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Review Article

Kinetic modeling and comparison of invitro dissolution profiles

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ABSTRACT

This review describes that the quantitative analysis of the values obtained in dissolution release tests are easier when mathematical formulas that express the dissolution results as a function of some of the dosage forms characteristics are used. From the theoretical analysis of the occurring process, these mathematic models are derived. In most of the cases the theoretical concept does not exist and some empirical equations have proved to be more appropriate. The dissolved amount of drug is a function of the test time when drug release from solid dosage forms has been described by kinetic models. Some commonly used analytical definitions of the functions are zero order, first order, Hixson–Crowell,Weibull, Higuchi, Baker–Lonsdale, Korsmeyer–Peppas and Hopfenberg models. Other release parameters, such as dissolution time, assay time, dissolution efficacy, difference factor (f1) and similarity factor (f2)can be used to characterize drug release profiles.

Key words: Dissolution, drug release kinetic models, model dependent method, model independent method, statistical model.

INTRODUCTION

After oral administration, Drug absorption from solid dosage forms is based on the release of the drug substance from the prepared drug product by using an active and inactive ingredientsand also based on the dissolution or solubilisation of the drug under physiological conditions, and the permeability across the GI (Gastro Intestinal) membrane. Due to this reason there is a need of an in vivo performance.[1, 2]In the drug bioavailability, dissolution is the rate limiting step. In the development of sustained release product, it is necessary that in-vitro release maintained in physiologic condition. The release patterns can be divided into those that release drug at a slow zero or first order rate and those that provide an initialrapid dose, followed by slow zero or first orderrelease of sustained component. To achieve plasma concentration of the drug inhumans in the development of sustained-release dosage forms is a main goal. Thedevelopment process can be accelerated andproducts introduced more rapidly than if suchpredictions are unavailable by achieving this goal.[3, 4, 5]The dissolution method and designs are set by considering the solubility, permeability,dissolution, and pharmacokinetics of the drugsubstance. The method for the comparison of invitro dissolution profile can be categorised into three categories.

1. ANOVA (Analysis of Variance) based model
2. Model dependent based approach
3. Model independent based approach.

ANOVA based method is not rely on the curve fitting procedures and also the dissolution data which are used in their native form. The analysis of this model is to show the difference in profiles of level and shape. A model-independent method uses the dissolution data in their native form. The model-dependent methods, however, are based on different mathematical functions, which describe the dissolution profile. Once a suitable function has been selected, the dissolution profiles are evaluated depending on the derived model parameters.

NEED OF MATHEMATICAL MODELLING

Several methods are specify to elucidate dissolution data as a function of time, but its dependence on dosage form characteristics can best be abstracted by using generic equationswhich mathematically interprets the dissolution curves in

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the function of other constraints related to delivery device. Kinetics of drug release can be determined by the use of such mathematical models. The quantitative analysis of the values obtained in dissolution study is easier when mathematical principles are used to describe the process. The mathematical modeling significantly accelerates the optimizationthe design of an existing and new deliverydevice to yield information on the efficiencyof various release models.

FACTORS INFLUENCING CHOICE OF MODEL

The choice of mathematical model is highly depend upon the class of drug (Class I, II, III, and IV), nature of excipients are used in the formulation, concentration of active ingredient and inactive ingredients used and also on the geometry of the delivery device.[3]

Several theories and kinetics models have been used for above mentioned factors to describe drugdissolution from conventional as well asmodified release dosage forms. Based on thesetheories, there are different models to representthe drug dissolution profiles, described below,where *f is* a function of *t* (time) related to theamount of drug dissolved from the pharmaceutical dosage forms.

Noyes-Whitney rule: Forestimation of thekinetics of drug release is a vital principle and it was offered by Noyes andWhitney in 1897 as the equation

dM/dt = KS (Cs - Ct)……..Eq.1

Where,

dM/dt = the rate of dissolution

S = surface area of the solid,

Ct = concentration of the solid in the bulkdissolution medium,

Cs= concentration of the solid in the diffusionlayer surrounding the solid,

K = diffusion coefficient,

L = diffusion layer thickness

The rate of dissolution dM/dt is the amount dissolvedper unit area per unit time and for most solids can beexpressed in units of $g \times cm^{-2} \times s^{-1}$. On the dissolutionrate of the solid, Ct has a negligible influence, when Ct is less than 15% of the saturated solubilityCs. Under such conditions,the dissolution of the solid is said to be occurringunder 'sink' conditions.[4]

Nernst and Brunner Film Theory: By using Fick's law ofdiffusion Brunner and Nernst used to establish a relationship between the constantin the equation (1) and the diffusion coefficientof the solute, as the equation:

K = DS/ hγ…….Eq.2

Where,

D = diffusion coefficient,

S = the area ofdissolving surface or area of the diffusion layer,

γ = the solution volume and

h = the diffusion layerthickness.

In formulating their theories, Nernst andBrunner assumed that thetransport processproceedsmuch slower than at the surface and thata linear concentration gradient is confined to thelayer of solution adhering to solid surface.Asthe actual surface is changed permanently with theprogress of dissolution processes during the usualdetermination of drug release,the ideal condition can never be achieved. In the Noyes- Whitney equation, the dissolution process correspondsto a first order reaction.[6, 7]

RELEASE KINETIC MODEL

To describe the overall release of drug from the dosageforms the number of kinetic models are available. Becausein a formulation qualitative and quantitative changesmay alter drug release and in vivoperformance. Productdevelopment by reducing the necessity of bio-studiesis always desirable when developing tools are used. The methods of approach to investigate thekinetics of drug release from sustained release formulation can be classified into three categories.

STATISTICAL METHODS

1. Exploratory dataanalysis method,

2.Repeated measuresdesign,

3. Multivariateapproach [MANOVA: Multivariate Analysis Of Variance][8, 9]

MODEL DEPENDENT METHODS

1.Zero order,

2. First order,

3. Higuchi,

4. Korsmeyer-Peppasmodel,

5. HixsonCrowell,

6. Baker-Lonsdalemodel,

7. Weibull model

8. Hopfenberg model

9. Gompertz model[13, 15]

MODEL INDEPENDENT METHODS

1. Ratio factors

2. Fit factors

- ✓ Similarity factor
- ✓ Difference factor
- ✓ Resign index[13 ,16]

Another method of classification:-

A.Empirical and semi empirical models(Higuchi, Peppas and Sahlin, Power law),

B.Mechanistic and empirical.

STATISTICAL METHODS

Exploratory Data Analysis methods: By the FDA exploratory data analysis methodsare not currently endorsed. For the improvement and understanding ofthe dissolution data of sustained release formulation, the methodis useful and therefore, its use is recommended. In the first step to compare dissolutionprofile data in both graphical and numericalmanner, thismethod can be used. By plotting the mean dissolution profiledata for each formulation with error bars extendingto two standard errors at each dissolution time point, the dissolution profile data are illustratedgraphically.95% confidence intervalsfor the differences in the mean dissolution profiles at each dissolution time point are evaluated and the data of the dissolution profiles are summarized numerically.

Multivariate approach (MANOVA): These methods were based upon repeatedmeasures designs where time is the repeated factorand percent dissolved is the dependent variable. Forstatistical methods, SPSS(**Statistical Product and Service Solutions)** 10.0 for Windows wasemployed. The calculated statistics of this methodwere, Pillai's Trace, Wilks' Lambda, Hotelling'sTrace, and Roy's Largest Root. Since the data were collectedas repeated measurements over time on thesame experimental unit, a repeated measures designwas applied. When compared to Student's "*t*-"andpaired "*t*-" tests, the major advantage of this designis increased precision.In repeated measures, ANOVA containingrepeated measures factors with more than two levels,additional special assumptions enter the picture:These are compound symmetry assumption and theassumption of spherocity. Because these assumptionsrarely hold, the MANOVA approach to repeated measures ANOVA has gained popularity in recent years. The compound symmetry assumptionrequires that the variances and covariances of thedifferent repeated measures are homogeneous. Thisis a sufficient condition for the univariate "F" testfor repeated measures to be valid. The spherocityassumption is a necessary and sufficient conditionfor the F test to be valid. When the compound symmetryor spherocity assumptions have been violated,the univariate ANOVA table will give erroneous results. Mauchly's test of spherocity results are usedfor the assumption of spherocity.[21]

MODEL DEPENDENT METHODS

On differentmathematical functions model dependent methods are established, which describe the dissolutionprofile. After the appropriate function designation, the dissolution profiles are estimateddepending on the derived model constraints. To determine the suitable drug release kinetic model, the nonlinearregression module of Statistica 5.0 was used. Quasi-Newtonand Simplex methods minimized the least squaresin non-linear regression analysis. The model dependent approaches includedzero order, first order, Higuchi, Hixson-Crowell,Korsmeyer-Peppas, Baker-Lonsdale, Weibull, Hopfenberg,Gompertz, Non-conventional order 1, Non-conventional order 2, Reciprocal powered time and regression models.

1. Zero-order model

From dosage forms drug dissolution that do notdisaggregate and release the drug slowly can be representedby the equation:

$$\mathbf{Q_0 - Q_t = K_0 t} \quad \text{.....Eq. 3}$$

Rearrangement of equation (3) yields:

$$\mathbf{Q_t = Q_0 + K_0 t} \quad \text{.....Eq.4}$$

Where,

Q_t =the amount of drug dissolved in time *t*,

Q_0 = the initial amount of drug in the solution (mosttimes, $Q_0 = 0$) and K_0 is the zero order release constantexpressed in units of concentration/time.

Plot: Data obtainedfrom in vitrodrug release studies were plotted ascumulative amount of drug released versustime, to study the release kinetics.

Application: Todescribe the drug dissolution of several types ofmodified release pharmaceutical dosage forms, some transdermal systems and in the matrix tablets with low soluble drugs in coatedforms, osmotic systems, etc. this model is generally used.[15]

2. First order model

To describeabsorption and elimination of some drugs, this model has been used. The release of the drugwhich followed first order kinetics can be expressedby the equation:

$$\boldsymbol{dC/dt = -KC} \quad \text{.....Eq. 5}$$

Where ***K***is first order rate constant expressed inunits of time^{-1}.

Equation (5) can be expressed as:

$$\mathbf{\log C = \log C_0 - Kt / 2.303} \quad \text{.....Eq. 6}$$

Where C_0= the initial concentration of drug, k = thefirst order rate constant, and t = time.

Plot:log cumulative percentageof drug remaining *vs.* time which would yield a straight line with a slope of **-K/2.303.**

Application: For dissolution of pharmaceuticaldosage forms such as those containing water-solubledrugs in porous matrices, this model has been used.[19]

3. Higuchi model

To describe drug release from a matrix systemwas proposed by Higuchi in 1961 was the first example of a mathematical model. Initially it wasconsidered for planar systems, then it wasextendedto porous systems and different geometrics.This model is based on the hypotheses that (i) in the matrix, initialdrug concentration is much higher thandrug solubility; (ii) onlyin one dimension (edge effect must be negligible), drug diffusion takes place;(iii) system thickness is grater then the drug particles; (iv) dissolution and matrix swelling arenegligible; (v) drug diffusivity is constant; and (vi)in the release environment, perfect sink conditions are always attained. Accordingly, model expressionis given by the equation:

$$f_t = Q = A\sqrt{D(2C - C_s)\,C_s\,t} \quad \text{Eq.7}$$

Where Q = the amount of drug released in time t perunit area A,

C = the drug initial concentration, *Cs* = the drug solubility in the matrix media and

D = thediffusivity of the drug molecules (diffusion coefficient)in the matrix substance.

Exceptwhen the total depletion of the drug, this relation is valid during all the time in the therapeuticsystem is achieved. Thedrug concentration in the matrix is lower than itssolubility and the release occurs through pores in thematrix, the expression is given by equation (8), to study the dissolution froma planar heterogeneous matrix system:

$$f_t = Q = \sqrt{\frac{D\delta}{\tau}(2C - \delta C_s)\,C_s\,t} \quad \text{Eq. 8}$$

Where D = the diffusion coefficient of the drug moleculein the solvent, δ = the porosity of the matrix,τ = the tortuisity of the matrix and Q, A, Cs and thave the meaning assigned above. Tortuisity is defined as the dimensions of radius and branching ofthe pores and canals in the matrix. In a general wayit is possible to simplify the Higuchi model as the simplified Higuchi model. [10]

$\mathbf{f_t = Q = K_H \times t^{1/2}}$……Eq. (9)

Where, K_H = the Higuchi dissolution constant.

Plot: Cumulative percentagedrug release versus square root of time.

Application: Todescribe dissolution of drug from several types ofmodified release pharmaceutical dosage forms, transdermal systems and matrixtablets with water soluble drugs this relationship can be used.

4. Korsmeyer – Peppas model

To find out the mechanism of drug release, first 60% drug release data were fitted in Korsmeyer Peppas model and the equation derived is as:

$\mathbf{M_t / M_\infty = Kt^n}$…….... (10)

WhereM_t / M_∞ = a fraction of drug released at time t, k = the release rate constant and n = the releaseexponent. The n value is used to characterize differentrelease for cylindrical shaped matrices.

For the case of cylindrical tablets, 0.45 ≤n correspondsto a Fickian diffusion mechanism, 0.45 < n <0.89 to non-Fickian transport, n = 0.89 to Case II(relaxation) transport, and n >0.89 to super case II transport. To find out the exponent of *n* theportion of the release curve, where M_t / M_∞< 0.6should only be used. [12]

Plot:log cumulative percentage drug release versuslog time, to study the release kinetics, data obtained from in vitro drug release studies were plotted.

5. Hixson Crowell

Hixson and Crowell (1931) suggest that the particles regular area is proportional to the cuberoot of its volume. They derived the equation:

$\mathbf{W_0^{1/3} - W_t^{1/3} = \kappa t}$…….. Eq. (11)

Where, $W_0$is = initial amount of drug in the pharmaceuticaldosage form,

W_t = remaining amountof drug in the pharmaceutical dosage form at time tand κ(kappa) is a constant incorporating the surface-volumerelation. The equation describes therelease from systems where there is a change in surfacearea and diameter of particles or tablets.

Plot: Cube root ofdrug percentage remaining in matrix versustime, tostudy the release kinetics, data obtained from in vitro drug release studies were plotted.

Application: This model is mainly applicable to that if the tablet dimensions diminish proportionally, where the dissolution occurs in planes that are parallel to thedrug surface,in such a manner that the initial geometricalform keeps constant all the time.[11]

6. Baker-Lonsdale model

From the Higuchi model, this model was developed by Baker andLonsdale (1974) anddescribed the drug release from spherical matricesaccording to the equation:

$$f_1 = \frac{3}{2}\left[1 - (1 - \frac{M_t}{M_\infty})^{2/3}\right] \frac{M_t}{M_\infty} = k_t \quad \text{.Eq. 12}$$

Where, the release rate constant, *k*, corresponds to the slope.

Plot: Data obtained from in vitrodrug release studies were plotted as[d (M_t / M_∞)] / dt with respect to the root of timeinverse, to study the release kinetics.

Application: Linearization of release data from several formulationsof microcapsules or microspheres, this model has been generally used.[13]

7. Weibull model

This model has been used for differentdissolution processes as the equation;

$$M = M_0\left[1 - e^{-\frac{(t-T)^b}{a}}\right]$$

…….Eq. 13

In this equation, Mis the amount of drug dissolvedas a function of time t. $M_0$is total amount of drug being released. Taccounts for the lag time measured as a result of the dissolution process. Parameter *a* denotes a scale parameter that describes the timedependence, while *b* describes the shape of the dissolutioncurve progression. For *b* = 1, the shape of thecurve corresponds exactly to the shape of an exponentialprofile with the constant *k = 1/a* (equation

$$\mathbf{M = M_0(1 - e^{-k\,(t\,-\,T)})}$$……..Eq. (14)

The shape of thecurve gets sigmoidal with a turning pointIf *b* has a higher value than 1,whereas if *b*haslower than 1 value then the shape of the curve wouldshow a steeper increase than the one with *b* = 1.

The time, when 50% (w/w) and 90% (w/w) ofdrug being in each formulation was released, wascalculated using the inverse function of the Weibullequation:

$$t_{(50\%\ resp.\ 90\%\ dissolved)} = (-\,a\ln\frac{M_0 - M}{M_0})^{1/b} + T$$

Eq. (15)

Application: For comparison of the release profiles of matrix type drug delivery this Weibull model is used.[14]

8. Hopfenberg model

To correlate the drug release from surface erodingpolymers so long as the surface area remains constantduring the degradation processHopfenberg has developed a mathematical model. Thecumulative fraction of drug released at time t wasdescribed as:

$$\mathbf{M_t / M_\infty = 1- [1- k_0 t / C_L a]^n}$$…….Eq. 16

Where k_0 = the zero order rate constant describingthe polymer degradation (surface erosion) process,C_L= the initial drug loading throughout the system, a = the system's half thickness (i.e. the radius for a sphere or cylinder), and n = an exponent that varieswith geometry n = 1, 2 and 3 for slab (flat), cylindricaland spherical geometry, respectively.

Application: To identify themechanism of release from the optimized oilispheresusing data derived from the composite profile,which essentially displayed site-specific biphasic release kineticsthis model is used.[15]

9. Gompertz model

By a simpler exponential model, the in vitro dissolution profile is oftendescribed known as Gompertz model, expressed by the equation:

$$\mathbf{X\,(t) = X_{max} exp\,[-\alpha e^{\beta log\,t}]}$$……..Eq. (17)

WhereX (t) = percent dissolved at time t divided by100; X_{max} = maximum dissolution; αdetermines theundissolved proportion at time t = 1 and described aslocation or scale parameter; β= dissolution rate perunit of time described as shape parameter. In the beginning thismodel has a steep increase and converges slowly to the asymptotic maximal dissolution.

Application: For comparison of the release profiles of drugs havinggood solubility and intermediate release rate, this model is widely used.[16, 17]

REGRESSION MODEL

For the formulation of many pharmaceutical dosage forms, statistical optimization designs have been previouslydocumented. [25]To optimize the formulation from in vitro release studyseveral types ofregression analysis are used. [26]

1. Linear or first order regression model. [27-29]

For determiningthe parameters of a linear system, linear regression is used. The empiricalmodel relating the response variable to the independentvariables are described by the followingequation:

$$\mathbf{Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2}$$.....Eq.(18)

Where Y represents the response, X_1 and X_2 representthe two independent variables. The parameterβ_0 signifies the intercept of the plane. β_1 and β_2,called partial regression coefficients, where β1measures the expected change in 'Y', the response,per unit change in X_1 when X_2 kept constant and viceversafor β2. The equation (18) can be rewritten in ageneral form as:

$$\mathbf{Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \ldots\ldots\ldots \beta_k X_k}$$……Eq. (19)

The model is a multiple linear regression model with 'k' regression variables. The modeldescribes a hyperplane in the k-dimensional space.

Further complex model (equation. 19) are often analysed by multiple linear regression technique byadding interaction terms to the first order linearmodel:

$$\mathbf{Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_{12} X_1}$$.....Eq.(20)

Where X_1 and X_2 are the interaction effects of twovariables acting simultaneously.

2. Quadratic model or second order regression model [30-32]

$$\mathbf{Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_{11} X_1^2 + \beta_{22} X_2^2 + \beta_{12} X_1 X_2}$$……Eq. 21

If we put, X_{21} = X3, $X_{22} = X_4$, $X_1 X_2$= X5 and $\beta_{11} = \beta_3$,$\beta_{22} = \beta_4$, $\beta_{12} = \beta_5$, then the above equation is

reducedto a linear model. Any model is linear if the (β) coefficients are linear, regardless of the shape of theresponse surface that it generates.

$$Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_3 X_3 + \beta_4 X_4 + \beta_5 X_5 \ldots\ldots\ldots\ldots \text{Eq.(22)}$$

The explanatory and response variables may bescalars of vectors. The resulting regression is called simple linear regression when both explanatory and response variables are scalars.The resulting regression is calledmultiple linear regressionwhen there are more than one explanatoryvariable. It should be noted that thegeneral formulae are the same for both cases. Therobust regression and least squares analysis aremostly used to solve linear regression models.

NON-LINEAR REGRESSION MODELS [33-34]

There are number of nonlinear regression techniques are used to obtain a more accurate regression.Due to the large number of dissolution media availablefor solid dosage forms, a statistical method tochoose the appropriate medium is critical for testingsolid dosage forms. It should be noted that an oftenused alternative is a transformation of the variablessuch that the relationship of the transformed variablesis again linear. The method was designedusing software to detect factors contributing to differencesin the dissolution process of the drug deliveredin dosage form.

1. Non- Convention Model 1

By the use of simple model known as nonconventional model 1, the in vitrodissolution profile can be described and expressed by the equation:

$$1-(1-F)^{1-n} = (1-n)\,k_{1-n}t \ldots\ldots \text{Eq. 23}$$

Where F is as fraction of drug released up to time t, k is parameter of model. On basis of non-linear regression, this model was calculated.

Application

For the determination of kinetics drug release from the nanoparticles,the non-conventional model 1 is useful.

2. Non- Convention Model 2

By the use another simple model known asnonconventional model 2, the in-vitrodissolution profile is described, expressed by theequation:

$$\frac{1}{(1-F)^{n-1}} - 1 = (n-1)\,K_{n-1} \ldots\ldots\ldots\ldots\ldots \text{Eq. 24}$$

Where F denotes fraction of drug released upto time t, k is parameter of model. This modelwas calculated on basis of non-linear regression.[17, 18, 19]

Application

For thedetermination of kinetics drug release from thenanoparticles, the non-conventional model 2 is useful.

MODEL INDEPENDENT METHODS[35, 36]

1. Ratio factors

Ratio tests are performed as ratios of percent drugdissolved, area under the dissolution curve, and meandissolution times of the reference formulation with thoseof a test formulation at the same sampling time. The mostcommon ratio test is performed by comparison of twomean dissolution times (MDTs), which are calculated by

$$MDT = \frac{\sum_i^n \bar{t}_i \Delta M_i}{\sum_i^n \Delta M_i}$$

Where *i* is the sample number, *n* is the number of dissolution sample times, $t_1 = t_{i-1} + t_1/2$is the time at midpointbetween t_i–1 and t_i, and ΔMiis the additional amount ofdrug dissolved between t_i–1 and t_i.

The variance of dissolution times (VTs) is estimated by

$$VT = \frac{\sum_i^n \left(\bar{t}_i - MDT\right)^2 \Delta M_i}{\sum_i^n \Delta M_i}$$

And the relative dispersion of dissolution time is given by

$$RD = VT / MDT^2$$

2. Fit factors

Fit factors include a difference factor *f*1 and a similarityfactor *f*2. The difference factor *f*1 calculate the % difference between the two curves at each time point and is a measurement of the relative error between two curves which is given by,

$$F1 = [(\sum_{t=1}^{n}(Rt - Tt)/ (\sum_{t=1}^{n}Rt)] \times 100$$

WhereRtand Tt are the percent drug dissolved of the referenceand test products, respectively, at each sample point i.

The similarity factor *f*2is a logarithmic reciprocal square root transformation of the sum of square error and is a measurement of similarity in the % dissolution between the two curves which is given by

$$F2 = 50 \times \log [(1 + (1 + (1/n) \sum_{t=1}^{n}(Rt - Tt)^2)^{-0.5} \times 100]$$

CONCLUSION

Reviews of the kinetic modeling on drug release exemplify that these models have beenpredictable to describe the relationship betweendrug dissolution and geometry on drug releasearrays mathematically. It is evident from thepharmaceutical literature that no singleapproach

is widely accepted to determine ifdissolution profiles are similar. The applicationand evaluation of model dependent methodsand statistical methods are more complicated,whereas the model independent methodspresent satisfactory model approach to the truerelationship between the dependent andindependent variables of the dissolution data.The disadvantages of the model independent methods are the values of f1 and f2 which aresensitive to the number of dissolution timepoints and the basis of the criteria for decidingthe difference or similarity between dissolutionprofiles is unclear. The limitation is that onlywhen the within-batch variation is less than15%, f2 equation should be used. Overall, thesemodels, though some are more complicated,helps the formulation and research scientists to forecast possible rate and mechanism of drugrelease.

Table 1: Some models with linear equations for graphical presentation [1]

Sr. no	Model name	Linear equation	Plot	
			X - axis	**Y- axis**
1	Zero order	$Q_t = Q_0 + K_0t$	Time	Cumulative amount of drug release
2	First order	$\log C = \log C_0 - Kt/ 2.303$	Time	Log cumulative percentage of drug
3	Higuchi model	$f_t = Q = K_H \times t^{1/2}$	Square root of time	Cumulative percentage of drug release
4	Hixson Crowell	$W_0^{1/3} - W_t^{1/3} = \kappa t$	Time	Cube root of drug percentage remaining
5	Korsmeyer Peppas	$M_t / M_\infty = Kt^n$	Time	Log cumulative percentage drug release
6	Baker Lonsdale	$f_1 = \frac{3}{2}\left[1 - (1 - \frac{M_t}{M_\infty})^{2/3}\right] \frac{M_t}{M_\infty} = k_t$	Root of time inverse	$[d(M_t/ M_\infty)] / dt$
7	Weibull	$M = M_0\left[1 - e^{-\frac{(t-T)^b}{a}}\right]$	Log [-ln(1-M)]	Log $(t- T_i)$

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