Pharm Methods, 2017; 8(2): 115-120
A multifaceted peer reviewed journal in the field of Pharm Analysis and Pharmaceutics
www.phmethods.net | www.journalonweb.com/phm

Original Article

Fabrication of Extended Release Tablets of Pramipexole: *In-vitro* Studies

Kambham Venkateswarlu[1]*, Heerasingh Thakur[2], Thumati Nagendra Bhaskar Babu[3]

[1]Department of Pharmaceutics, JNTUA-Oil Technological and Pharmaceutical Research Institute, Jawaharlal Nehru Technological University Anantapur, Anantha-puramu-515001, Andhra Pradesh, INDIA.
[2]Drug Safety Scientist, Cognizant Technology Solutions, Hyderabad, Telangana, INDIA.
[3]Ph.D Scholar, Department of Pharmaceutics, GITAM Institute of Pharmacy, GITAM University, Visakhapatnam, Andhra Pradesh, INDIA.

ABSTRACT

In this study, Extended release (ER) tablets of Pramipexole (PMPL) to be taken once daily were prepared and evaluated. Formulations were developed using different polymers and excipients in varying concentrations to get the desired extended release period of 24 h. The granules were prepared by wet granulation method and evaluated for angle of repose (AR), bulk density (BD), tapped density (TD), Carr's index (CI) and Hausner's ratio (HR). The granules showed satisfactory flow properties. The compressed tablets were evaluated for weight variation, hardness, friability, drug content, thickness and *in-vitro* drug release. Formulation (F9) containing Sodium carboxy methyl cellulose (SCMC- 10%) and both grades of Micro Crystalline Cellulose (MCC PH101, MCC PH102) as diluents gave the desired release for once a day administration. The drug release was found to be followed first order kinetics and particularly diffusion with non-fickian transport mechanism. *In-vitro* release pattern of drug from the optimized formulation F9 was found to be similar (i.e. the similarity factor f2 was found to be 66.43) with the marketed product MIRAPEX ER and showed better drug release pattern than the marketed product. It was revealed from the results that the formulation F_9 could be the suitable candidate for the effective treatment of Parkinson's disease as once daily formulation.

Key words: Dissolution studies, Extended release tablets, Parkinson's disease, Pramipexole, Wet granulation.

Correspondence:
Kambham Venkateswarlu,
Department of Pharmaceutics, JNTUA- Oil Technological and Pharmaceutical Research Institute, Ananthapuramu, Andhra Pradesh, INDIA.
Phone no: 91-9441701016

E-mail: k.v.reddy9441701016@gmail.com, k.v.pharmacy@jntua.ac.in
DOI : 10.5530/phm.2017.8.18

INTRODUCTION

Extended release drug delivery systems popularly known as prolonged or timed release delivery systems. They are defined as those that allow at least a two-fold reduction in dosing frequency, as compared to the drug presented in a conventional dosage form, such as a solution or conventional solid dosage forms.[1] Drug efficacy generally depends on the ability of the drug to reach the target site in sufficient quantity to maintain therapeutic levels for the desired time period. Orally administered drugs must overcome several obstacles to reach their desired targets. Orally administered drugs subject to the first pass effect generally exhibit non-linear pharmacokinetics. Until the liver's metabolic capacity has been exceeded, the amount of such drugs in the bloodstream is significantly lower than the amount administered. This metabolic elimination of the given dose results in reduced bioavailability. However, once the administered dose exceeds the liver's metabolic capacity, a significant increase in the drug concentration in the bloodstream may be obtained. The first pass phenomenon presents particular difficulties in the maintenance of therapeutic levels of an orally administered drug over an extended period such as 12 or 24 h.[2]

In practice dopamine agonists play an important role in the therapy of Parkinson's disease, because of the corresponding receptors are targeted directly. Most of the pharmaceuticals show their effect directly at the D_2 receptors, whereas the role of different types of receptors is still unknown. All dopamine agonists have a direct effect to the dopamine receptors; they differ in respect to half-life and special effects to different subtypes of dopamine receptors (D_1, D_2 and D_3). The latest dopamine agonists have advantages because of the long half-life, which improves the sense of a continuous postsynaptic activation of the receptors. A mono therapy of Parkinson's disease is possible with dopamine agonists and is used in early stages.[3] PMPL is a non-ergotamine full agonist at the D_2 subfamily of dopamine receptors, with higher selectivity for D_3 than for D_2 and D_4 dopamine receptors.[4]

Extended release formulations are having fewer fluctuations in plasma concentrations over the time period compared to immediate release formulations. A considerable research has been done on PMPL for prolonged release but those were not clear.[3-4] Hence, the step has been taken to develop PMPL extended release tablets as a monotherapy for the treatment of Parkinson's disease and to reduce the dosing frequency from three times a day to once a day.

MATERIALS AND METHODS

Materials

The pure drug PMPL was obtained from Paras Impex, India and remaining ingredients such as MCC PH101 and MCC PH102 from Accent Microcell Industries, India, Lactose monohydrate and Magnesium stearate from Signet Chemicals, India, SCMC from Aditya Chemicals, India, Hydroxy propyl methyl cellulose K4M (HPMC K4M) from FMC Biopolymer, India, Hydroxy propyl methyl cellulose K100M (HPMC K100M) from Dow Chemicals, India, Eurdragit L100 from Evonik, India, Hydroxy propyl methyl cellulose E3CPS (HPMC E3CPS) and Plasdone K90 from Colorcon Asia, India, Colloidal silicon dioxide from Waker Silicones, India, and other chemicals used were of analytical grade. The marketed product MIRAPEX ER was purchased from local pharmacy.

Methods

Fourier Transform Infrared (FTIR) studies

IR spectroscopy has its application in the studies of drug-excipient interactions. Samples of pure drug and its physical mixtures were prepared by KBr disc method and scanned from 4000 cm^{-1} to 400 cm^{-1} using FTIR

(Bruker, USA). The IR spectrum of pure drug was compared with the IR spectrum of its physical mixture for spectral changes.[5]

Evaluation studies

Micromeritic studies

The flow characteristics of granules were known by flowability studies such as AR,[6] BD,[7] TD,[8] CI[9] and HR.[10]

Preparation of PMPL ER tablets

The ER tablets were prepared by wet granulation method. Ingredients (Table 1) such as Lactose monohydrate, MCC PH 101, SCMC, Eudragit L100, HPMC K 100M, MCC PH102 were sifted through mesh size 40 separately and collected in polybags. Lactose, MCC PH101, SCMC and Eudragit L 100 were loaded in Rapid Mixer Granulator (RMG-3510, Saral Engineering, India) and mixed for 15 min by setting impeller at slow speed. Drug-binder solution was prepared by taking Plasdone K90 and PMPL into a SS 316 container which already consists of purified water with the arrangement of stirrer and stirring was continued till a clear solution obtained. The drug binder solution along with dry mixed powder were taken into a granulator and mixed for 3 min by setting impeller at slow speed and chopper set to off. Additional quantity of purified water was added to the wet mass and further mixed for 1 min. Then the obtained wet granules were unloaded from the granulator and drying was done by fluid bed drier for 5 min at temperature of 55-65°C. LOD was checked using LOD apparatus at 105°C till constant weight is reached and It should not be more than 3% w/w. The dried granules were sifted through sieve #20 and over sized granules collected separately, which were then milled using 1.5 mm screen at medium speed with knives followed by sifted through sieve #20. The dried granules, Extra granular part (HPMC K100M, MCC PH102, SCMC) and colloidal silicon dioxide were loaded into Octagonal blender and blended for 10 min. Magnesium stearate was added to the above mixture and further blended for 5 min. Finally the formulation blend was compressed into tablets by RIMEK rotary tablet punching machine using 9.5 mm round standard concave punch tooling.[3]

Post compression studies

The prepared PMPL ER tablets were evaluated for Weight variation,[11] Friability,[12] Thickness[13] and Hardness test[14] according to the methods described in earlier studies.

Drug content

The tablets were tested for their drug content uniformity by Reverse Phase - High Pressure Liquid Chromatography (RP-HPLC) (Agilent LC 1200). Twenty tablets containing PMPL were exactly weighed and ground into a fine powder. From this powder, an amount of the tablet powder equivalent to 25 mg PMPL was transferred into a 25 ml standard flask containing 10 ml of diluent and shaken for 10 min. The volume was made up to the mark with diluent and mixed well. The solution was filtered through a 0.45 µm membrane filter. The filtered solution was appropriately diluted with diluent to obtain a concentration of 100 µg/ml. From this solution, 5 µl was injected into the HPLC system. The area under the peak was noted and the drug content in the tablets was quantified using the calibration graph or regression equation.[15]

In-vitro drug release

In-vitro dissolution studies of the extended release tablets of PMPL formulations were carried out in pH 1.2 hydrochloric acid medium for first 2 h, which was then replaced with the same volume of a phosphate buffer solution pH 6.8 kept at 37°C ± 0.5°C using USP dissolution apparatus-II (Lab India, India). One tablet was used in each test. Aliquots of the dissolution medium (5 ml) were withdrawn at specific time intervals and replaced immediately with equal volume of fresh medium. The samples were filtered through membrane filter disc and analyzed for drug content by measuring area with HPLC. Drug concentration was calculated from the standard curve and expressed as cumulative percent drug release.[16-17]

Similarity factor

The similarities between two dissolution profiles were determined by model independent procedure such as similarity factor (*f2*) and it was performed according to the method described in earlier studies.[18]

Table 1: Formulation of PMPL ER tablets

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Intra granular addition												
PMPL	0.375	0.375	0.375	0.375	0.375	0.375	0.375	0.375	0.375	0.375	0.375	0.375
Lacotse monohydrate	17.22	-	17.22	17.22	41.22	41.22	41.22	41.22	41.22	69.82	53.22	41.22
MCC PH 101	40	40	85.6	73.6	67.6	73.6	55.6	43.6	43.6	19	43.6	43.6
SCMC	-	-	-	-	-	-	12	12	18	12	12	12
Eudragit L 100	-	-	12	12	6	-	6	6	6	12	6	6
HPMC E3 CPS	2.4	-	-	-	-	-	-	-	-	-	-	-
Plasdone K90	-	-	4.8	4.8	4.8	4.8	4.8	3.6	3.6	3.6	3.6	3.6
HPMC K4M	-	19.62	-	-	-	-	-	-	-	-	-	-
HPMC K 100M	120	100	100	100	100	100	100	100	100	100	100	100
MCC PH 102	52.8	72.8	12.8	12.8	12.8	12.8	12.8	14	14	10	14	14
Extra granular addition												
Eudragit L 100	-	-	-	12	-	-	-	-	-	6	-	12
SCMC	-	-	-	-	-	-	-	12	6	-	-	-
Colloidal silicon dioxide	4.8	4.8	4.8	4.8	4.8	4.8	4.8	4.8	4.8	4.8	4.8	4.8
Magnesium stearate	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.4	2.4
Total weight (mg)	240	240	240	240	240	240	240	240	240	240	240	240

Drug release kinetics

The dissolution profile of F9 was fitted to Zero order, First order, Higuchi and Korsmeyer Peppas model to ascertain the kinetic modeling of the drug release and it was performed according to the method explained in earlier studies.[19]

Significance studies

Statistical analysis was performed by one way and two way ANOVA using Graph Pad Prism 6 and significance was set at $p<0.05$. The results were calculated as avg (n=3) ± standard deviation (SD).

RESULTS AND DISCUSSION

PMPL extended release tablets were prepared by wet granulation method using different polymers and excipients. In all the formulations, the dose of PMPL was kept constant at 0.375 mg and the final weight of the tablet was at 240 mg. The proposed dosage form was intended to decrease the dosing frequency thereby it favors the better treatment and enhances patient compliance.

FTIR Studies

The drug excipients incompatibility refers to the physical or chemical interactions between the excipients and active ingredient which may influence the drug safety and efficacy through its detrimental effect on the drug stability and bioavailability. The compatibility of the drug with excipients was investigated by FTIR spectroscopy. The characteristic absorption peaks of pure drug were found at the wave numbers of 3427.53, 2937.11, 1589.26, 1312.55 and 756.33 cm^{-1} responsible for functional groups of N-H stretching, C-H stretching, C=C stretching, C-N stretching and C-H bending respectively. All these characteristic peaks were observed in the spectrum of physical mixture (Figure 1), hence it indicates that there were no chemical interactions between the pure drug and the excipients. Thus the chosen excipients for the formulations were found to be compatible with the API.

Precompression evaluation of granules

The results of micromeritic studies are represented in table 2. The mean BD of the granule blend was found to be in the range from 0.472 to 0.510 gm/ml and for TD, found to be in the range from 0.557 to 0.626 gm/ml. The CI values varied from 13.23 to 18.36 % (good to fair flowability) and HR from 1.12 to 1.22 (good to fair flowability). The AR values were in the range of 25°.53' to 29°.25', which indicates the good flowability of the granules.[20] It was evident from the Micromeritic studies that all the formulations possessing acceptable flow properties, hence, the granules of all the formulations were selected for further studies.

Post compression evaluation of tablets

The results of physical evaluation of tablets are represented in table 3. The hardness of tablets found to be in the range of 12.0 to 12.6 kg/cm^2. Friability values ranged from 0.52 to 0.88% and the results were complied with the official limits. Both the hardness and friability studies confirmed that all the tablets possessing sufficient strength to withstand the mechanical breakdowns during the shipping etc. The weight variation values ranged from 1.17 to 4.15% and found to be within the prescribed pharmacopoeial limits (7.5%).[21] The thickness values of all the formulations were ranged from 4.12 to 4.72 mm and tablets possessing the uniform thickness. PMPL tablets contain not less than 90% and not more than 110% of the labeled amount of PMPL. Drug content (94.23 to 101.73%) was found be uniform within the batches of the different tablets.

Dissolution studies

In-vitro dissolution studies were performed for all the formulated tablets using USP-II tablet dissolution apparatus employing rotating paddle method at 100 rpm using pH 6.8 phosphate buffer solutions as dissolution medium and the temperature of medium was maintained at 37 ± 0.5°C. The results of *in-vitro* drug release data and similarity factor are given in table 4. As per the results of dissolution studies, formulations from F1 to F12 satisfied the desired sustained release of 24 h but failed show maximum drug release within specified time except F9 and formulation F9 showed similar dissolution profile as that of the innovator with

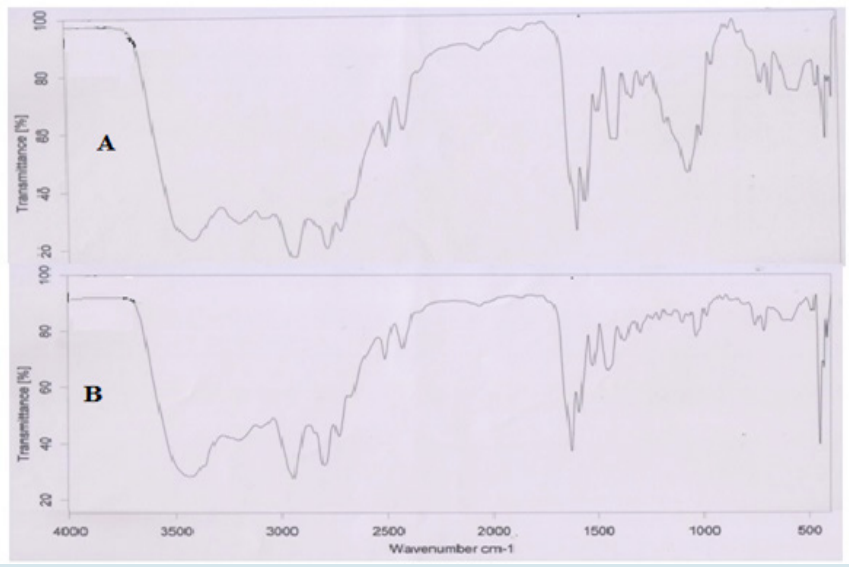


Figure 1: FTIR studies. A) IR spectrum of physical mixture, B) IR spectrum of pure drug.

Table 2: Flowability studies

Formulation	BD (gm/ml)	TD (gm/ml)	CI (%)	HR	AR (°)
F1	0.49±0.004989	0.578±0.009933	15.06±0.70277	1.17±0.009428	29°.25'±0.742
F2	0.51±0.000943	0.626 ±0.001633	18.36±0.33993	1.22±0.008165	27°.75'±0.881
F3	0.486±0.01275	0.585 ±0.006182	17.93±1.26578	1.12±0.004714	26°.12'±1.240
F4	0.47±0.005888	0.544 ±0.001633	13.93±0.54365	1.15±0.009428	27°.07'±0.951
F5	0.474±0.002494	0.552 ±0.003266	13.93±0.88065	1.15±0.012472	29°.14'±0.980
F6	0.496±0.001633	0.572 ±0.001633	13.23±0.47140	1.14±0.009428	26°.66'±0.815
F7	0.519±0.008055	0.606 ±0.005888	14.23±0.65489	1.14±0.012472	28°.36'±0.542
F8	0.514±0.002494	0.594 ±0.002494	13.43±0.66499	1.15±0.009428	27°.66'±0.271
F9	0.487±0.003399	0.567 ±0.002494	13.86±1.28149	1.15±0.012472	26°.05'±1.146
F10	0.519±0.001247	0.601 ±0.002494	13.53±0.38586	1.15±0.004714	28°.76'±0.346
F11	0.484±0.000943	0.557 ±0.012365	14.5±1.349074	1.13±0.008165	29°.08'±0.686
F12	0.496±0.00094	0.576±0.001633	13.7±0.141421	1.15±0.004714	25°.53'±0.779

Values expressed in avg±SD (n=3)

Table 3: Post compression studies

Formulation	Weight variation (%)	Friability (%)	Thickness (mm)	Hardness (kg/cm2)	Drug content (%)
F1	2.16±0.045	0.75 ±0.011	4.16±0.01	12.5±0.32	99.12±0.65
F2	2.95±0.173	0.88 ±0.021	4.70±0.02	12.3±0.52	97.43±2.35
F3	3.52±0.416	0.82 ±0.032	4.66±0.02	12.0±0.33	98.31±2.21
F4	3.36±0.174	0.85 ±0.010	4.42±0.02	12.5±0.23	101.23±3.25
F5	2.75±0.192	0.76 ±0.022	4.70±0.03	12.1±0.44	96.04±3.84
F6	4.15±0.057	0.72 ±0.033	4.67±0.03	12.6±0.18	94.08±0.93
F7	1.22±0.114	0.66±0.021	4.42±0.03	12.3±0.25	100.52±2.34
F8	1.17±0.325	0.56±0.020	4.71±0.02	12.2±0.14	96.83±4.27
F9	1.37±0.337	0.52±0.016	4.69±0.01	12.0±0.35	97.93±0.91
F10	1.41±0.692	0.68±0.021	4.72±0.02	12.4±0.23	95.23±2.25
F11	1.44±0.184	0.54±0.038	4.12±0.03	12.3±0.06	96.71±0.57
F12	1.38±0.436	0.66±0.021	4.56±0.03	12.0±0.32	99.13±1.62

Values expressed in avg ± SD (n=3)

Table 4: *In-vitro* dissolution profiles of developed formulations with similarity factor and innovator

Time (h)	% Cumulative Drug Release												
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	Innovator
1	22.5±2.77	19.8±1.23	10.8±2.45	7.9±2.10	14.9±2.94	19.3±2.35	10.9±2.47	13.0±2.81	15.2±2.56	8.3±2.90	10.4±2.89	12.6±3.05	20.3±1.53
2	35.4±2.53	30.7±4.43	17.0±2.56	12.8±1.84	22.8±4.01	29.5±3.74	17.7±2.40	20.9±1.66	23.6±3.90	12.8±2.61	17.1±3.23	18.9±4.66	27.9±1.86
4	50.7±1.18	45.2±3.30	26.7±4.04	20.6±2.01	40.0±2.75	47.8±3.26	27.6±4.40	32.1±3.87	37.2±4.23	21.0±2.68	26.4±1.93	29.7±4.52	36.5±1.94
6	58.9±3.10	56.0±4.73	34.7±3.91	27.6±0.26	50.3±3.35	59.2±3.67	36.7±3.97	41.2±1.52	47.3±5.32	27.8±4.88	37.3±2.03	39.4±3.81	47.4±1.34
9	68.8±1.65	67.9±3.24	44.9±3.96	35.6±0.62	60.9±4.64	70.2±4.87	47.4±4.87	53.0±3.42	61.0±2.07	38.4±3.16	49.4±4.69	50.1±4.05	51.1±1.68
12	76.2±2.17	76.1±6.12	52.5±3.48	46.6±1.94	68.1±4.34	77.2±4.65	57.1±2.77	61.6±2.61	71.0±3.59	46.9±1.51	60.0±1.95	58.5±3.08	59.4±1.45
16	78.4±4.44	80.1±2.97	64.1±3.51	51.8±1.63	76.4±3.38	82.5±3.81	69.8±4.84	71.5±2.72	82.0±2.89	57.0±2.58	67.8±2.84	66.5±3.79	71.8±1.85
20	82.6±3.41	82.5±2.17	66.9±3.37	59.5±0.84	80.6±4.82	85.7±4.59	74.6±3.99	78.6±3.14	91.3±3.66	64.7±1.71	73.6±4.09	71.8±2.16	80.2±1.14
24	87.6±3.80	88.2±2.86	75.3±1.79	67.1±0.41	86.0±3.82	87.3±4.90	81.7±2.70	86.0±4.52	97.0±3.89	72.0±3.04	80.2±3.80	77.1±3.15	93.5±1.12
f2	45.60	48.69	45.81	36.04	59.48	47.22	51.51	63.66	66.43	46.81	58.12	65.19	--

Table 5: *In-vitro* **drug release kinetics of the formulation F9**

Formulation	Zero order	First order	Higuchi	Korsmeyer-peppas	Drug release mechanism
	r2	r2	r2	n	
F9	0.928	0.966	0.995	0.601	Non-fickian diffusion

the similarity factor of 66.43. Formulation F9 consists of more concentration of SCMC than that of other formulations and its concentration was distributed in the ratio of 3:1 in intra granulation and extra granulation. This formulation was also having the combination of diluents MCC PH101 and MCC PH102 in the ratio of 3:1. The earlier studies were performed with same method but they didn't confirm their results by significant studies and similarity factor studies. All the formulations were sustained the drug release for desired time of 24 h but didn't show significant drug release except F9 ($p<0.05$). The formulation F9 showed significant and maximum drug release in 24 h followed by it was subjected to kinetic studies and it was also a more than that of the innovator.

Drug release kinetics

The drug release kinetics was performed for the formulations F9 and followed first order kinetics, particularly showed the drug release mechanism of diffusion with non-fickian transport (Table 5).

CONCLUSION

Extended drug delivery system is an approach to improve the therapeutic effect of potent drugs. In this study PMPL extended release tablets were prepared for the monotherapy of parkinson's disease and the dosing frequency of the drug was reduced from three times a day to once a day due to the extended release formulation, hence an objective of this study was achieved. Based on the experimental results, formulation F9 showed the better drug release for a period of 24 h with the maximum drug release of 97% and similarity factor of 66.43. Drug release mechanism was found to be diffusion with non-fickian transport. When compared to the marketed product, formulation F9 showed better results, hence there is a lot of scope for future *in-vivo* studies.

ACKNOWLEDGEMENT

None

CONFLICT OF INTEREST

Authors declared that there is no conflict of interest.

ABBREVIATIONS USED

ER: Extended release; **PMPL:** Pramipexole; **AR:** Angle of repose; **BD:** Bulk density; **TD:** Tapped density; **CI:** Carr's index; **HR:** Hausner's ratio; **SCMC:** Sodium carboxy methyl cellulose; **MCC:** Micro Crystalline Cellulose; **HPMC K4M:** Hydroxy propyl methyl cellulose K4M; **HPMC K100M:** Hydroxy propyl methyl cellulose K100M; **HPMC E3CPS:** Hydroxy propyl methyl cellulose E3CPS; **FTIR:** Fourier Transform Infrared; **RMG:** Rapid Mixer Granulator; **RP-HPLC:** Reverse Phase-High Pressure Liquid Chromatography; **ANOVA:** Analysis of Variance; **Avg:** Average; **SD:** Standard deviation.

REFERENCES

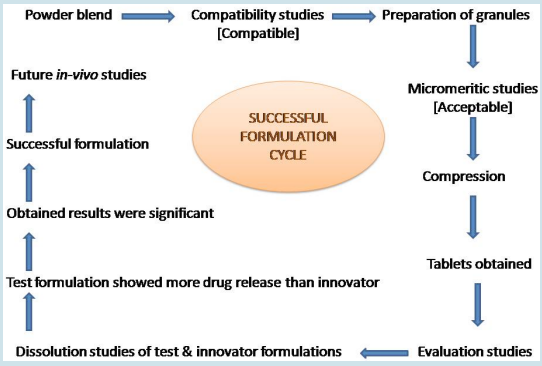
1. Venkateswarlu K, Shanthi A. Formulation and evaluation of sustained release Glipizide matrix. IOSR J Pharm Biol Sci. 2012;2(5):17-23. https://doi.org/10.9790/3008-0251723.
2. Chauhan MJ, Patel SA. Formulation Optimization of Pramipexole Dihydrochloride Prolong Release Tablets by Implementation of Design of Experiment Tool. Inventi Impact: Pharm Tech. 2013;2013(1):55-60.
3. Sudhamani T, Dande JK, Rajarajan S. Formulation and *in vitro* optimization of extended release tablets of Pramipexole dihydrochloride monohydrate for Parkinson's disease. Int J Pharm Sci Res. 2014;5(3):874-81.
4. Rakesh SSS, Anbazhagan S, Basaveswara Rao MV. Joginapalli Sreekanth. Design and Evaluation of Extended Release Tablets of Pramipexole dihydrochloride monohydrate. Int J Pharm Sci Rev Res. 2015;30(1):361-6.
5. Venkateswarlu K, Preethi JK. Formulation development and *in vitro* evaluation of mouth dissolving tablets of pioglitazone hydrochloride. Pharmatutor. 2016;4(12):37-42.
6. Venkateswarlu K. Fabrication and Evaluation of Glibenclamide Microspheres for Sustained Release. Int J Pharm Pharmacogn Res. 2017;5(2):78-87.
7. Venkateswarlu K, Chandrasekhar KB, Ramachandra R. Development and *in-vitro* Evaluation of Reconstitutable Suspension of Flucloxacillin. Marmara Pharm J. 2016;20(3):280-7. https://doi.org/10.12991/mpj.20162082023.
8. Venkateswarlu K, Chandrasekhar KB. Formulation and *in-vitro* evaluation of lacidipine oral disintegrating tablets: enhancement of solubility and dissolution rate. Int J Life Sci Pharm Res. 2016;6(2):16-26.
9. Venkateswarlu K, Thirumalesh Naik SB, Chandrasekhar KB. Formulation and *in vitro* evaluation of orlistat orodispersible tablets for enhancement of dissolution rate. Int J Pharm Pharm Sci. 2016;8(4):236-41.
10. Naik TSB, Venkateswarlu K, Chandrasekhar KB. Formulation and *in vitro* evaluation of Pregabalin mini tablets for sustained release. Pharm Lett. 2016;8(2):277-83.
11. Venkateswarlu K, Chandrasekhar KB. Development of stavudine sustained release tablets: *in-vitro* studies. Future J Pharm Sci. 2016;2(2):37-42. https://doi.org/10.1016/j.fjps.2016.08.002.
12. Venkateswarlu K, Preethi JK, Kiran BSS. Formulation Development and *in vitro* Evaluation of Floating Tablets of Ciprofloxacin HCl. Asian J Pharm. 2016;10(4):271-8.
13. Venkateswarlu K, Chandrasekhar KB. Development and Statistical Optimization of Sustained Release Gastro Retentive Floating Tablets of Cephalexin. Marmara Pharm J. 2016;20(2):172-83. https://doi.org/10.12991/mpj.20162070534.
14. Thirumalesh Naik SB, Venkateswarlu K, Chandrasekhar KB. Formulation and in-vitro evaluation of orodispersible tablets of olanzapine for the improvement of dissolution rate. J Chem Pharm Res. 2016;8(1):177-81.
15. Vijayabhaskar K, Venkateswarlu K, Thirumalesh Naik SB, Kiran Jyothi R, Nethra Vani G, Chandrasekhar KB. Preparation and *in vitro* Evaluation of Ranitidine Mucoadhesive Microspheres for Prolonged Gastric Retention. Br J Pharm Res. 2016;10(2):1-12. https://doi.org/10.9734/BJPR/2016/22670.
16. Venkateswarlu K, Rangareddy A, Naga Mallikarjuna Raja B, Hemraj Sharma, Kanaka Narasimhaiah. A validated stability indicating RP-HPLC method for estimation of Armodafinil in pharmaceutical dosage forms and characterization of its base hydrolytic product. Pak J Pharm Sci. 2017;30(1):023-8.
17. Venkateswarlu K, Preethi JK, Kiran BSS. Formulation Development and *In-vitro* Evaluation of Floating Tablets of Ciprofloxacin HCl. Asian J Pharm. 2016;10(4):271-8.
18. Mukesh CG, Krishnakant GS, Neelima RM, Chirag DS, Vinita UV, Rikita KD. Assessment of Similarity Factor Using Different Weighting Approaches. Dissolution Tech. 2005;12(4):22-7. https://doi.org/10.14227/DT120405P22.
19. Thirumalesh Naik SB, Venkateswarlu K, Chandrasekhar KB. Formulation and

evaluation of Oxybutynin chloride extended release matrix tablets. Indo Am J Pharm Res. 2016;6(01):4179-84.

20. Nirosha M, Kishore Kumar Reddy B, Heerasingh T, Manasa S. Formulation and *in vitro* Evaluation of Quetiapine Fumarate Extended Release Tablets using Natural Polymers. Lat Am J Pharm. 2017;36(2):392-8.

21. Venkateswarlu K, Preethi JK, Chandrasekhar KB. Formulation and *in-vitro* evaluation of loperamide immediate release tablets by liquisolid technique. Adv Pharm Bull. 2016;6(3):385-90. https://doi.org/10.15171/apb.2016.050 ; PMid:27766222 PMCid:PMC5071801.

PICTORIAL ABSTRACT



SUMMARY

- The extended release tablets of Pramipexole were successfully prepared and evaluated.
- All the pre and post compression parameters were complied with the official limits. All the formulations showed extended release of drug for the desired time of 24 h but the formulation F9 showed maximum drug release of 97% within 24 h.
- When compared to the innovator drug, the developed formulation showed more drug release with the similarity of 66.43.
- F9 followed first order kinetics and particularly diffusion with non-fickian transport mechanism

ABOUT AUTHORS

Mr. Kambham Venkateswarlu: Has completed his masters in Pharmaceutical Sciences (Pharmaceutics) from Jawaharlal Nehru Technological University Anantapur, Ananthapuramu, Andhra Pradesh, India and also completed more than 30 certifications from various international organizations like World Intellectual Property Rights Organization [WIPO], Switzerland and Alison, Ireland. He is also a recipient of Two Honorary Doctorates from LADC Institute, USA. Recently his biography was listed in Marquis Who's Who in the World as top 3% biographies in the country and also recipient of more than 10 National and International Awards. He has authored 5 International Books and more than 60 international scientific publications, amongst those, more than 15 were published in SCI indexed journals and also presented more than 10 scientific papers in various national and international conferences or seminars. He is also a one of the regular article writers for business magazines such as South Asia Ingredients magazine and member in several pharmacy associations like IPA etc. He is also acting as a Reviewer for the well known publishers such as Bentham Sciences, Science Domain International and some other ESCI Indexed journals such as Marmara Pharmaceutical Journal etc. He is involving in research since July-2012 [>4 Years] and these have been achieved within the span of 25 years of age.

Mr. Heerasingh Thakur: Worked as a Drug Safety Scientist in cognizant Technology Solutions, Hyderabad, Telangana. He has published one research article and 3 articles are under process.

Mr. Thumati Nagendra Bhaskar Babu: Is pursuing his PhD in GITAM Institute of Pharmacy, GITAM University, Visakhapatnam, A.P., India.