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Release Kinetic Determination of Once a Day Prolong Release Tablets of Pramipexole Dihydrochloride Using Model-Dependent Approaches

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ABSTRACT

The aim of presented research work was to determine release kinetic pattern of Pramipexole dihydrochloride prolong release tablets using model dependent approaches. Various release kinetic models like Zero order, First order, Higuchi, Korsmeymer-Peppas, Hixson–Crowell and Weibull were applied to developed prolonged release tablet of Pramipexole dihydrochloride. The criteria for selecting the most appropriate model was lowest sum of square of residuals. Residual values between predicted and observed data were used to calculate the sum of squares of residuals. Lowest sum of square of residuals indicate the minimum variance between the predicted and observed dissolution data. The entire release profile was compared by taking the absolute difference (residual) between the predicted and observed calculated AUC data.

KEYWORDS

Pramipexole dihydrochloride, Zero order, First order, Higuchi, Korsmeymer-Peppas, Hixson–Crowell, Weibull, sum of square residual, Prolong release.

INTRODUCTION

Over the past few decades, significant medical advances have been made in the area of drug delivery with the development of controlled release dosage forms and large variety of formulations delivered by oral controlled release dosage forms. The release pattern can be divided into those that release drug at a slow zero or first order rate and those that provide an initial rapid dose, followed by slow zero or first order release of sustained component. The purpose of the controlled release systems is to maintain drug concentration in the blood or in target tissues at a desired value as long as possible[1]. In other words, they are able to exert a control on the drug release rate and duration[2].

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For this purpose, generally, controlled release system initially release part of the dose contained in order to attain rapidly the effective therapeutic concentration of the drug. Then, drug release kinetic follows a well-definedbehaviour in order to supply the maintenance dose enabling the attainment of the desired drug concentration. Controlled release formulations are important tool for utilization of modern concept of therapeutic treatment to increase effectiveness, improve patient compliance, reduce drug administration frequency and reduce side effect related to dosing. Mathematical modelling turn out to be useful approach in development of controlled release formulation for prediction of release kinetic before the release system are realized. It allows the measurement of some important physical parameters, such as the drug diffusion coefficient and resorting to model fitting on experimental release data. Mathematical model

development requires the comprehension of all the phenomena affecting drug release kinetic[3]; it has a very important value in the process optimization of such formulations. The model can be simply thought as a mathematical metaphor of some aspects of reality that, in this case, identifies with the ensemble of phenomena ruling release kinetic. For this generality, mathematical modelling is widely employed in different disciplines such as genetics, medicine, psychology, biology, economy and obviously engineering and technology.

MATERIAL AND METHODS

MATERIALS

Pramipexole dihydrochloride, hypromellose (HPMC K15M), Carbomer homopolymer type B (Acrypol 971 P), corn starch, magnesium stearate, colloidal anhydrous silica and isopropyl alcohol were procured from Hetero drugs Limited, Colorcon Asia private limited, Corel pharmachem Limited, Roquette, Macron fine chemicals, Evonik Industries AG and Finar chemicals Limited respectively. All ingredients were used of pharmaceutical grade.

METHOD

Materials used to formulate Pramipexole prolonged release tablets are mentioned in Table 1. Base granules prepared with hypromellose and corn starch by addition of mixture of isopropyl alcohol and water (70:30), Pramipexole dihydrochloride, hypromellose, carbomer homopolymer type B, colloidal anhydrous silica and magnesium stearate were added as extragranular. Lubricated blend was compressed into tablets using tooling on a rotary tablet press. The compression force was adjusted to obtain tablets with hardness in the range of 90-130 N.

Dissolution Study of Prepared Formulation

Dissolution profile of prepared Pramipexole dihydrochloride tablets 1.05 mg were performed ine office of generic drug (OGD) recommended dissolution medium (500 ml, 0.05M phosphate buffer pH 6.8 at 37 ± 0.5 °C, USP Type I, 100 RPM). Sample aliquots (5 mL) were withdrawn at 2, 4, 6, 8, 12, 18 and 24 hours and replaced with equal volumes of fresh medium. Drug content was determined by HiperfomanceLiquid Chromatography (HPLC) at262 nm wavelength. The mean data (n = 6) were used. Percentage cumulative drug release (% CDR) was measured against time.

Table 1: Optimised formulation composition of Pramipexole prolonged release tablets 1.05 mg

Formulation Ingradients	**Quantity mg per tablet**
Intragranular	
Hypromellose (HPMC K15M)	124.00
Corn Starch	152.88
Binder	
Isoproyl alcohol: Purified water	Quatity sufficient (in ratio of 70:30)
Extragranular	
Pramipexole dihydrochloride	1.50
Hypromellose (HPMC K15M)	53.00
Carbomer homopolymer type B (Acrypol 971P)	4.14
Colloidal ahnydrous silica	2.68
Magnesium stearate	1.80
Theoretical average weight of tablets	**340.00 mg**

Note: 1.50 mg Pramipexole dihydrochloride monohydrate equivalent to 1.05 mg Pramipexole.

Model-Dependent Approaches

In vitro drug release data were fitted to kinetic models as follows

Qt versus t (Zero order)4

Log Qt versus t (First order)5

Qt versus square root of t (Higuchi)6

log %Qt versus log %t (Korsmeymer-Peppas)7

Qt versus cube root of t (Hixson–Crowell)8

log Qt versus log t (Weibull)9

Where Qt is the amount of drug released at time t.

The criteria for selection the most appropriate model was lowest sum of square of residuals and highest regression value. Residual values between predicted and observed data were used to calculate the sum of squares of residuals. Lowest sum of square of residuals indicate the minimum variance between the predicted and observed dissolution data. Highest regression values indicate linearity in release profile.

The entire release profile was compared by taking the absolute difference (residual) between the predicted and observed calculated AUC data.

RELEASE KINETIC CALCULATION AND DISCUSSION

Various kinetic models were applied in release profile of optimize formulation in order to determine release kinetic pattern. In following table 2 to 8, data are shown of Qt versus t (Zero order), Log Qt versus t (First order), Qt versus square root of t (Higuchi), log %Qt versus log %t (Korsmeymer-Peppas), Qt versus cube root of t (Hixson–Crowell) and log Qt versus log t (Weibull) respectively where observed release profile means drug release observed actually and predicted release profile means data are set in such a way that regression value more than 0.99.

Table 2: % Deviation in Release Profile for the Optimized Batch from the Weibull model

Log t	Predicted Weibull release profile		Observed Weibull release profile		Absolute difference in AUC
	Log Q t	AUC	Log Q t	AUC	
0.00	0.00		0		
0.30	1.59	0.24	0.53	0.0795	0.0256
0.60	1.71	0.05	0.96	0.193943	0.0200
0.90	1.77	0.05	1.44	0.361236	0.0984
1.08	1.85	0.07	1.69	0.247784	0.0303
1.26	1.92	0.09	1.92	0.273457	0.0328
1.38	1.96	0.05	2.08	0.2052	0.0235

Table 3: % Deviation in Release Profile for the Optimized Batch from the Hixson-Crowell model

Cube root of time (minute)	Predicted Hixson-Crowell release profile		Observed Hixson-Crowell release profile		Absolute difference in AUC
	Q t	AUC	Q t	AUC	
1.26	39	24.51176	39.00	24.51176	0
1.58	51	17.02258	51.00	17.02258	50.87306
1.99	59	14.26507	63.00	21.39761	4.529934
2.27	70	23.41201	73.00	21.28364	53.27882
2.60	84	34.06309	84.00	26.76386	0
2.85	92	21.79887	92.00	21.79887	0

Table 4: % Deviation in Release Profile for the optimized Batch from the Korsmeymer-Peppas model

Log % t	Predicted Korsmeymer-Peppas release profile		Observed korsmeymer-Peppas release profile		Absolute difference in AUC
	Log % Q t	AUC	Log % Q t	AUC	
-1.69897	-0.40894	0.347384	-0.368	0.31261	0.00121
-1.39794	-0.29243	-0.1804	-0.29243	-0.11702	0.00402
-1.09691	-0.22915	-0.07894	-0.22915	-0.07894	0.00000
-0.92082	-0.1549	-0.0749	-0.18	-0.04958	0.00064
-0.74473	-0.07572	-0.06594	-0.14	-0.03331	0.00106
-0.61979	-0.03621	-0.02696	-0.113	-0.01829	0.00008

Table5: % Deviation in Release Profile for the optimized batch from the Higuchi model

Square root of time (minute)	Predicted Higuchi release profile		Observed Higuchi release profile		Absolute difference in AUC
	Q t	AUC	Q t	AUC	
1.414214	39	27.57716	31	21.92031	32
2	51	20.48528	42	18.77817	2.914214
2.828427	59	19.31371	57	36.2132	285.5929
3.464102	70	34.60891	70	40.90144	39.59592
4.242641	84	53.9472	84	53.9472	0
4.898979	92	36.56648	95	50.27891	188.0307

Table 6: % Deviation in Release Profile for the optimized batch from the first order model

Time (minute)	Predicted first order release profile		Observed first order release profile		Absolute difference in AUC
	Log Q t	AUC	Log Q t	AUC	
2	1.591065	1.591065	0.36	0.36	1.5129
4	1.70757	0.349517	0.53	0.51	0.0256
8	1.770852	0.379691	0.91	2.28	3.61
12	1.845098	0.74246	1.27	3.6	8.1796
18	1.924279	1.187719	1.8	7.95	45.6976
24	1.963788	0.829679	2.31	10.71	97.6144

Table 7: % Deviation in Release Profile for the optimized batch from the zero Order model

Time (minute)	Predicted Zero order release profile		Observed Zero order release profile		Absolute difference in AUC
	Q t	AUC	Q t	AUC	
2	39	39	11	11	784
4	51	36	19	24	144
8	59	48	36	102	2916
12	70	110	52	160	2500
18	84	210	77	375	27225
24	92	168	100	483	99225

Table 8: Result of model fitting for optimized batch

Model	SSR
Zero-order	132794
First-order	156.6401
Higuchi	548.133
Korsmeyer-Peppas	0.00701
Hixon-crowell	108.681
Weibull	0.2305

The criteria for selection the most appropriate model are lowest sum of square of residuals (SSR) value. Residual values between predicted and observed data were used to calculate the sum of squares of residuals, The entire dissolution profile was compared by taking the absolute difference (residual) between the predicted and observed calculated AUC data. Lowest sum of square of residuals (SSR) in Korsmeyer-Peppas (0.00701) indicated the minimum variance between the predicted and observed dissolution data. Lowest SSR indicates; in optimize formulation drug release follow Korsmeyer-Peppaskinetic.

CONCLUSION

Release kinetic is an integral part of formulation development because if the kinetic of drug release is known, one can also advance for the establishment of in vivo in vitro (IVIVC) correlation. Mathematical approach is one of scientific methods to optimize and evaluate the error in terms of deviation in AUC for the release profiles of formulated products during the formulation development stage. Mathematical model approach is important in research and development because of its simplicity and their inter-relationships may minimize the number of steps in final optimization, thereby improving the formulation development process.

REFERENCES

1. Langer RS, Wise DL, Medical applications of controlled release, applications and evaluation, Vol. I and II, CRC Press, Boca Raton, 1984.

2. Robinson JR, Lee VHL, Controlled drug delivery, Marcel Dekker, Inc. New York, Basel 1987.

3. Cartensen JT, Modeling and data treatment in the pharmaceutical sciences., Technomic Publishing Co. Inc., New York, Basel 1996.

4. Brazel CS, Peppas NA, “Modeling of drug release from swellable polymers”, Eur. J. Pharm. Biopharm. 2000, 49, 47–58.

5. Lapidus H, Lordi NG, “Some factors affecting the release of a water-soluble drug from a compressed hydrophilic matrix”. J. Pharm. Sci. 1966, 55, 840–843.

6. Higuchi T, “Mechanism of sustained action medication: theoretical analysis of rate of

release of solid drugs dispersed in solid matrices". J. Pharm. Sci. 1963, 52, 1145–1148.

7. Korsmeyer RW, Gurny R, Doelker E, Buri P, Peppas NA, "Mechanisms of solute release from porous hydrophilic polymers". Int. J. Pharm. 1983, 15 (1), 25–35.

8. Hixson AW, Crowel JH, "Dependence of reaction velocity upon surface and agitation: theoretical considerations". Ind. Eng. Chem. 1931, 23, 923–931.

9. Thakkar VT, Shah PA, Soni TG, Parmar MY, Gohel MC, and Gandhi TR, "Goodness-of-Fit Model-Dependent Approach for Release Kinetic of Levofloxacin Hemihydrates Floating Tablet", Dissolution technology, February 2009, 35-39.

