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NUMERICAL SIMULATION ON-TIME EVALUATION OF PLASMA DRUG CONCENTRATIONS FOR ONE-COMPARTMENT MODEL IN PRESENCE OF DRUG INFUSION

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Abstract

In the present numerical study, we apply an ODE IVP to plasma drug concentrations for a one-compartment model in presence of drug infusion. The solution procedure is done in a Matlab environment. The outcome shows that the infusion rate at time t = 4 h is discontinuous but the corresponding plasma concentration-time profile looks smooth at that time.

Keywords: Drug Infusion, Pharmacologic Modeling (PK), Plasma Drug concentration, Matlab, Simulation.

I. Introduction

The fields of pharmacokinetics (PK) and pharmacodynamics (PD) are covered by pharmacologic modelling (PD). PK refers to "what the body does to a drug," that is, how it is absorbed, distributed, and removed, whereas PD refers to "what a drug does to the body," that is, how it interacts with receptors and associated signalling pathways up to the whole body level. Modelling outcomes is based on the time course of medication concentrations and effects.

PK employs compartmental models either empirically to gain a good fit to experimental data or physiologically to develop cross-species predictive models (physiologically-based PK, or PBPK). PD models use direct and/or indirect response mechanisms to convert drug concentrations at the pharmacologic site of action, or biophase, into biological effects. PK-PD models, when combined, are a powerful tool.

In the most frequent cause of first-order kinetics, when a drug is infused intravenously at a constant rate, a plateau concentration will be reached progressively [VIII]. There is no medicine in the body when the infusion begins, thus there is no excretion. The amount of drug in the body grows, yet the rate of removal decreases as the drug concentration rises. As a result, the rate of elimination will continue to

increase until it catches up to the rate of infusion. The amount of drug in the body then remains constant, indicating that it has achieved a steady-state or plateau. The factors affecting the steady-state plasma drug concentration are (i) Infusion rate (r): The steady-state drug concentration is proportional to the infusion rate. As a result, a faster infusion rate means a greater steady-state plasma drug concentration. (ii) Clearance (CL): A medication with a higher clearance will have a lower plasma drug concentration at a plateau. The drug's elimination half-life, which is governed by clearance and volume, determines how long it takes to reach the plateau. As a result, the volumetric effect only affects the time it takes to reach the plateau, not the steady-state concentration. The drug plasma concentration is 93.75 percent of the steady-state plasma concentration after four elimination half-lives. Similarly, when changing infusion rates, the time it takes to reach a new steady state is determined by the drug's half-life [III]. The decrease in plasma drug concentration when an infusion is stopped follows an exponential curve. The constant rate infusion method is used to ensure that the medicine is exposed to the patient at the same rate over an extended period. For the concentration to achieve a therapeutic target, the drug infusion rate must be adjusted to the patient's clearance.

The current investigation considers the differential equation for drug plasma concentration considering a one-compartment model in presence of drug infusion [V, VI].

The paper is prepared as follows: in Section II, we elucidate the model. We perform simulation, i.e., align the model to the plasma drug concentrations for a one-compartment model with drug infusion in Section III and IV to examine the outcomes. We finally close the study in Section V.

II. Mathematical Model & Materials

The model is the following differential equation [IV, VII]

$$\frac{dc}{dt} = \frac{r(t)}{V} - c\frac{CL}{V} \tag{1}$$

with

$$r(t) = \frac{Dose}{t_R}, \qquad for\ 0 \le t \le t_R$$

$$= 0, \qquad for\ t_R > t_R \tag{2}$$

and

$$c(0) = 0 \tag{3}$$

where

c: plasma drug concentrations (mg/L),

t: time (hr),

r: drug infusion rate (mg/hr),

V: volume of distribution (L),

CL: clearance of drug (L/hr),

Dose: given dose (mg),

t_R: infusion time (hr).

Equations (1)–(3) constitute an ODE IVP including the infusion rate (r) as a forcing function, which is a part of PK models to describe drug input [II].

III. Simulations

Matlab routine ode45 [I] is used to solve the equations (1-3). We perform the simulation for the following particular case:

Table 1. Data for simulation

Parameter	value
V	25.2 L
CL	4.32 L/hr
Dose	400 mg
t_R	4 hr

The results are shown in Fig. 1 for time evaluation of plasma concentration along with drug infusion input.

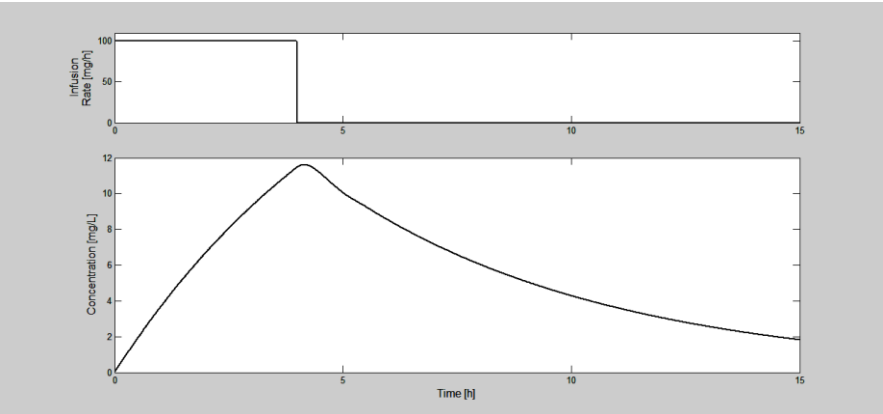

Fig. 1. Time variation of plasma concentration along with drug infusion input.

IV. Discussions

Time evaluation of plasma concentrations for a one-compartment model with drug infusion input is shown in Fig 1. For better visualization of the model, the infusion rate is added as the upper graph and the lower graph illustrates the time course of plasma concentrations for the time interval [0, 15 hr]. Astonishingly, the infusion rate is discontinuous at time t = 4 h, but the variation of plasma concentration is smooth there.

V. Conclusions

In the present numerical study, we take up an ODE IVP and apply it to plasma drug concentrations for a one-compartment model in presence of drug infusion. Matlab ode45 is employed for the solution. Results show that the infusion rate at time t = 4 h is discontinuous but the corresponding plasma concentration-time profile looks smooth at that point.

Transparency Declaration

The authors declare that no conflict of interest to report the present study.

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