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Pharmaceutical Nanotechnology: Bio-pharmaceutical Support in Candidate Drug Selection

Abstract

Drug selection is one of the important steps in new drug development. There are multiple factors that contribute to new drug formulation. Biopharmaceutical considerations along with physiological and pharmaceutical parameters are more helpful in defining the process. Various GIT restrictive barriers are challenges for many new drug developments. New drug formulation advantages over the traditional molecules should be cost-effective, therapeutically superior and compliant as compared to previously used active agents. Drug selection compromises multiple steps including preliminary studies in the lab (screening) to the formulation of the dosage form to in-vitro studies along with in-vivo studies. These led to the clinical trials after the selection had been made. Wide drug selection techniques are employed to save costs along with adverse drug effect profiles. It also includes safety for animal studies and in humans.

Key Words: Drug screening, Drug development, Biopharmaceutical Aspects

Introduction

Administration through the oral route has been the most accepted and convenient route for disease management. Although the oral route is the most suitable way of delivering drugs, it encompasses a large number of obstacles within GIT which makes it not a straightforward way of administration. The oral route is one of the safest and most effective routes in the drug delivery system. There are numerous efforts going on to modify or change the molecule or its dosage form so that it would be easy to administer through the oral route. It is predicted that 40–60% of newly discovered chemicals are poorly soluble in water (PWSD). When prepared as standard oral dosage forms, PWSD candidates often present biopharmaceutical problems that result in variable absorption, low bioavailability, high pharmacokinetic variability, and uptake that is dependent on food (Bio-enabling forming technologies, such as lipid-based formulations, solid dispersions, or nanosized drug formulations, are frequently needed for new therapeutic candidates. Clinical development may be slowed or delayed because the development of such more complex delivery systems often demands more resource investments than the development of a traditional oral dose form (Kuentz 2011). Finding an appropriate formulation method for a particular drug candidate as soon as feasible is essential to achieving the biopharmaceutical goals and facilitating quick, cost-effective development (O'driscoll and Griffin 2008). Both in vitro and in vivo research are impacted by the potential therapeutic compounds' physicochemical and biological characteristics. The selection of drug candidates with a higher chance of success in the development process is aided by the invention and selection of molecules possessing drug-like characteristics (Yazdanian 2013).

Description

The main problems of GIT in delivering drugs for systemic circulation are

- Lining of Stomach,
- Small and large intestine luminal portion,
- The presence of GIT enzymes,
- Physical hurdles such as epithelium &
- Liver.

These problematic hurdles are necessary for human beings. Because they can affect the drug properties

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by controllable water available, electrolytes and also the tiny creatures bacteria/ viruses produced toxins may be inflated to handle (Lamont 1992). Normally the path is followed by the drug particles to reach the systemic circulations (in solution form) so, it effectively passes the GIT and intestinal mucosa. Although the rate controlling step for oral drug absorption and movement across the membrane is dissolution. Before this, the drug in GIT must be in the desired simple molecular state. To improve the absorption of drugs it is proposed that the delivered entity must be in smaller particulates and this effect can enhanced by site-specific targeted drugs. Undissolved large crystalline structures and liposomes are less absorbed from GIT (Cu and Saltzman 2009).

Stages of drug release

The cascade of phenomena such as the release of the drug from its delivery system, i.e., the crossing of NCE in the mucosa, association/deterioration in the mucosal membrane, and the drug passed into the systemic circulation by crossing the intestinal membrane in its molecular state, which is schematically shown in Figure 1.

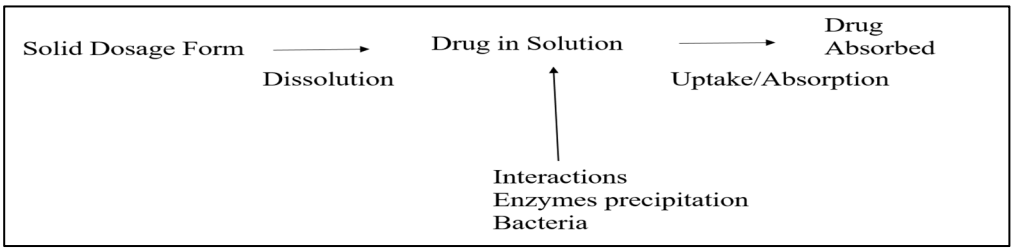

Figure 1

Development of New Drug Products

For fast and complete drug dissolution and movement of NCE particles across the membrane effective methodologies are developed to reach different site actions involved in and after/ between the processes need to be evaluated properly (AL Harvey *et al.*, 2015). By combining the information obtained from the stream of phenomenon (e.g., solubilisation, dissolution, permeation, or instability related to metabolism) accruing in the body as rate-limiting steps could be utilized to determine such development models. These well-designed and optimized methods could be utilized in the discovery of new chemical entities which further aid in selecting the best drug candidate with a well-defined PK-PD profile (pharmacokinetic and pharmacodynamics. This is not a single step, it comprises multiple analytical steps which collect huge amounts of data to obtain desired output by setting different parameters nowadays.

Screening and optimization

For optimization and justification of new chemical entities, various circumstances in corresponding like dissolution, solubilisation, permeation along stability, toxicity and duration of action etc. These all variables can be rationally utilized by using different applied statistical tools (Eriksson *et al.*, 1999). This point is vital to account for because a drug made orally bioavailable by increasing its potency if previously it is not suitable as an oral drug. In the screening of a drug candidate, the dissolution and solubility rate of the drug compound can be affected by these parameters in biological processes while studying the outcome of the drug. In case of improper/incomplete distribution of the drug in the approved system, showed that this NCE will not dissolve in blood receipt after *in-vivo* studies (drugs with low water-soluble capacity). Hence, this new chemical entity is considered as having no probable outcome for use in human beings due to less solubility and less permeability profile. So the handling of this issue became hard to resolve and required a somewhat mechanistic approach to cross the membrane. These circumstances can interfere with some consequences. These outcomes can be affected by natural mechanisms present in the human body such as membrane efflux pumps required to cross the mucosal membrane (glycoproteins) (Hunter and Hirst, 1997) or transformation of the drug during movement and adherence with the material in the experimental system (Table 1). Describing these moderate transport issues of NCE is crucial to addressing the development of official concealing methodologies.

Table 1. Stated problems during permeation of drug transport across the membrane.

- *Adsorption to systems used materials*
- *Little drug solubility due to the Complexation of ions in the buffer*
- *Metabolism/ degradation of drug entity in the gut or in the intestinal parts: where small activities of the cells can be affected.*

- *Systematic response issues*
- *Undissolved large water molecules layer in mucus is responsible for less absorption of drugs.*

Drug discovery process

In the discovery process of a new drug compound, the selection of the most suitable new chemical entity is the major part of price determination and clinical trials follow. Some basic criteria for drug absorption across the membrane according to biopharmaceutical concerns are stated as:

High diffusion constant (determined using in vitro assays such as intestinal perfusions, Using chambers, Caco-2 cell monolayers, etc.) overall the gastrointestinal tract [delayed or prolonged delivery formulations]. Transport of drugs across the membrane or interaction by the help of a carrier or passively is highly water-soluble drugs, over a spacious range of pH (e.g., pH 1–7). Somewhat deterioration in lower GIT e.g., intestinal homogenates, intestinal luminal fluids, or incomplete first-pass effect of microsomal formulations to the gastrointestinal parts such as intestines, stomach and liver. Drugs absorbed in the *in-vivo* testing of animals can be correlated with human GIT.

These parameters are not as easy as they seem to be, developing a correlation between in-vitro in-vivo studies, by relating potency concentrations and therapeutic index ratio in safety margin level for new chemical drug (NCD). Although the absorption rate and permeation level, be examined critically for NCD. Moreover, the physical and chemical nature of this NCD described in the latter pre-formulation data evaluation further helps to optimize the functions of that entity that support it to declare a powerful chemical drug postulant.

Bio-pharmaceutical Aspects

Bio-pharmaceutical data collected in the selection of new chemical entities related to the attributes of NCD molecule (e.g., bioavailability, enzymatic stability, homogenization, membrane transport, resistance to fluids at the site of action and dissolution) is significant to obtain successive formulation systems. This data is foremost vital, such as,

- To determine vital dosage forms and technologies,
- To develop biopharmaceutical aim for formulating selected dosage forms,
- To describe later biopharmaceutical aspects required to attain aims and objectives
- With the help of retrospective data for an explanation of various studies used in developing an optimized dosage form.

Therefore, effectively accomplished NCD molecule testing decreased the chance of an error in the final selected delivery system, outcomes avoiding vital biopharmaceutical conditions for that new chemical compound. That's why, this sort of data is also responsible for an effective advancement procedure based on scientific technology, while hit and trial methods are negated.

Best fit model for bio-pharmaceutical assessment

To relate the testing outcomes of such NCD with the human body with the help of underlying mechanisms can be described by its physiological, physical and chemical characteristics. They represent a best fit bio-pharmaceutical model for IVIV correlation if it could describe stated parameters. Not a solitary step can relate these parameters at the same time from starting of production to the final screening step. They differ for all different types of developments. So not a single describing process can direct all gathered data to discover a new chemical drug delivery method or new chemical compound. Much time and collected information is required to do so. In the last 2 decades, various methodologies referred to for drug screening technology development. This composed information could help us to study simple primary parameters regarding drug dissolution then absorption. Also, guide us about the data collection and after gathering this data how to analyse and utilize it for further functionalization and development. These procedures helped us to select

an NCD and develop an optimized dosage form considered for use in humans.

Conclusion

After going through multiple steps, a new drug has been developed in the new formulation. The advantages of this development would be cost effectiveness, safety in side effects, and more compliance along with better adherence. The idea behind drug discovery initiatives is the hope that a novel, effective medication can be found and made available to treat human suffering. The program is advanced by the efficacious data and good indications. On the other hand, human safety has to come first when choosing and evaluating a therapeutic medication candidate. Demands for safety from the public and regulatory bodies are higher than ever in the wake of multiple unanticipated adverse events seen in human trials in recent years.

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