounds. It is a common practice in isolation of these bioactive compounds that a number of different separation techniques such as TLC, column

chromatography, flash chromatography, Sephadex chromatography and HPLC, should be used to obtain pure compounds. The pure compounds are then used for the determination of structure and biological activity. Beside that, non-chromatographic techniques such as immunoassay, which use monoclonal antibodies (MAbs), phytochemical screening assay, Fourier-transform infrared spectroscopy (FTIR), can also be used to obtain and facilitate the identification of the bioactive compounds.

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