RESEARCH PAPER

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Computer aided analysis of *in vitro* release data of a Sustained release Product

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Isoniazid microcapsules were prepared using ethylcellulose as coating polymer and by phase-separation and coacervation process involving non-solvent addition. *In vitro* dissolution was done and the release data were analysed by computer for different kinetic equations e.g. zero order, first order, square root, cube root, binomial equation, weibull equation and logarithmic ligistic plots. Statistical parameters such as sum of deviation, sum of square deviation and standard error of estimates in each case were determined and compared.

THE main aim in designing a sustained release preparation is to deliver the drug at desired and predetermined rate. Hence it is essential to study selected release patterns of drug from the sustained release products and their thorough statistical analysis.

MATERIALS AND METHODS

Isoniazid, I.P., Ethylcellulose GR (viscosity of a 5% w/w solution in 80:20 toluene : ethanol by weight at 25° approximately 14 cp, BDH) polyisobutylene (mol. wt. 380, 000, density 0.918 g/ml), Toluene AR (Sarabhai M Chemical, India), Petroleum Ether (60° - 80°, E. Merck) were used.

1. Preparation of Microcapsules

Ethylcellulose was dissolved in toluence, polyisolutylene (PIB) was added in different amounts to improve the yields and surface characteristics of microcapasules. Dry isoniazid powder was added in the mixture with continuous stirring. Petroleum ether was added slowly. When microcapsules have just formed the whole system was chilled by application of ice on the outside of the beaker and chilled pet-ether was further added to harden the microcapsules which were then filtered and dried in air. Reproducible batches were prepared with core and coat ratios 1:1 and 1:2.

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2. *In vitro* Dissolution study

In vitro drug release from microcapsules were studied in USP-XX basket type Dissolution Test Apparatus. About 900 ml glass distilled water was taken as dissolution medium. The basket was covered with a # 100 mesh nylon screen. The instrument was adjusted at 37° ± 0.1° and rotated with 100 rpm (±2%). Samples were withdrawn from dissolution medium at different time intervals and drug was assayed in Hitachi UV spectrophotometer at 266 nm.

3. Statistical Analysis of *in vitro* dissolution data in Computer

A programme has been developed in BASIC language (Chart-1) to calculate the desired parameters such as sum of deviations (SDEV), sum of square deviations (SDEVSQ), Standard Error of

Estimates (SERR), Correlation coefficients and rate constants. In each case, two tests of data one is experimental and the other is theoretical according to a particular equation used, are compared to determine these parameters. The following regression equations have been used to develop the programme in BASIC.

1. *Zero Order Kinetics:*

$M = Ko.t+A$ M = Mass of drug release at time t,
Ko = Zero order release rate constant
A = t_0, i.e. lag time.

2. *First Order Kinetics :*

$\ln \frac{Ma}{Ma-M} = K1\ (t-to)$ Mα = total mass dissolved at finite time
K_1 = First order dissolution rate const.

3. *Square Root equation (Higuchi Model) :*

$M = Ks \sqrt{t-to}$ Ks = Square root dissolution rate const.

4. *Cube Root Equation :*

$M = M\alpha\ [M\alpha^{1/3} - Kc\ (t-to)]^3$ Kc = cube root dissolution rate const.

5. *Weibull Function :*

Log [-ln (1-M/Mα)] = b.log(t-to)-Loga
a = Scale parameter b = Shape parameter,

6. *Bionomial Equation :*

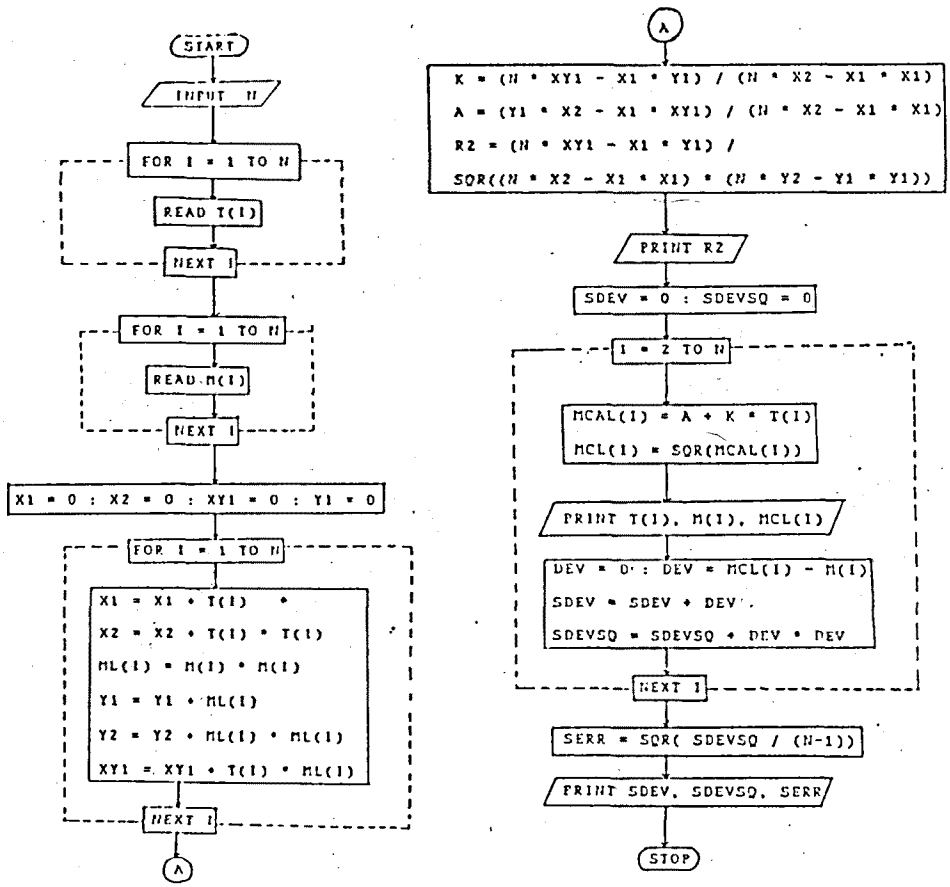

CHART - I : Computer program in BASIC for square root equation (Higuchi Model) of drug release as a model for kinetic equation and for calculation for correlation-coefficient, sum of Deviation (SDEV), sum of Square Deviation (SDEVSQ), Standard Error of Estimate (SERR)

Isoniazid : Ethylcellulose = 1:2, PIB conc. 9% w/w

Kinetic Equations	SDEV	SDEVSQ	SERR	COREL-CO-EFF
Zero order kinetics	-3.738E-04	10588.99	29.70549	0.999845
First order kinetics	-347.229	91492.21	87.31752	0.947769
Square Root Equation	66.83115	5015.906	22.39622	0.99086
Cube Root Equation	-43.69608	54920.67	67.65148	0.99989
Logarithmic Ligistic Equation	-91.04809	3449.823	16.95539	0.982071
Binomial Equation	6.39343E-03	698.192	7.627758	0.999989
Weibull Equation	100.4657	5754.529	25.2862	0.945566

$M = A+B.t+c.t^2$ A, B, C. are constant

7. Logarithmic Logistic Plots :

$$\ln \frac{M}{1-M} = a + Bt \quad a, B \text{ are contants}$$

RESULTS AND DISCUSSION

It is found from the above table that the higher degree of correlation was obtained with the Hixoncrowell, cube root, binomial, logarithmic logistic and zero order kinetics. The cube root equation was considered suitable since the surface area of the core material decreases, the shape of the core appeared to be remained unchanged and sink conditions were maintained during the entire release process. From the weibull distribution data, the shape parameter with lesser than unity showed dissolution curve with steeper initial slope than consistent and with the higher than unity shows dissolution curves having upward curvature following a smooth turning point. In the similar way the binomial and zero-order equations are also significant.

In conclusion, the principal advantage is that each set of data can be reduced to a simple linear equation which replaces the usual plot of percent drug release Vs. time. The instanttaneous rate of release of drug at any time during the test can be determined on a sound mathematical basis. Interpolation values can also be readily calculated rather than relying on graphical determination of such values drawn through a series of points by visual observation only.

From the above view points it can further be concluded that the higher degree of good fitting can be obtained from different kinetic models and the required parameters can be easily calculated based on whether a successful and promising sustained release drug delivery system can be designed and developed.

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