Scholars Academic Journal of Pharmacy (SAJP) **ISSN 2320-4206 (Online)**
Sch. Acad. J. Pharm., 2015; 4(1): 10-15 **ISSN 2347-9531 (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublisher.com

Research Article

Formulation and In-Vitro Characterization of Methyl Phenidate Extended Release Capsules

Sudheer*, Muneer Syed, D. Srinivas Rao
K.C. Reddy Institute of Pharmaceutical Sciences, Guntur, Andhra Pradesh.

***Corresponding author**
Sudheer
Email: muneerkcrp@gmail.com

Abstract: The present work involves Controlled release Methylphenidate Hydrochloride capsules development in order to meet the required bio-availability and its *in-vitro* release pattern and the preformulation studies, Physical drug excipient compatibility studies, Analytical method development, Manufacturing of capsules filled with drug loaded pellets and Evaluation procedures for pellets and capsules were studied. The size of pellets (841-1190µm) was found to be within the range of standard sieves. Bulk density of all formulations of Methylphenidate Hydrochloride pellets were found to be in the range of 0.61- 0.67 gm/ml. Tap density of all formulations of Methylphenidate pellets were found to be in the range of 0.63-0.74 gm/ml. The moisture content of all the formulations was found to be within the range of 1.52 – 1.94 %. The compressibility of all formulations was found to be within the range of 14.81-20.45. Stability studies were conducted for optimized formulation (F7) at two different storage conditions 25ºc ± 2ºC /60%RH ± 5% , 40ºC ± 2ºC /75%RH ± 5%for a period of 90 days. The formulation was found to be stable with respect to physical appearance, percentage moisture content, percentage drug content and percentage drug release. The optimized formulation has consistent release profile to provide the drug release for longer duration of 10 hours. FTIR studies have shown that there were no considerable interactions between drug and excipients. The short term stability study also indicates no change in the physical characteristic of drug content.
Keywords: Methylphenidate Hydrochloride, FTIR, Preformulation studies

INTRODUCTION

Extended release dosage forms [1-5] were designed to achieve a prolonged therapeutic effect by continuously releasing the drug over an extended period of time after administration of a single dose. Extended release dosage form allows at least two fold reduction in dosage frequency as compared to that drug presented in conventional dosage forms.

A controlled drug delivery system [6-7] was usually designed to deliver the drug at particular rate. Safe and effective blood levels were maintained for a period as long as the system continues to deliver the drug. This predetermined rate of drug release was based on the desired therapeutic concentration and the drug's pharmacokinetics.

MATERIALS &METHODS:

Methylphenidate Hydrochloride was obtained from Sun Pharma, Mumbai. Sugar Spheres (#20-#25) from Arun Pharma, Cambodia. Manufacturers of PVP k30 and PEG6000 are ISP Pharma, California and Clarient, Columbia respectively and all other chemicals used are obtained from S.D. Fine Chem. Ltd., Mumbai.

The preformulation studies like determination of melting point, solubility, and pH and partition coefficient were performed for Methylphenidate Hydrochloride and polymers.

Compatibility studies:

FT-IR Spectroscopy:

The compatibility studies were carried out by taking a mixture of drug and excipients. A part of mixture can be exposed to different storage conditions like $40^0C \pm 2^0C$ / 75% RH ±5% and control samples were to be kept at $2\text{-}8^0C$. They were tested with respect to their physical and chemical aspects. These samples were collected at regular intervals and subjected to FT-IR.

Preparation of Capsules:

Accurately weighed quantities of raw materials and measured quantities of solvents were dispensed and transferred to manufacturing area. PEG 6000 was dissolved in specific amount of water under stirred conditions. To this solution, PVP K30 was added and stirred under same conditions until a clear solution was obtained. Then Methylphenidate Hydrochloride was added under same stirred conditions

until get a clear solution.

Drug Loading

Weighed quantity of sugar spheres were loaded, and drug solution was coated onto sugar spheres.

Coating Solution Preparation [8-10]

Solution-1: Ethyl Cellulose N-45 was dissolved in specific quantity of IPA under stirred conditions. Solution-2:PEG6000 and HPMC E5 was dissolved in specific quantity of water under stirred conditions. Now the solution-2 was added to EC solution under stirring and was continued until a clear solution was obtained. Finally talc was added and stirred.

The dried pellets were loaded onto coating pan and coated with controlled release coating solution. The weight of pellets equivalent to 381mg Methylphenidate Hydrochloride were filled into hard gelatin capsules of size.1 by capsule filling machine.

Table 1: Ingredients used for the preparation of Capsule

S. No.	Ingredients	Quantity(%w/w)							
		F1	F 2	F 3	F 4	F 5	F 6	F 7	F 7
	Sugar Spheres(#20-	83.85	83.47	83.1	82.8	82.9	82.33	82.86	82.86
	Methylphenidate	10.5	10.5	10.5	10.5	10.5	10.5	10.5	10.5
3	PVP K30	3	3	3	3	3	3	3	3
4	PEG 6000	0.5	0.6	0.7	0.8	0.8	0.8	0.5	0.5
5	Purified Water	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
6	Ethyl cellulose N-45	1.5	1.75	2.0	2.0	2.0	2.5	2.3	2.3
7	HPMC E5	0	0	0	0.2	0.1	0.125	0.115	0.115
8	PEG 6000	0.15	0.175	0.2	0.20	0.2	0.25	0.23	0.23
9	IPA	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
10	Talc	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5

Evaluation of pellets

Evaluation tests for Drug Loaded Methylphenidate pellets:

a. Physical description:

0.5g of pellets were transferred into a dry Petri dish or dispensed on a white card. Observed the content visually and results of physical description are mentioned in

b. Sieve analysis:

The particle size of the pellets after drug loading was evaluated by mechanical sieving using a series of sieves with aperture size 1, 0.85, 0.71, 0.60mm. A sample load of 100g was placed on the sieve and shaken by mechanical shaker. The weight of pellets retained on each sieve were determined and mean particle size have been determined.

c. Bulk density and Tap density:

Bulk density was determined by USP method-I. 20g of pellets was taken and poured into a measuring cylinder. Bulk volume of pellets was noted results shown in Table 2.

Bulk density= Mass of pellets/ Bulk Volume.

d. Water content by KF Titration:

30ml of methanol was taken in a clean, dried Karl Fischer titration flask and titrated with KF reagent until the end point to neutralize the free water. Methylphenidate pellets were powdered finely. Accurately weighed quantity of 0.5gm of sample is transferred to the titration flask and dissolved by stirring and titrate with KF reagent to the end point and percentage water content was calculated by following formula and results were shown in Table 3.

% Water Content = V×F×100/W×100

f. Hausner's ratio:

It indicates the flow properties of powder and is measured by the ratio of tapped density to bulk density.

Hausner's ratio=Tapped density/Bulk density

Evaluation tests for capsules containing pellets

a. Weight variation test

20 intact capsules were selected randomly and weighed and average weight is calculated. Individual weight of each capsule is determined. According to USP, none of the individual capsule weight should be less than 90% and more than 110% of the average weight.

b. Lock length

The lock length can be determined by Vernier calipers. The empty capsule cap and body were measured individually to know the lock length of the capsule.

RESULTS & DISCUSSIONS

FT-IR Spectroscopy:

Methylphenidate hydrochloride, PVP K30, HPMC E5, are subjected to FT-IR spectroscopy. The FT-IR spectrums are interpreted and the functional

groups C-H-2900cm^{-1}, C=O- 1740cm^{-1}(stretching) are identified in Methylphenidate hydrochloride. The functional groups C-N, C-O-1330cm^{-1}(stretching), N-H-1530cm^{-1}(bending) are observed in PVPK30. The following functional groups are identified in HPMC E5 polymers O-H-1330cm^{-1}, C-H- 2960cm^{-1}(stretching), C=C - 1680cm^{-1}. From the spectrum of drug and excipient mixture, no interaction of drug and polymers have been observed and shown in (Fig 1-6) and % drug release shown in Fig-7.

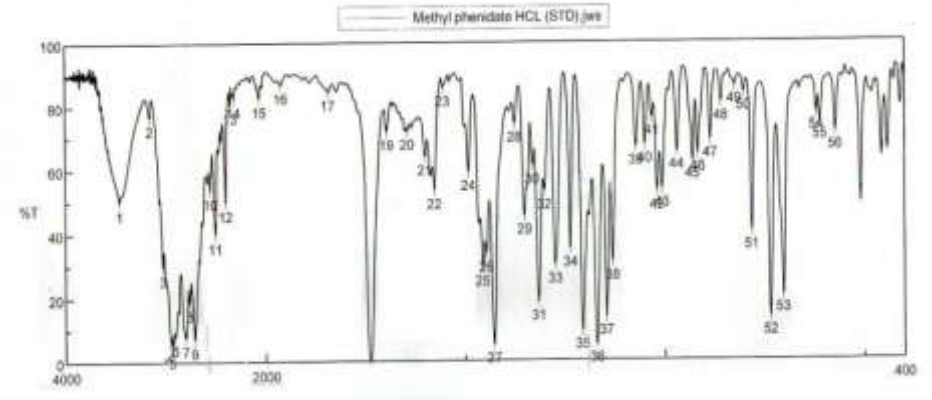

Fig 1: FTIR Spectra of Methylphenidate Hydrochloride

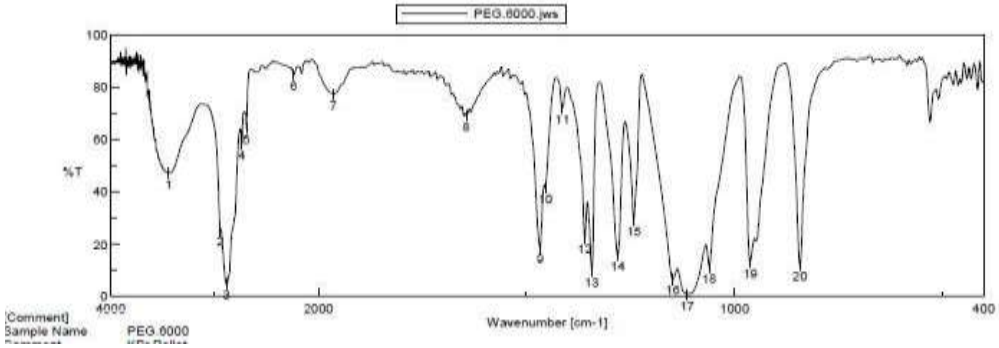

Fig 2: FTIR Spectra of PEG-6000

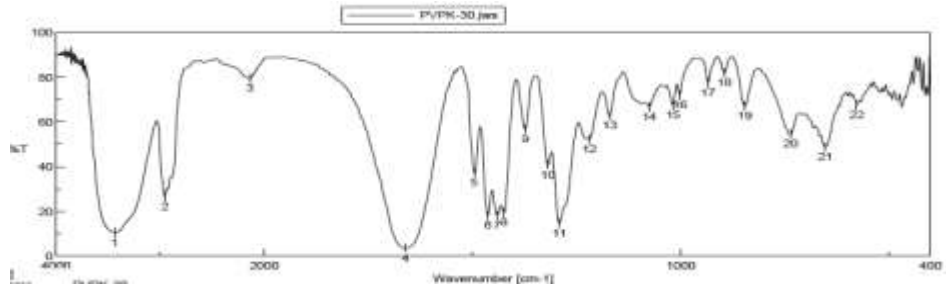

Fig 3: FTIR Spectra of PVPK-30

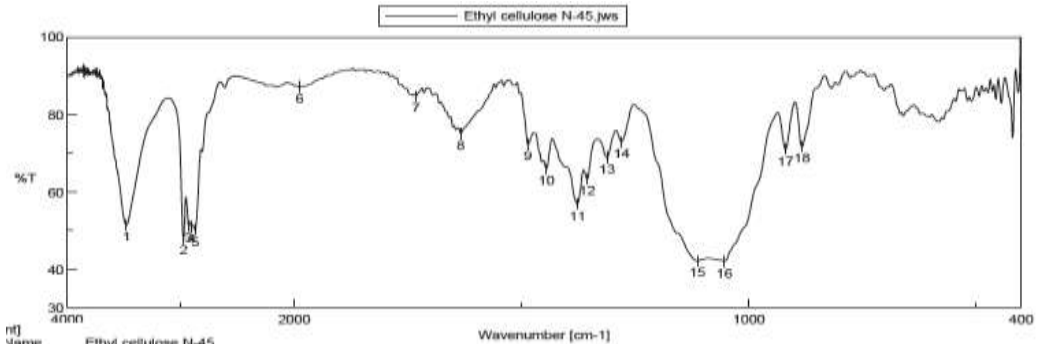

Fig 4: FTIR Spectra of Ethyl cellulose N-45

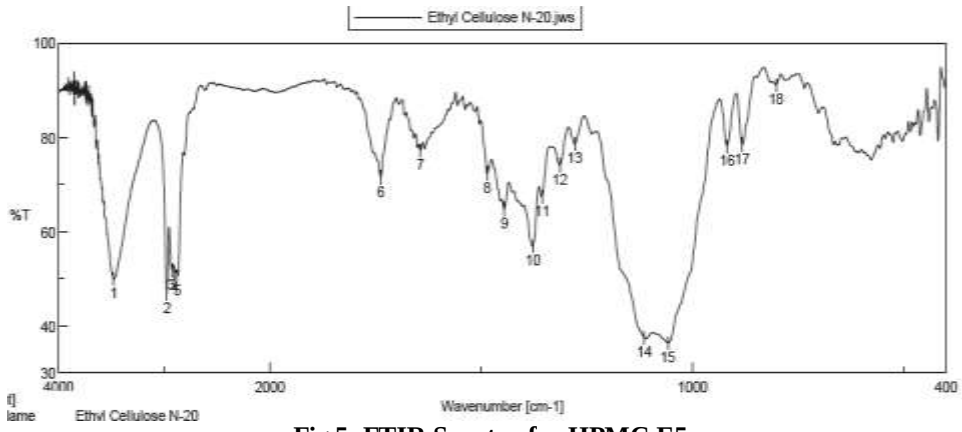

Fig 5: FTIR Spectra for HPMC E5

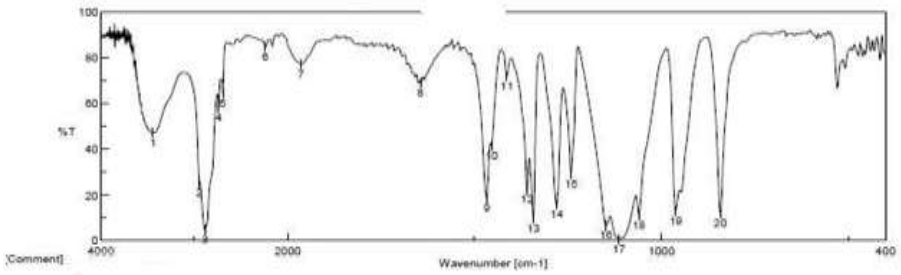

Fig 6: FTIR Spectra of Physical mixture

Evaluation of drug loaded pellets:

Physical description:

0.5g of pellets were transferred into a dry petri dish or dispensed on a white card. The contents were observed visually. It was found that Methylphenidate Hydrochloride is a white to off white powder.

Table 2: Results of Bulk density and Tap density

S. No	Formulation	Bulk Density (gm/ml)	Tap Density (gm/ml)	Hausner ratio:
1	F 1	0.89 ± 0.01	0.80 ± 0.1	1.04
2	F 2	0.83 ± 0.04	0.70 ± 0.03	1.04
3	F 3	0.82 ± 0.03	0.75 ± 0.04	1.04
4	F 4	0.81 ± 0.02	0.78 ± 0.05	1.04
5	F 5	0.84 ± 0.01	0.71 ± 0.01	1.04
6	F 6	0.88 ± 0.03	0.70± 0.04	1.00
7	F 7	0.83 ± 0.04	0.75± 0.03	1.04

Table 3: Results of % Moisture content

S. No	Formulation	% Moisture Content
1	F 1	1.94
2	F 2	1.85
3	F 3	1.82
4	F 4	1.79
5	F 5	1.73
6	F 6	1.52
7	F 7	1.52

Evaluation of capsules containing pellets:

Weight variation & drug content:

Capsules containing Methylphenidate formulations have shown the average weight & drug content uniformity in the range of 453.5-455.9 & 98.3%-100.5%.

Lock length:

Empty capsule cap length and width: 10.2mm, 6.58mm Empty capsule body length and width: 16.82mm, 6.5mm Filled capsule length and width: 19.22, 6.8mm. Lock length of the capsules containing pellets was found to be 7.8mm

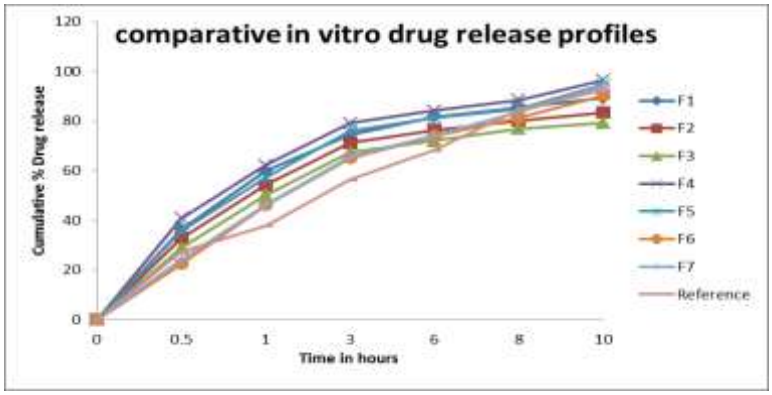

Fig 7: Comparative In-vitro drug release profiles.

Kinetic analysis of dissolution data:

The release rate kinetic data for the F7 is shown in Tabl4. As shown in Fig 8-9, drug release data was best explained by zero order equation, as the plots showed the linearity (r^2 = 0.821). As the drug release was best fitted in zero order kinetics, indicating that the rate of drug release is concentration independent.

Table 4: Results of release kinetics:

Release kinetics	R^2	Intercept	Slope
Zero order	0.821	23.91	7.734
First order	0.426	0.115	1.049
Higuchi	0.956	28.051	7.801
Korsmeyer peppas	0.818	-0.739	1.809

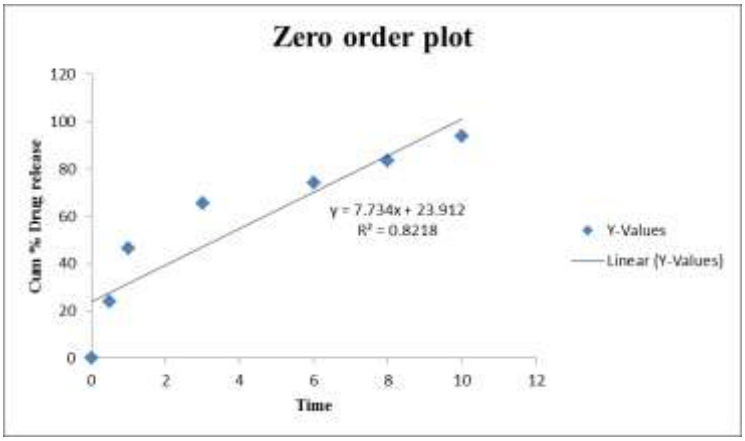

Fig 8: Zero Order Graph of Optimized Formulation (F7)

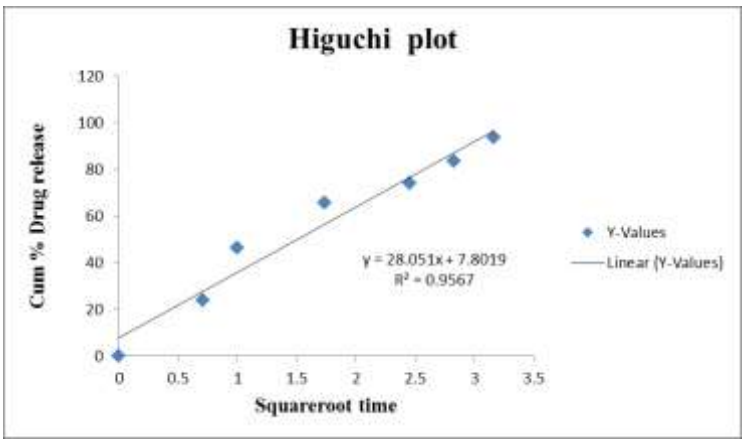

Fig 9: Higuchi Plot of Optimized Formulation (F7)

CONCLUSION

In the present study, the optimized formulation has consistent release profile to provide the drug release for longer duration of 10 hours. The short term stability study also indicates no change in the physical characteristic of drug content and the comparison of dissolution profiles between the Methylphenidate Hydrochloride extended release capsules 40mg and the reference drug, showed no major changes in the dissolution profiles. Hence, it can be concluded that the Methylphenidate Hydrochloride extended release capsules were successfully developed and evaluated.

REFERENCES

1. Chein Yie W; Novel Drug Delivery System 2nd Edition Marcel Dekker., New York, 1992, p: 139.
2. Nagaraju R, Jwapna Y, Hari B R, Rajesh K; Design and evaluation of delayed and extended release tablets of mesalamine**.** Journal of Pharmaceutical Science and Technology, 2010; 2(1):103-110.
3. Liebermann HA, Kanig JL, Febige L; The theory and practices of industrial pharmacy. 3rd ed. Bombay: Varghese publication. 1987;293-294.
4. Jain K; Gastroretentive Drug Delivery in progress in controlled and novel drug delivery system, 1st edition., CBS Publisher and distributer, new Delhi., 2004; 82-90.
5. Allen LV, Ansel HC; Pharmaceutical dosage forms and drug delivery systems. Lippincott Williams & Wilkins. 2013; 268.
6. Chein YW; Controlled and modulated drug delivery systems, Encyclopedia of Pharmaceutical Technology. New York: Dekker; 1990; 281-313.
7. Abdul S, Chandewar AV, Jaiswal SB; A flexible technology for modified-release drugs: Multiple-unit pellet system. Elsevier Journal of Controlled Release, 2010; 147(1):2–16.
8. Srivastava S, Mishra G; Fluid Bed Technology: Overview an parameters for process selection. International Journal of Pharmaceutical Sciences and Drug Research, 2010; 2(4):236-246.
9. Thoma K, Bechtold K; Influence of aqueous coatings on the stability of enteric coated pellets and tablets. European Journal of Pharmaceutics and Biopharmaceutics, 1999; 47(1):39–50.
10. Altaf AS; Modified release capsules of Ambroxil prefprmulation and evaluation. Pelagia Research Library, 2011;2(3):1-19.