Available online at www.pelagiaresearchlibrary.com

Pelagia Research Library

Der Pharmacia Sinica, 2012, 3 (1):111-116

Der Pharmacia Sinica
ISSN: 0976-8688
CODEN (USA): PSHIBD

Formulation and Evaluation of Pseudoephedrine hydrochloride Extended Release Tablets

Vamshi Krishna Madishetty[1*], Vijaya kumar Bontha[1], Anitha Kakkerla[2]. Raju Koraboina[2]

[1]Department of pharmaceutics, Jangoan Institute of Pharmaceutical Sciences, Jangaon, Warangal, Andhra Pradesh, India
[2]Deparment of Pharmaceutics, Talla Padmavathi Pharmacy College, Warangal, Andhra Pradesh India.

ABSTRACT

The formulation of pseudoephedrine Hydrochloride (HCl) extended release was prepared by using different polymers (HPMC and ethocel) and with different diluents (dibasic calcium phosphate anhydrous, dibasic calcium phosphate dihydrate, lactose anhydrous and DCL-15). The experimental work including preformulation studies, formulation development and evaluation. The results of the present study point out that the type and level of excipients influence the rate and extent of pseudoephedrine HCL extended release. The insoluble diluents especially dibasic calcium phosphate causes that the drug to be release at a slower rate and to lesser extent than the soluble diluents (lactose) was investigated. The effect of pseudo polymorphic form of dibasic calcium phosphate on the dissolution profile was studied. Analysis of dissolution profile on the basis of Higuchi's model suggested that the drug release mechanism basically swelling and diffusion controlled.

Key words: Pseudoephedrine HCl, Hydroxyl propyl methyl cellulose, Extended release, Release kinetics, Pseudo polymorphism.

INTRODUCTION

The extended release dosage form of pseudoephedrine HCl was formulated in such a manner to make the availability of the drug over an extended period of time following administration[1,2]. A typical controlled release system is designed to provide constant or nearly constant drug levels in plasma with reduced fluctuations via slow release over an extended period of time [3,4].

Pseudoephedrine is a sympathomimetic amine that is; its mechanism of action relies on its indirect action on the adrenergic receptor system. It has weak agonistic activity at α and β adrenergic receptors. Its foremost mechanism of is to cause to release of endogenous noradrenalin from storage vesicles in pre synaptic neurons. This pseudoephedrine is used to alleviate the symptoms of seasonal allergic rhinitis associated with sneezing, nasal and lachrymal secretion. When the pseudoephedrine administered the vasoconstriction in the nasal mucus membrane, reduces tissue hyperemia, edema and nasal congestion. Other beneficial effects may include increasing the drainage of sinus secretions and opening of obstructed Eustachian tubes [5,6].

The present work aim to develop extended release matrix tablet of pseudoephedrine HCl using different polymers and excipients.

MATERIALS AND METHODS

Pseudoephedrine HCL complimentary sample from natco pharma, Hyderabad. HPMC K100M and DCP[natco pharma]. Ethocel from glennmark pharmaceuticals pvt ltd, Mumbai. Sodium stearate from S.D fine chemicals, Mumbai. Aerosil from Merck specialties, Mumbai.

Formulation of tablets:

- pseudoephedrine HCl , HPMC K100M, ethyl cellulose, PVP K-30, directly compressible lactose(DCL-15), lactose anhydrous, DCP anhydrous, DCP dihydrate, talc, colloidal silicon dioxide, magnesium stearate were weighed according to the table given for formulations (P1 to P9) and passed through #40 sieve.
- The above material was loaded into double cone blender and mixed at 30rpm for 15 min.
- Slugs were prepared by using rotary tablet compression machine by using 12mm flat punches and reduce the size by using cutter mill.
- The prepared granules were passed through #24 sieve.
- Required amount of magnesium stearate was added to above granules and blended in double cone blender for 2 min at 30rpm.
- At final lubricated granules were compressed to tablets by using rotary tablet compression machine using 8mm round flat punches.

Table No.1: Formulation Development of Pseudoephedrine HCl ER Tablets

S. No.	Trials				
	Method of Formulation	**slugging**	**Slugging**	**Slugging**	**Slugging**
	Ingredients	P1	P2	P3	P4
1	Pseusdoephedrine HCl	120	120	120	120
2	Talc	5	4	4	4
3	Magnesium stearate	2	2	2	2
4	Colloidal silica	3	2	2	2
5	HPMC K100M	160	160	160	160
6	Ethyl cellulose	40	40	40	40
7	DCL -15	50	-	-	-
8	PVPK-30	20	20	20	20
9	Lactose anhydrous	-	50	35	25
10	DCP anhydrous	-	-	15	25
11	Magnesium stearate	-	2	2	2

Table No.2: Formulation Development of Pseudoephedrine HCl ER Tablets

S.No.	Trials					
	Method of Formulation	**Slugging**	**Slugging**	**Slugging**	**Slugging**	**Slugging**
	Ingredients	P5	P6	P7	P8	P9
1	Pseusdoephedrine HCl	120	120	120	120	120
2	Talc	4	4	4	4	4
3	Magnesium stearate	2	2	2	2	2
4	Colloidal silica	2	2	2	2	2
5	HPMC K100M	160	160	160	160	160
6	Ethyl cellulose	40	40	40	40	40
7	PVPK-30	20	20	20	20	20
8	Lactose anhydrous	-	45	15	25	-
9	DCP anhydrous	50	-	-	-	-
10	DCP dihydrate	-	5	35	25	50
11	Magnesium stearate	2	2	2	2	2

RESULTS AND DISCUSSION

The formulation of pseudo ephedrine HCl extended release tablets prepared by using different polymer(HPMC, Ethocel) with different diluents (DCP, Talc, lactose anhydrous and DCL-15) and then evaluated for post compression parameters in-vitro drug release kinetics.[7].

Table No.3. Post compression study of pseudoephedrine HCl ER tablet

Trails	Average Wt (mg)	Thickness (mm) (Mean ± S.D.)	Hardness (kg/cm^2)	Friability	Drug content (in %) (Mean ± S.D.)
P1	395-410	4.01±0.1	4-6	0.21	101.53 ± 7.89
P2	394-409	4.02±0.2	4-6	0.45	98.58 ± 0.99
P3	397-408	4.01±0.4	4-6	0.78	97.22 ± 1.78
P4	396-409	4.04±0.3	4-6	0.41	99.29 ± 1.07
P5	396-404	4.02±0.2	5-6	0.12	99.24 ± 2.68
P6	396-405	4.01±0.3	5-6	0.65	96.24 ± 0.81
P7	395-406	4.02±0.1	5-6	0.73	97.90 ± 1.92
P8	396-403	3.98±0.2	5-6	0.63	101.18 ± 1.84
P9	396-402	4.04±.03	4-6	0.53	100.54 ± 1.35

In-vitro dissolution study of pseudoephedrine HCl ER tablet

Table No.4. comparative dissolution profile of extended release tablets containing pseudoephedrine HCl.

Time (hrs)	Cumulative % drug release									
	Inno.	P 1	P 2	P 3	P 4	P 5	P 6	P 7	P 8	P 9
2	31.81	55.96	58.75	54.24	50.23	45.26	56.26	48.45	45.24	42.28
4	55.5	77.28	68.36	66.13	62.45	55.92	73.92	64.23	56.13	50.63
6	64.23	95.88	80.65	88.65	79.08	63.63	89.23	79.6	74.23	70.56
8	77.96	99.27	90.75	95.11	88.28	78.76	97.42	89.26	89.62	85.66
10	86.96	99.65	98.05	97.16	92.67	89.72	99.23	96.76	100.28	92.73

Figure 1: Zero order release kinetics

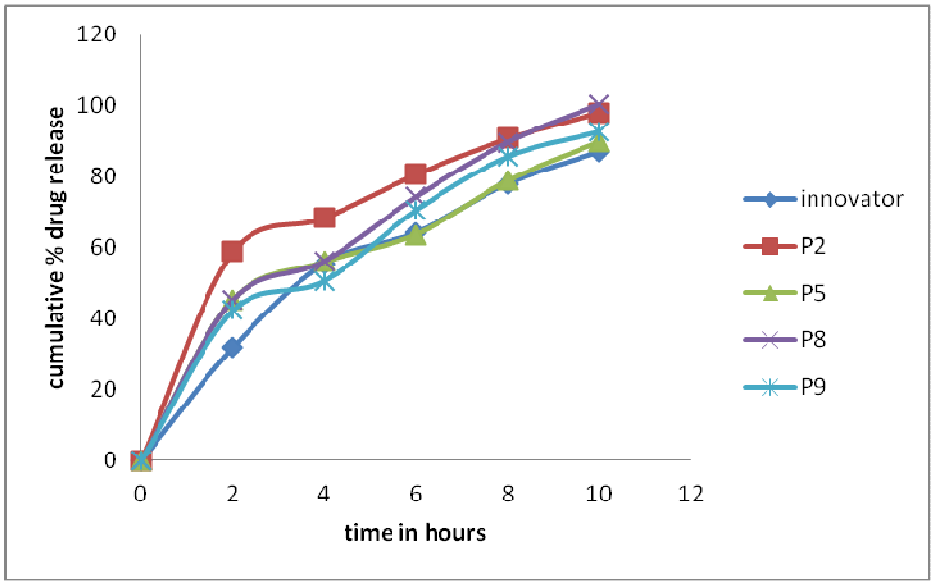


Figure 2: First order release kinetics

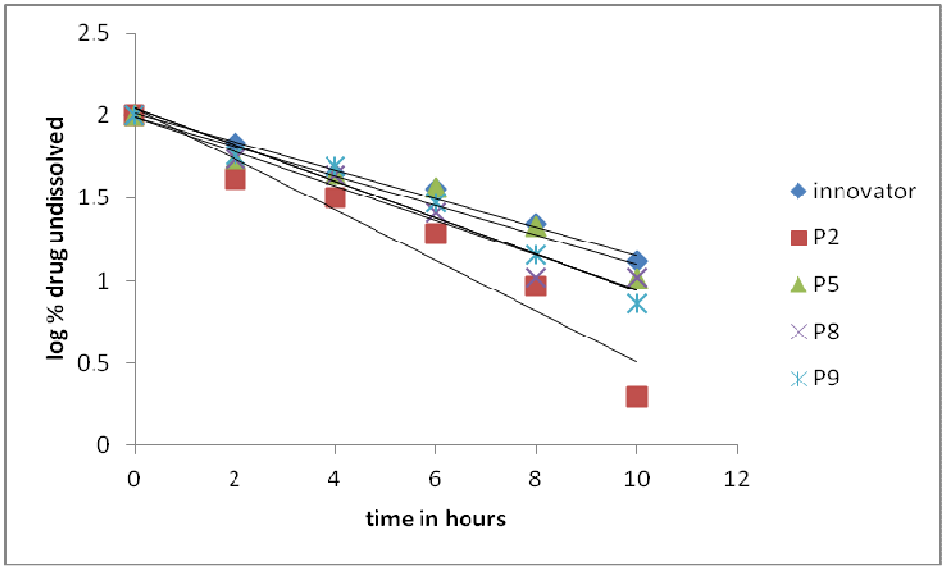
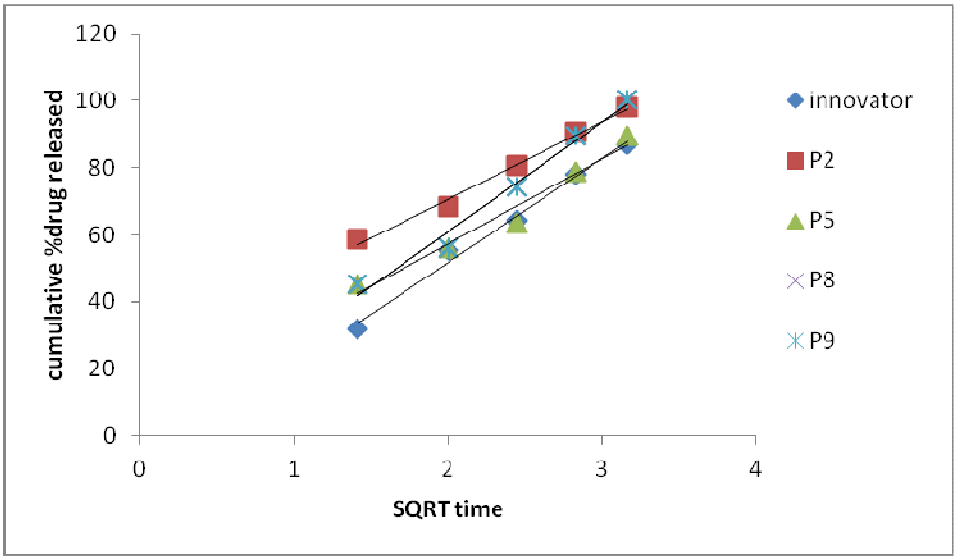


Figure 3: Higuchi model:



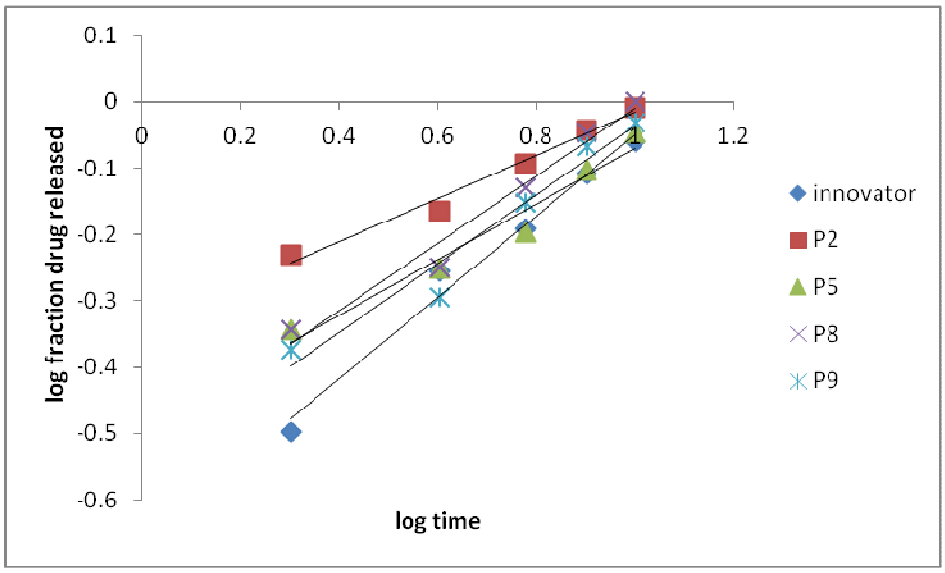
Drug release kinetics

Drug release kinetics of formulated pseudoephedrine HCl Extended Release tablets was explained by studying the results obtained from different kinetic models. The results were shown in table 4. By comparing the correlation coefficients of kinetic models several conclusions can be drawn. The correlation coefficients of all the formulations for first order release kinetics were found higher when compared to those for zero order kinetics indicating that the drug released from all the formulations followed first order kinetics. Data from the korsemayer model suggested that drug release from formulations P8 and P9 was non-fickian (anomalous) diffusion. Analysis of the dissolution profile the basis of Higuchi model suggested that drug release from P5 and P9 was basically swelling and diffusion controlled[7]. By comparing the dissolution profile of marketed formulation with formulated pseudoephedrine HCl ER tablets for similarity factor (f2) and dissimilarity factor (f1) of all formulations. Formulation P5 showed the highest f2 value 60.24 and lowest f1 value 5.313 and P9 also shown closest values to the P5.

Table No. 5- study on drug release kinetics

Formulation	Zero order	First order	Higuchi	n value
Innovator	0.981	0.994	0.994	0.614
P1	0.950	0.977	0.950	0.379
P2	0.933	0.953	0.933	0.511
P3	0.993	0.958	0.972	0.394
P4	0.993	0.996	0.993	0.400
P5	0.962	0.980	0.962	0.418
P6	0.934	0.987	0.934	0.370
P7	0.990	0.992	0.934	0.438
P8	0.988	0.988	0.990	0.510
P9	0.997	0.999	0.988	0.519

Figure 4: Korsemeyer-Peppas model:



The effect of the type of diluents used in the formulation on drug release was characterized by drug to be released slower rate and to a lesser extent than soluble excipient. The incorporation of different pseudo polymorphic form of excipients also showed a significant effect on dissolution rate[8,9]. Compare P4, P5 & P8, P9, in P4, P5 formulations consists anhydrous form of DCP and P8, P9 formulations consists dehydrate form of DCP as diluents. Comparatively dissolution rate was slowed down in case of P4, P5 in compare to P8, P9. it is may due to hydration of DCP in molecular level and strongly traps water which is absorbed by tablet initially and not utilized for drug dissolution.

In the present investigation pseudoephedrine HCl ER tablets were prepared and evaluated. The prepared tablets were checked for the quality of the tablet under uniform condition of manufacturing process. The post compression evaluation found that weight variation 400±5 mg, hardness 4-6 kg; thickness 4.0±0.2 mm; % drug content values are in the range of 95% to 102%; friability less than 1% and found to be within compendial limits prescribed. The in-vitro drug release study was carried out using USP type II dissolution test apparatus and demineralized water used as dissolution medium.

The effect of the type of diluents used in the formulation on drug release was shown a significant effect reported. The comparative study was done for drug with innovator product and results were showed in table 5.

CONCLUSION

Thus it can be concluded that the pseudoephedrine HCl ER tablets prepared by using HPMC K100M, DCP anhydrous and DCP dihydrate with optimum concentration shown in trials P5 and P9. It was found that drug release follows first order kinetics and mode of release is swelling and diffusion controlled. The results of this study provide useful information in formulation optimization during development of controlled release tablet formulations.

REFERENCES

[1] Alfonso RG, Remington's, The science and practice of pharmacy, 20th edition, pp.903-929.
[2] Leon Shargel, Phd, Rph, Applied Biopharmaceutics and Pharmacokinetics, 5th edition, **2005**, pp.37, 45-46, 251-263.
[3] Leon lachman, Herbert A Libermann, Joseph L.Kanig, Theory and practice of industrial pharmacy, 3rd edition: pp.431-439.
[4] Owens TS, Dansereav RJ, Saker A, *Int.J.Pharm* **2005**; 288,109-122.
[5] www.drugsbank.com.
[6] Satoskar R S, Bhandarkar S D, Ainapure S S, Pharmacology and Pharmacotherapeutics, 18th edition, 262-265.
[7] Verma VS, Kaushal AM, Garg A, Garg S, *Am. J. Drug Deliv*. **2004**, 2(1), 43-57.
[8] Y. Kawashima H, Takeuchi T, Hino T, Niwa T.L, Lin F, Sekigawa M. Ohsa, *Int. J. Pharm*. **1993**, 99, 229–238.
[9] Costa P, Souse JM, *Eur. J. Pharm. Sci*. **2001**,13,123-133.
[10] Anitha K, Sandeep G, Raju J, Prabhakhar VR. *Der pharmacia sinica*, **2010**, 1(3);46-54.
[11] Shreeraj H. Shaha, Jayvadan K. Patelb, Nirav V. Patelc. *Der pharmacia sinica*, **2010**, 1(3); 232-244.
[12] Prabakaran L, Vishalini M. *Der pharmacia sinica*, **2010**,1(1);147-165.
[13] Apparao P, Jyothi, Prabhakarreddy V, Raju J, Shashidher B. *Der pharmacia sinica*, **2011**,2(3);176-192
[14] Abhijit NM, Smita KP, Atul S P, Prasad P, Nachiket S D. *Der pharmacia sinica*, **2010**, 1(2),130-135.s