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Short Communication

Allometry Scaling in Drug Development

Murugesh Kandasamy*

Department of Pharmaceutical Chemistry, International Medical University, Malaysia

***Corresponding author:** Murugesh Kandasamy, Lecturer, Department of Pharmaceutical Chemistry, International Medical University, No. 126 JalanJalil Perkasa 19, Bukit Jalil 57000 Kuala Lumpur, Malaysia, Tel: +603-27317703; Email: MurugeshKandasamy@imu.edu.my

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Introduction

Allometry is about the study of body size and its outcomes, it is described as 'by a different measure', and in allometric system the proportions are changed in a regular fashion [1]. Allometry, which is the oldest of the approaches and still widely applied in biology, is concerned with the study of the relationship between the size and function of components of the body and growth or size of the whole body [2]. Alternatively, to study the species change in a specific factor which correlates with difference in size of the species. Allometry is centered on the prediction (an exact prediction) by considering the physiological, anatomical and biochemical parallels among animals, which can be explained by mathematical models. It is now an established fact that many physiological processes and size of the organ that exhibit a power-law relationship with the body weight of the species. This relationship is defined as the scientific source of allometric scaling [3,4].

Extrapolation of animal pharmacokinetic parameters to predict in humans is a vital tool in drug discovery and development. Allometric scaling has many components, and many different ideas and methods have been recommended to enhance the prediction of pharmacokinetic parameters from animals to humans. The simple allometric approach is based on the power function $Y=aW^b$, where Y is the parameter of interest, W is bodyweight, a and b are the coefficient and exponent of the allometric equation, respectively. Where the bodyweight of the species is plotted against the pharmacokinetic parameter of interest on a log-log scale. Volume of distribution, clearance, and half-life are the three most important pharmacokinetic parameters than can be predicted [5]. Interspecies pharmacokinetic scaling can be expressed on the assumption of physiological, anatomical, and biochemical parallels among animal species [6,7]. Interspecies allometric scaling can be demonstrated by using two approaches:

a. Physiological-based models

b. An empirical allometric method. Physiological models provide a mechanistic-based prediction of drug disposition.

Above models require size of the organ, blood flow rates, blood to tissue partitioning and metabolic and chemical reaction rates. Plasma protein binding, enzymatic kinetic parameters and in vitro and in vivo clearance data may also be combined to predict in a physiologically-based prediction. These ideas have been used by many researchers [8-11] to predict the kinetic behavior of drugs. Physiological based models have limited use in drug discovery and development because it is costly, time consuming and complexity in calculating.

To perform allometric scaling and to predict pharmacokinetic parameters in humans at least three animal species are generally required. It is postulated that the more the number of animals, greater the chances of precise predictions of pharmacokinetic parameters. However, allometric scaling for more species are time consuming and costly [3]. Earlier, some of the researchers used less than two species to predict pharmacokinetic parameters in humans.

To develop a potential clinical compound, accurate pharmacokinetic and toxicokinetic studies are conducted initially in laboratory animals for example. Mice, rats, etc. With the help of initial data it is easier to screen the potential therapeutic clinical compounds in the process of drug discovery and development. This extrapolation of data, described as interspecies allometric scaling, may be helpful in the prediction of a suitable dose for first-time administration to humans.

The main objective of allometric scaling is to predict a safe and effective dose for the first to human for first time dose administration. Recently, allometric scaling of pharmacokinetic parameters has drawn tremendous responsiveness to predict human pharmacokinetic parameters and lot of suggestions were given to improve the predictive performance of allometric scaling. Allometry, which is the oldest of the approaches and still widely applied in biology, is concerned with the study of the relationship between the size and function of components of the body and growth or size of the whole body. This short communication gives a brief idea about the prediction of pharmacokinetic parameters from animal data to predict human pharmacokinetic parameters in amid of wide variety of physiological and anatomical differences. Though the approaches are not perfect, but draw prominence to apprehend and fine tune the concept of allometric scaling.

References

1. Boxenbaum H (1984) Interspecies pharmacokinetic scaling and the evolutionary-comparative paradigm. Drug Metab Rev 15(5-6): 1071-1121.

2. Sarrus PF, Rameaux JF (1839) Rapport surun memoire addressee l'Academieroyale de Medecine, Bull. Acad R Med Paris, pp. 1094-1100.

3. Mahmood I (2007) Application of allometric principles for the prediction of pharmacokinetics in human and veterinary drug development. Adv Drug Deliv Rev 59(11): 1177-1192.

4. Mahmood I, Balian JD (1999) The pharmacokinetic principles behind scaling from preclinical results to phase I protocols. Clinical Pharmacokinetics 36(1): 1-11.

5. Mordenti J (1986) Man versus beast: Pharmacokinetic scaling in mammals. J Pharm Sci 75(11): 1028-1040.

6. Durk MR, Pang KS (2010) Physiologically based pharmacokinetic modeling for absorption, transport, metabolism and excretion. J Pharmacokinet Pharmacodyn 37(6): 591-615.

7. Bischoff KB (1975) Some fundamental considerations of the applications of pharmacokinetics to cancer chemotherapy. Cancer Chemother Rep 59(4): 777-793.

8. Sugita O, Sawada Y, Sugiyama Y, Iga T, Hanano M (1982) Physiologically based pharmacokinetics of drug-drug interaction: A study of tolbutamide-sulfonamide interaction in rats. J Pharmacokinet Biopharm 10(3): 297-316.

9. Lin JH, Sugiyama Y, Awazu S, Hanano M (1982) Physiological pharmacokinetics of ethoxybenzamide based on biochemical data obtained in vitro as well as on physiological data. J Pharmacokinet Biopharm 10(6): 649-661.

10. Farris FF, King FG, Dedrick RL, Litterst CL (1985) Physiological model for the pharmacokinetics of cis-dichlorodiammineplatinum (II) (DDP) in the tumored rat. J Pharmacokinet Biopharm 13(1): 13-39.

11. Rowland M, Robert LD (2012) Principles of Clinical Pharmacology. (3rd edn), (32): 531-540.