INTRODUCTION
Among different stages of drug development, in vitro dissolution has been a concern. Under some circumstances dissolution can be used as a tool for the quantification of bioequivalence [4]. Lots of theories/kinetics models dictate drug release from immediate and modified release delivery systems. There are number of models to represent the drug dissolution profiles where \( f(t) \) is a function of \( t \) (time) related to the amount of drug dissolved from the pharmaceutical delivery system. The quantitative analysis of values obtained in the dissolution profile is facilitated by the usage of a kinetic equation that mathematically modifies the dissolution curve in function of some parameters related with the pharmaceutical delivery systems [6]. In some cases, the equation can be simplified by a theoretical interpretation of the process, as for example zero order release. In particular, with tablets, capsules, coated forms or prolonged release systems that theoretical equation does not exist and sometimes a more adequate empirical fundament is used. The type of drug, solubility, its polymorphic form, crystallinity, particle size, and amount in the dosage form can influence the kinetic model [7, 8]. A water-soluble drug incorporated in a matrix device is mainly released by diffusion, while for a low water-soluble drug the self-erosion of the matrix device will be the principal release mechanism [9, 10]. To accomplish these studies the cumulative profiles of the dissolved drug are more commonly used in opposition to their differential profiles [11, 12, 13]. To compare dissolution profiles between two drug products model dependent (curve fitting), statistic analysis and model independent methods can be used [14, 15].
IN-VITRO RELEASE MODELS:

The kinetics of drug release is ascertained by plotting the values of *in-vitro* diffuse study of rifampicin noisome formulations S 1, S 2 and S 3 with different kinetic models like zero order (cumulative percentage drug diffused Versus Time), first order (log cumulative percentage drug retained Versus Time), Higuchi model (cumulative percentage drug diffused Versus √Time), Korsmeyer - Peppas model (log cumulative percentage drug diffused Versus log Time) [16, 17]. The linear regression ($r^2$) values shown in Table 3 obtained were interpreted with the Diffusion exponent (n) of Table 1 to obtain the kinetic models. The values of *in-vitro* diffuse study of rifampicin noisome formulations S 1, S 2 and S 3 were published by the author and cited[17, 19].

RESULTS AND DISCUSSION

In-vitro release and kinetic models:

The drug release mechanisms from the dosage forms are best described by various kinetic models. The use of *in-vitro* drug diffusion profile to predict *in-vivo* bio-function was found to be cost based development of novel drug delivery systems [18].

| Diffusion exponent (n) | Drug transference mechanism | Rate as a function of time |
|------------------------|-----------------------------|---------------------------|
| 0.5                    | Fickian diffusion            | $t^{-0.5}$                |
| 0.5 < n < 1.0          | Anomalous transport         | $t^{n-1}$                 |
| 1.0                    | Case-II transport            | Zero order release        |
| Higher than 1.0        | Super Case-II transport      | $t^{n-1}$                 |

Table 1: Types of diffusional release mechanisms from polymeric matrix

| Time in (hrs) | S 1 | S 2 | S 3 |
|---------------|-----|-----|-----|
| 1             | 9.60| 10.67| 12.80|
| 2             | 15.47| 17.60| 19.20|
| 3             | 19.73| 22.40| 25.07|
| 4             | 26.13| 28.27| 29.87|
| 5             | 32.53| 34.67| 35.73|
| 6             | 37.33| 40.53| 41.60|
| 7             | 43.20| 45.33| 45.87|
| 8             | 48.00| 49.07| 51.73|
| 9             | 52.80| 56.00| 58.13|
| 10            | 62.40| 63.47| 65.07|
| 11            | 68.27| 69.87| 72.00|
| 12            | 72.53| 73.60| 77.33|
| 13            | 77.33| 79.47| 83.20|
| 14            | 82.13| 84.80| 86.93|
| 15            | 88.00| 89.60| 90.67|
| 16            | 91.73| 94.40| 93.87|
| 17            | 95.47| 96.53| 98.13|

Table 2: Comparative *In-vitro* Release Study of Rifampicin Niosomes: (n=3)

Coefficient of correlation ($r^2$) values for Zero order plots indicates that the rifampicin release from the noisomes was slow and steady. It is shown in the Graphs 1, 5 and 9. Coefficient of correlation ($r^2$) values for Zero order plots indicates that the mechanism of rifampicin release from the niosomes followed independent of concentration and the rate was zero order release, it was slow and steady for all formulations from S 1, S 2 and S 3. It is shown in the Graphs 1, 5 and 9.

First order plots show that the ($r^2$) values suggest the rifampicin release rate was in relationship with concentration of rifampicin in noisomes for all the formulations from S 1, S 2 and S 3. It is shown in the Graphs 2, 6 and 10. First order plots show that the ($r^2$) values suggest the rifampicin release rate was concentration dependant due to nonlinearity of all the rifampicin noisome formulations from S 1, S 2 and S 3. It is shown in the Graphs 2, 6 and 10.

The curve of Higuchi plot represents two different release rates: first part is nonlinear then followed by a linear release for all the formulations from S 1, S 2, to S 3. It is shown in the Graphs 3, 7 and 11.
Graph 1 Zero Order Kinetics of S1

\[ y = 5.6868x + 3.4946 \]
\[ R^2 = 0.9967 \]

Graph 2 First Order Kinetic Release of S1

\[ y = -0.076x + 2.2064 \]
\[ R^2 = 0.8771 \]

Graph 3 Higuchi Model of S1

\[ y = 26.088x - 18.594 \]
\[ R^2 = 0.9447 \]

Graph 4 Korsmeyer - Peppas Model of S1

\[ y = 0.853x + 0.9324 \]
\[ R^2 = 0.9948 \]

Graph 5 Zero Order Kinetics of S2

\[ y = 5.7069x + 5.2153 \]
\[ R^2 = 0.9957 \]

Graph 6 First Order Kinetic Release of S2

\[ y = -0.0803x + 2.189 \]
\[ R^2 = 0.8518 \]
Graph 7: Higuchi Model of S2

\[ y = 26.297x - 17.266 \]
\[ R^2 = 0.9521 \]

Graph 8: Korsmeyer - Peppas Model of S2

\[ y = 0.8089x + 0.9928 \]
\[ R^2 = 0.9961 \]

Graph 9: Zero Order Kinetics of S3

\[ y = 5.7285x + 6.7699 \]
\[ R^2 = 0.9927 \]

Graph 10: First Order Kinetic Release of S3

\[ y = -0.0726x + 2.1311 \]
\[ R^2 = 0.909 \]

Graph 11: Higuchi Model of S3

\[ y = 26.492x - 16.055 \]
\[ R^2 = 0.9562 \]

Graph 12: Korsmeyer - Peppas Model of S3

\[ y = 0.7601x + 1.0549 \]
\[ R^2 = 0.9922 \]
The pattern of release from the rifampicin niosomes was found to be an initial- nonlinear suggests burst release and a linear diffusion-controlled steady slow release. The initial burst release might be because of smaller size range particles with lesser surface diameter accounts for faster diffusion of drug molecules and surface adsorbed molecules that are available at higher rates from rifampicin niosomes to the medium resulting in nonlinear curve. Then the linear part of the curve accounts for steady slow release of rifampicin from the niosomes was controlled and transference of rifampicin might be by diffusion (depicts Fick’s law of diffusion) results in a linear part of the curve. It is shown in the Graphs 3, 7 and 11. The plot of in-vitro drug release values in Korsmeyer - Peppas model showed good linearity of the release pattern from the \( r^2 \) values for all the formulations from S 1, S 2, to S 3 where the release of the drug from niosome is governed by diffusion indicative of best fit to non-swelling controlled release systems. It is shown in the Table 3 and Graphs 4, 5 and 12.

**Table 3: Comparative Diffusion Coefficients \((r^2)\) of Niosome Formulations: \((n=3)\)**

| Kinetic Models | S 1  | S 2  | S 3  |
|----------------|------|------|------|
| Zero           | 0.996| 0.995| 0.992|
| First          | 0.877| 0.851| 0.909|
| Higuchi        | 0.944| 0.952| 0.956|
| Korsmeyer      | 0.944| 0.996| 0.992|
| Peppas         |      |      |      |

**Conclusion**

The study revealed *in vitro* kinetic models were well fit for non-swelling controlled release systems for all the formulations from S 1, S 2 to S 3. The release pattern is well explained by mass transfer following a non-Fickian model which involves more than one type of release phenomena of Case II transport mechanism. The results revealed that all the formulations were best explained by zero order release.

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