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Editorial

The Importance of DMPK Researches

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Editorial

The discovery and development of new pharmaceuticals drugs present a mounting challenge, marked by increasing complexity and costs. Late-stage failures, particularly in phase III trials, carry significant financial burdens. Notably, attrition rates are higher during phase II and submission phases. Consequently, drug discovery initiatives have heavily invested in frontloading activities aimed at mitigating risks and minimizing attrition during the early stages of drug development [1].

Thus, early screening and optimization of drug metabolism and pharmacokinetics (DMPK), alongside considerations of physicochemical properties, have emerged as pivotal factors. These efforts aim to ensure that compounds exhibit desirable attributes such as solubility, permeability, oral bioavailability, suitable half-life, clearance for dosing regimens, and lack of drug-drug interactions [1]. Such criteria constitute integral components of rational drug discovery, necessitating the utilization and further refinement of well-established in vitro, in vivo, and in silico methodologies [2,3].

Numerous studies have elucidated the influence and significance of descriptors encompassing both calculated physical and chemical properties and ADME (Absorption, Distribution, Metabolism, and Excretion) properties of compounds. These descriptors furnish reliable in silico insights, facilitating informed decision-making throughout the drug development pipeline [4]. Emphasizing the assessment of developability risks associated with a molecule's progression into clinical development, these studies enhance the prospects of success for novel drug candidates. Consequently, there is a pressing need for the advancement of machine learning methods and in silico programs to provide more nuanced assessments of drug-like properties to researchers.

With a contemporary outlook, recognizing the pivotal role of animal models in predicting pharmacokinetics during the preclinical phase underscores the importance of adopting alternative methodologies. The inherent limitations and discrepancies between human and animal physiology necessitate innovative approaches to circumvent erroneous pharmacokinetic predictions. Consequently, there is a growing momentum towards reducing and ultimately prohibiting animal testing in drug discovery. In this context, in vitro tests utilizing human-derived cells have emerged as effective alternatives [5].

Microfluidic technology has garnered attention as a transformative tool in cell-based assays, offering platforms such as cell-on-a-chip, single/multiple organ-on-a-chip, and body-ona-chip. By faithfully replicating in vitro environments, these platforms facilitate the maintenance of cellular function and morphology, as well as the emulation of organ interactions. Notably, body-on-a-chip models integrating multi-organ functions hold promise for predicting complex organ interactions [5,6].

Moreover, physiologically-based pharmacokinetic (PBPK) modelling and in vitro system technologies have emerged as invaluable tools for comprehending the ADME processes of drugs in the early stages of drug discovery. The insights gleaned from these studies contribute significantly to advancing our understanding of the therapeutic effects of drugs on human pathophysiology. Continued progress in preclinical trials is imperative to ensure a streamlined and cost-effective drug development process, ultimately yielding safer medications.

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