PHARMACO-KINETIC PREDICTION OF THE DRUG DISTRIBUTION PROFILE IN A HUMAN PHYSIOLOGICAL SYSTEM

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ABSTRACT
Drugs are medicinal substances that are administered mostly orally and then metabolized in the gastro-intestinal tract (G.I.T) and subsequently assimilated in the blood stream. The paper highlights computerized solutions of a simplified mathematical model that adequately simulates the drug distribution profile in a human physiological process. The result shows the mechanism or the process of absorption in the blood vessels X(t) and the initial build up in the G.I.T and predicts that the ingested drug concentration reduces exponentially in the G.I.T due to metabolic action and then starts from an infinitesimal amount in the blood stream and increases to a threshold value as it is being distributed to various parts of the human body.

Keywords: Sublingual Pack, Oesopharynx, Gastro-intestinal Tract, Transdermal, Vena Cava, Villi.

1.0 INTRODUCTION

Drugs are chemical substances that interact with living system through chemical process by binding the regulatory molecules and then activating or inhibiting normal body process. These substances are normally administered to achieve a beneficial therapeutic effect on some process within an individual or for their toxic effects on regulatory processes in Parasites infecting a patient. Such deliberate therapeutic application may be considered a proper role of the medical pharmacology which often is defined as the science of substances designed to prevent, diagnose and treat disease and ailments. In practice drugs used in clinical settings are formulated in a variety of ways to suit the route of administration as well as other pharmacokinetic variables of the particular drug (Bernet et al, 1990).

The popular route of oral drug administration is apparently the commonest and most convenient means used in therapeutic medicine. Examples include parenteral, suppositories, transdemal, intrathecal, inhalational, tropical (Rubino et al, 2000). The Gastro-Intestinal tract of a man has large surface area that start from the mouth and oesopharnx and terminates in the anus. This G.I.T endowed with a rich supply of blood vessels and capillaries especially the Vill, of the smaller lower abdomen that enable extensive absorption of drugs taken by oral route (Koloduy et al, 1974) has shown that the sublingual packs are retained in the buccal cavity where they are absorbed by tributaries (Iingual veins) of the internal jugular vein that finally empties into the superior vena cava that rains into the right heart (Mendelson et al, 1974). Hence sublingual tablets are rapidly distributed throughout the body. The volume of distribution is a pharmaco-kinetically important factor that determines drug concentration in the blood or plasma and is in turn affected by drug clearance, drug half- life, blood flow, drug bioavailability, drug metabolism all of which are important pharmaco-kinetic parameters (Schaefer et al, 1975).

2.0 MATERIALS AND METHOD OF SIMULATION/ANALYSIS

The pharmaco-kinetic model for the drug delivery in a man's physiological system was derived considering the material balance equation for the two important compartments Fig. 2.0 (G.I.T) and blood stream as:

(Compartment One) $\frac{dx_1}{at} = r - k_1x_1$ (1)

(Compartment Two) $\frac{dx_2}{at} = k_1x_1 - k_2x_2$ (2)

Combining (1) and (2) we obtain

$\frac{d^2x_2}{dt^2}$ + (K_1 + K_2) $\frac{dx_2}{at} + k_1k_2x_2 = r$ (3)

Let r = $Re^{-\propto t}$ (4)

The solution to equation (1) and (2) respectively become

$X_1 = \frac{R}{K_1 - \propto}[e^{-\propto t} - e^{k_1t}]$ (5)

$X_2 = \frac{K_1R}{(\propto - k_1)(\propto - k_2)(k_1 - k_2)}[(k_1 - k_2)e^{-\propto t} + (\propto - k_1)e^{-k_2t} - (\propto - k_2)e^{-k_1t}]$ (6)

The initial conditions include $X_1(0)$ = 1mg, $X_2(0)$ = 0 and $X_2^1(0)$ = where

X(t) = mass of drug in the GIT; $X_2(t)$ = mass of drug in the blood stream, r=rate of drug delivery (mg/Sec), R = Initial rate, mg/sec, $\propto$ = characteristic Constant (min^{-1}) for the Patient, t = time (hour).

3.0 RESULTS AND DISCUSSION

After the drug ingestion into the body through the various routes it got to the blood stream through which it reached its target organs and tissues. The result showed that the drug concentration depletes in the G.I.T as metabolic action takes place while it accumulates gradually until it reached a threshold in the blood stream before assimilation and distribution took place necessitating the down ward trend figure 1 for $X_1(t)$ and $X_2(t)$. the increased value of $X_2(t)$ at the early stage is the absorption process into the blood stream and then the subsequent decrement due to delivery to target organs and tissues as clinical response begin to manifest either beneficially or otherwise. The algorithm for computing $X_1(t)$, $X_2(t)$ is shown figure 4 while the block diagrams for the control of body temperature, Pressure and blood sugar level is given figure 3 and figure 5 respectively. Pharmacokinetic variables characterizing a healthy individual include body temperature 36^{oC} (normal) 38^{oC} (high); Blood glucose level 72-99mg/dl (normal), 140mg/dl and above (high). The blood pressure $\frac{120}{80}$, mmHg up to $\frac{129}{85}$ mmHg is normal while $\frac{140}{90}$ mmHg is high. The top number is the Systolic which measure the force the heart exerts on the wall of the arteries each time it beats while the bottom number is the Diastolic which measures the force the heart exerts on the wall of the arteries in between beats. The normal resting heart rate for adults ranges from 60 to 100 beats per minute. A lower heart resting rate implies more efficient heart function and better cardiovascular fitness. MATLAB Program was written for equations (1) and (2) implementable on an XP 500 series HP laptop HP laptop and used to generate the profiles presented in figure 1.

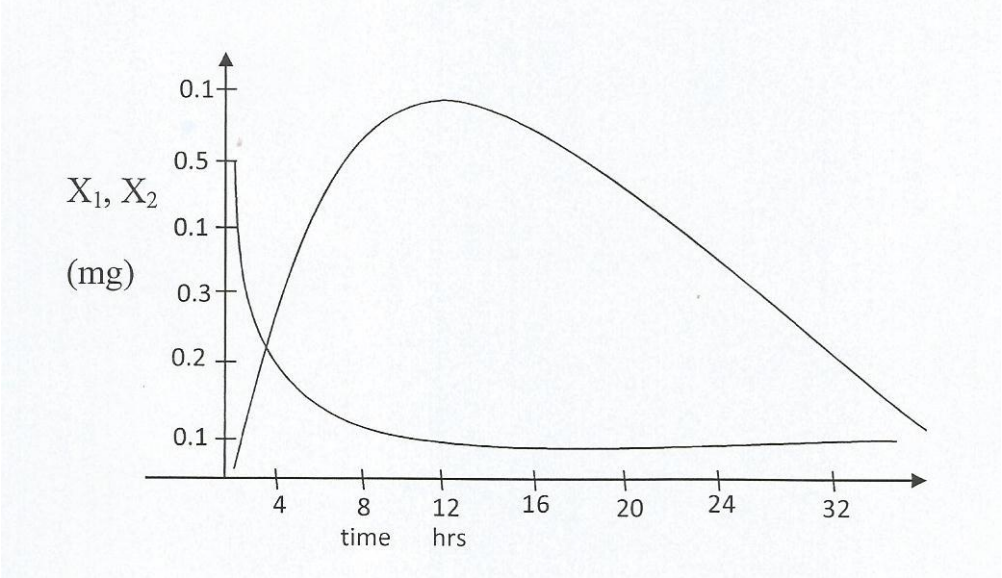

Figure 1: X_1, X_2 Vs time

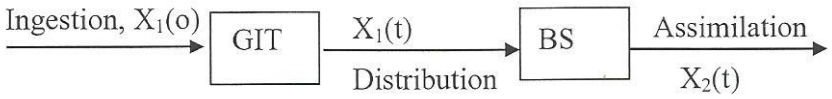

Figure 2: Two Compartment Process

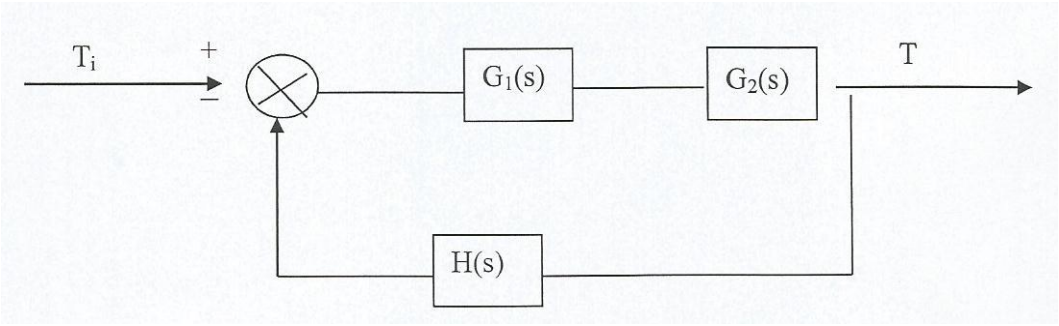

Figure 3: Block diagram for the Clinical Control of Body Temperature

T_i = normal body temperature
T = measured body temperature
G_1 = Transfer foundation for the G.I.T
G_2 = Transfer function for the blood stream
H(s) = Transfer function for a measuring element (clinical Thermometer)

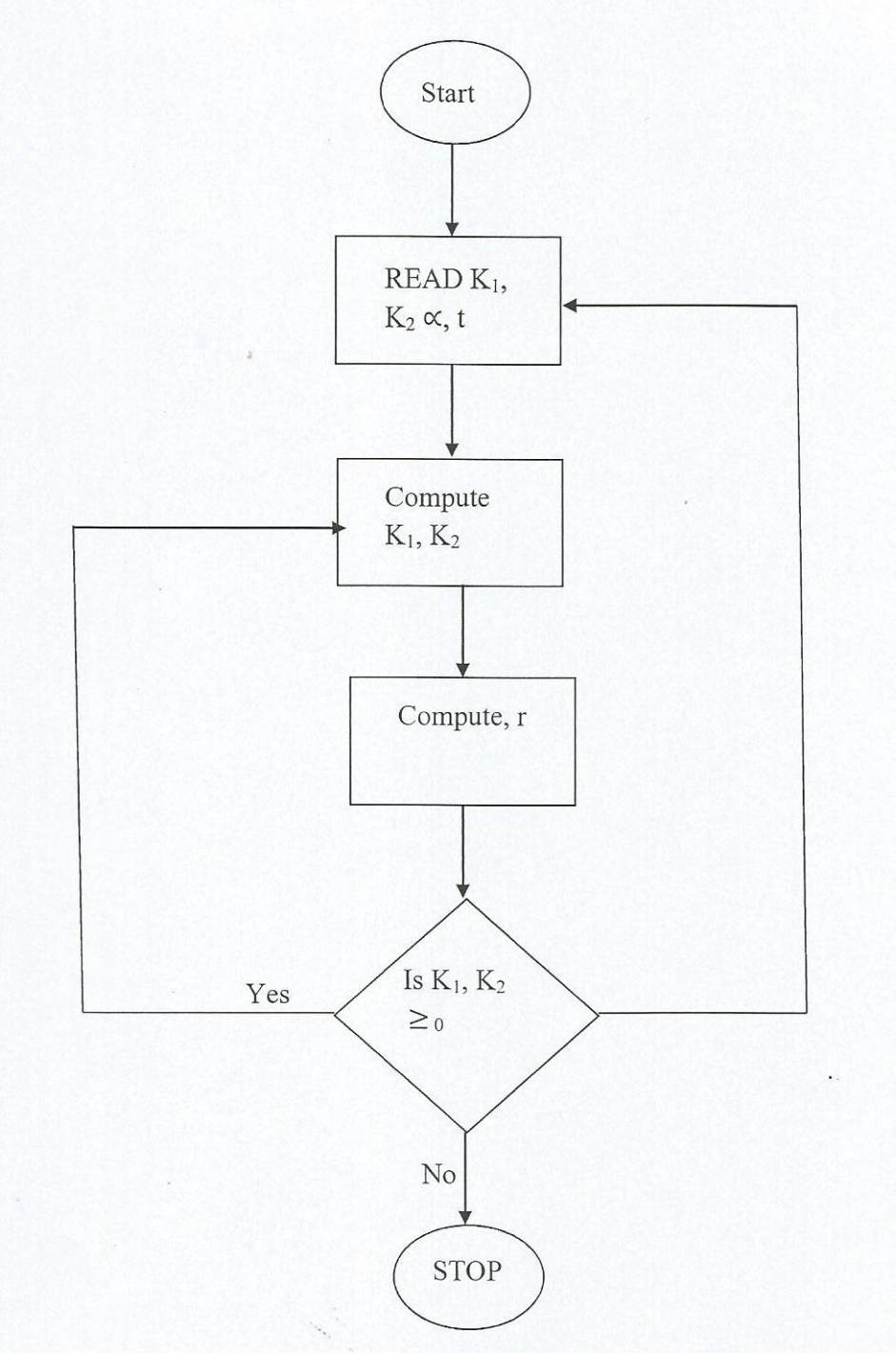

Figure 4: Algorithm for Computing X_1, X_2, r

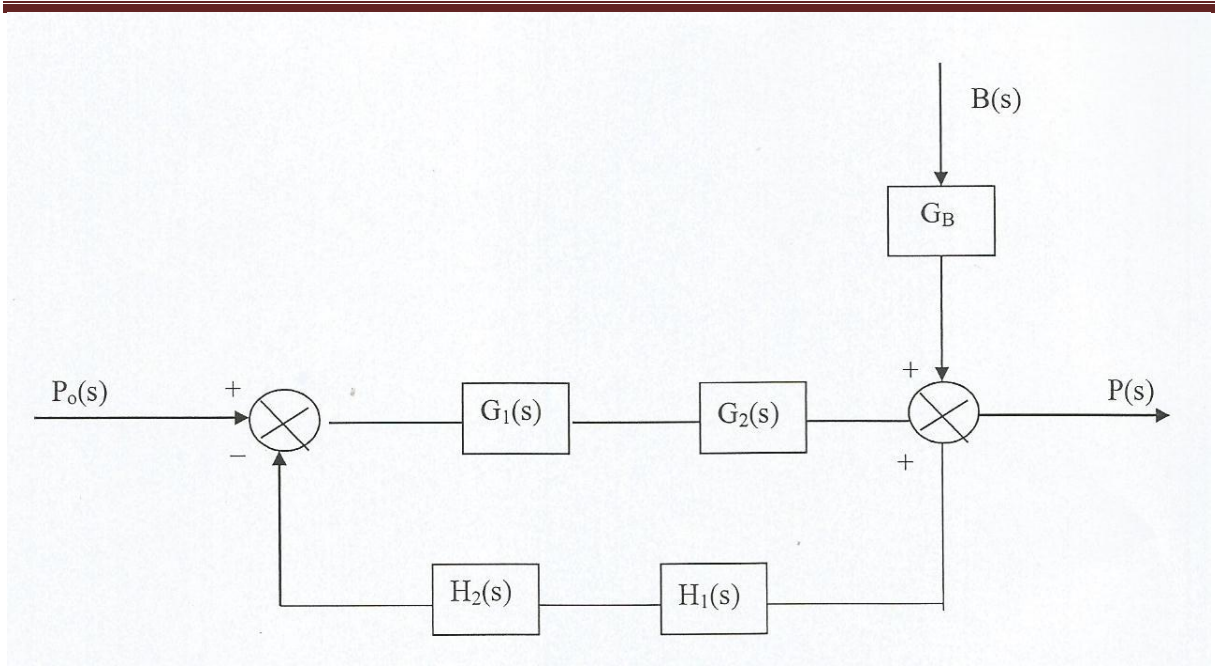

Figure 5: Block Diagram for the Control of Body Blood Pressure and Sugar Level

$G_B(s)$ = Transfer function for the Vanae Cavae
B(s) = Body blood sugar concentration, mg/l
$H_1(s)$ = Transfer function for the measuring element (blood pressure monitor)
$H_2(s)$ = Transfer function for the measuring device (blood sugar meter)

CONCLUSION

The dose, frequency of administration required to achieve effective therapeutic blood and tissue levels and effects vary in different individuals or patients because of individual differences in drug distribution and rates of metabolism and assimilation. The differences are determined by genetic factors and non-genetic variables such as age, sex, liver size, liver function, body rhythm, body temperature, nutritional and environmental factors. These variables are taken into consideration in obtaining values for K_1 and K_2 as well as $\propto$ the pharmaco-kinetic parameters. This highlights the application of chemical engineering principles in the medical field.

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