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FORMULATION AND EVALUATION OF DELAYED RELEASE TABLETS OF IMIDAPRIL USING HYDROXY PROPYL METHYL CELLULOSE

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Abstract

In this insight of designing delayed release tablets of imidapril, results were can be conducive as the formulated tablets gave satisfactory results for various physicochemical parameters like hardness, friability, thickness, weight variation and content uniformity. Here in this study HPMC and cellulose acetate acts as barriers to release the drug after a desired lag time. Imidapril Core in cup tablet shows a delayed release pattern. Out of all the formulations F8 was found to be efficient and it was optimized based on its drug release pattern. It was observed that P4 F8 formulations were found to shows maximum drug release and it was optimized due to its release after a lag time. The physicochemical interactions between the drug and the polymer was studied by the FTIR studies and found to be no interactions.

Keywords: Delayed release tablets, Imidapril, HPMC, compatibility studies.

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INTRODUCTION

Traditionally, Drug delivery means simple chemical absorbed from the gut or from site of delivery. However, living organisms are not zero order in their requirement or response to drugs. These systems are referred as most potent which acts according to circadian cycle and exhibits desired pharmacological action with reduced side effects. Diseases targeted for chronopharmaceutical formulations need enough scientific background of chronopharmaceutical drug delivery system. Certain diseases or disorders include cardiovascular diseases, hypercholesterolemia, ulcer, asthma, arthritis, duodenal ulcer, cancer, diabetes, and neurological diseases [1-9]. If the organization in time of living system including man is borne in mind, it is easy to conceive that not only must the right amount of the right substance be at right place but also this must occur at the right time. According to the numerous studies revealed that the drug side effects or kinetics of the drug can be modified by such circadian time & or the timing of drug application within 24 hrs of a day.

MATERIALS AND METHODS

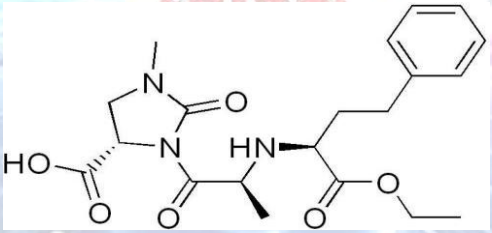

Fig. 1: Structure of Imdidapril Hydrochloride

Drug-Excipient Compatibility Study

IR studies was performed to characterize the physic-chemical interactions between the drug and polymer.1-2 mg of solid fine powder of drug and 200-300 mg of dry powder of KBr (IR grade) were taken in a mortar and mixed well with the help of a spatula. FTIR spectrophotometer is the instrument which is used for Spectrum measurement at a wavelength region of 4000-400cm^{-1} using KBr disk method now thus obtained IR spectra is compared with the standard drug spectra to determine whether any interactions between the polymers and drug [10-13]. Imidapril is obtained from Chandra Labs, Hyderabad, Cross povidone, Talc, from MYL CHEM Mumbai, Magnesium stearate, MCC, Cellulose acetate from S.D Fine chem. LTD.

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Formulation of core tablets by direct compression

Direct compression method is used for the preparation of the inner core tablets. As shown in Table powder mixtures of imidapril, microcrystalline cellulose , cross-carmellose sodium (Ac-Di-Sol) ,SSG, crospovidone ingredients were dry blended for 20 min which is followed by addition of Magnesium Stearate. The mixtures were then further blended for 10 min., KBr hydraulic press is used for the compression of 180mg of resultant powder at a pressure of 1 ton, with a 8mm punch and die to obtain the core tablet [14-21].

Table 1: Composition of core tablets

Ingredients	F 1	F2	F 3	F 4	F5	F6	F7	F8	F9
Imidapril	10	10	10	10	10	10	10	10	10
Crospovidone	9	13.5	18	-	-	-	-	-	-
CCS	-	-	-	9	13.5	18	-	-	-
SSG	-	-	-	-	-	-	9	13.5	18
Magnesium stearate(1%)	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8
MCC	159.2	154.7	150.2	159.2	154.7	150.2	159.1	154.7	150.2
Total wt	180mg	180mg	180mg	180mg	180mg	180mg	180mg	180mg	180mg

Formulation of Core in Cup Tablets by direct compression:

The cellulose acetate propionate coating cup which is impermeable was applied around the core tablet and the composition of the impermeable membrane composition. The 12 mm diameter is filled with the 100mg of cellulose acetate propionate powder to form a flat surface powder bed by gentle compaction. Now the core tablet is place in the middle of the powder bed inside the cavity and again it is surrounded with the remaining amount (60 mg) of the coating powder tocover fully the core tablet with the coating material. On the top, hydrophilic polymer (HPMC) was added and the bed was compressed directly by using 12mm flat punch to produce the desired core-in-cup system.

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In-vitro Dissolution methods for Imidapril core in cup tablets

In –vitro Dissolution studies of Pulsatile delivery systems was done with the conventional paddle method of press coated tablets were performed at 37 ± 0.5 °C using phosphate buffer pH 6.8 in USP II paddle method at 50 rpm. at pre-determined time intervals 5 ml of aliquot was withdrawn and filtered, now it is replaced with the fresh dissolution medium maintaining the temperature constant. UV spectrophotometer is used to analyze the samples at 238nm [21-26]. The lag time and percentage release was determined of the each formulation.

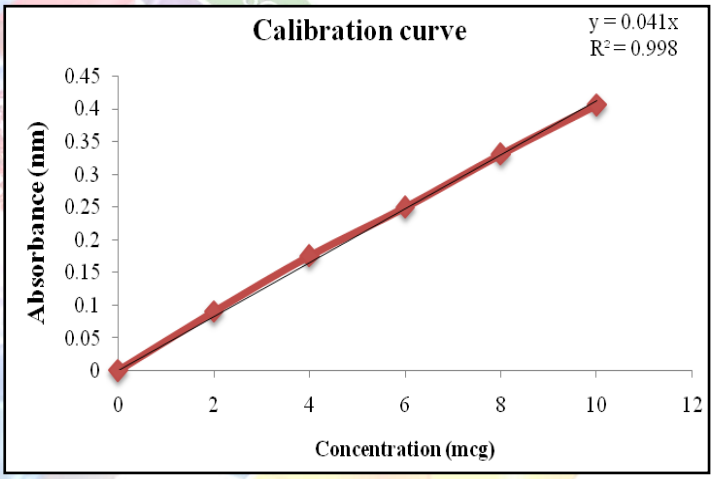
RESULTS AND DISCUSSION

Calibration curve of Imidapril in phosphate buffer

Table 2: Concentration and absorbance of Imidapril in phosphate buffer

Concentration in mcg	Absorbance at 238nm
0	0
2	0.090
4	0.175
6	0.249
8	0.330
10	0.405

Fig. 2: Calibration curve for Imdidapril



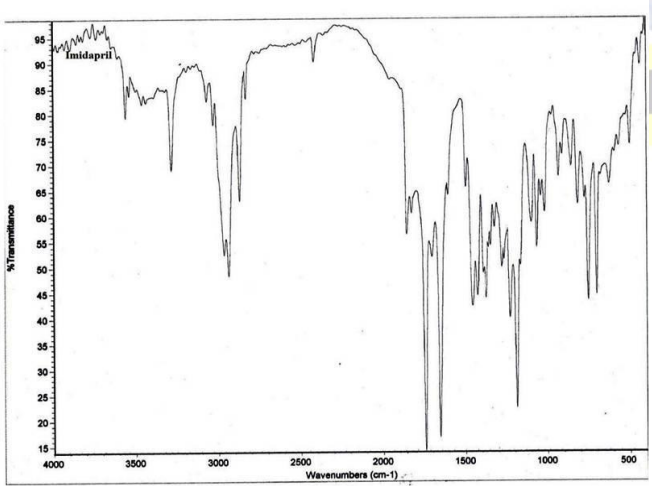


Fig.3: FTIR of the Imidapril

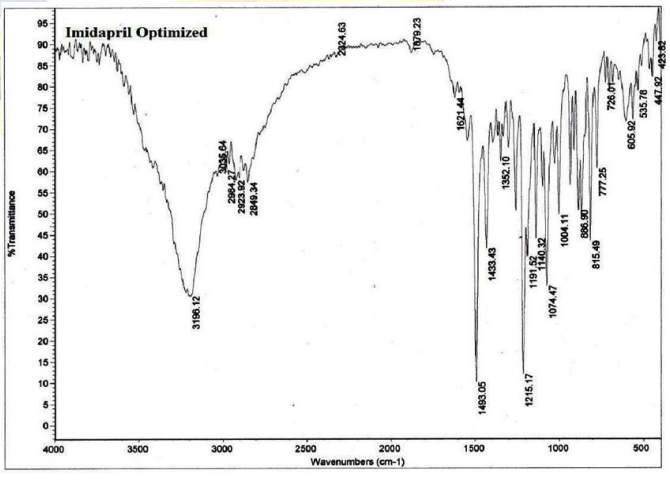


Fig. 4: FTIR of the Optimized Imidapril formulation

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Table 3: Dissolution for core tablet

Dissolution Time (Min)	Core formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
5	30	33	25	27	28	33	32	40	35
10	42	44	35	35	38	42	40	62	45
15	55	68	42	48	50	53	52	75	55
20	64	77	58	56	58	60	62	82	65
30	75	81	69	68	70	71	70	97	74
45	84	96	78	80	82	84	82	-	86
60	94	101	85	88	91	91	92	-	94

Table 4: Physical Evaluation Parameters for Core Tablets

S. No	Physical parameter	F 1	F 2	F 3	F 4	F 5	F 6	F 7	F 8	F 9
1	**Weight variation**	181	180	180	179	178	180	182	180	180
2	**Hardness (Kg/cm^2)**	4	4.2	4.3	4.1	4.3	4.4	4.2	4.3	4.4
Other Parameters										
3	**Thickness (mm)**	3.25	3.22	3.24	3.24	3.4	3.50	3.20	3.18	3.26
4	**Friability %**	0.4	0.55	0.62	0.54	0.62	0.57	0.65	0.52	0.54
5	**Disintegration time**	3 min 55se	3min 30 sec	2min	2min 30sec	2min 12sec sec	1 min30 sec	1min 30 sec	1min	1min 45 sec

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CONCLUSION

In this stand point and the above experimental results it can be concluded that, Formulated tablets gave satisfactory results for various physicochemical parameters like hardness, friability, thickness, weight variation and content uniformity. HPMC and cellulose acetate has predominant effect on the lag time, while also shows significant effect on drug release. Imidapril Core in cup tablet shows a delayed release pattern. Out of all the formulations F8 was found to be efficient and it was optimized based on its drug release pattern. In-vitro release rate studies showed that the maximum drug release was observed in P4 F8 formulations was optimized based on less amount of drug release during lag time. FT-IR studies revealed that there was no interaction between Imidapril and the polymers.

REFERENCES

1. Listair CR, Jonathan CDS, Walter K, Richard WB, Ross JM, Howard NES, et al. Investigating the coating-dependent release mechanism of a pulsatile capsule using NMR microscopy. J Control Rel 2003; 92:341-7.
2. Samanta MK, Suresh NV, Suresh B. Development of Pulsincap Drug Delivery of salbutamol sulphate for drug tareting. Indian. Pharma Science. 62(2):102-7.
3. Seshasayan A, Sreenivasa RB, Prasanna R, Ramana Murthy KV. Studies on release of Rifampicin from Modified Pulsincap Technique. Indian J Pharma Sci 2001:337-9
4. Sangalli ME, Maroni A, Zema L, Busetti C, et al. 2001. In vitro and in vivo evaluation of an oral system for time and/or site-specific drug delivery. J Control Rel 2001; 73:103 110.
5. Zahirul Khan MI, Zeljko P, Nevenka K. A pH-dependent colon targeted oral drug delivery system using methacrylic acid copolymers. I. Manipulation of drug release using Eudragit® L100-55 and Eudragit® S100 combinations. J Control Rel 1999; 58:215 222.
6. Howard NES, Clive GW, Peter GW, Massoud B, Julei SB, Alan CP. Evaluation of PulsincapTM to provide regional delivery of dofetilide to the human GI tract. Int J Pharm2002; 236:27 34.
7. Sungthongjeen, SatitPuttipipatkhachorn, OrnlaksanaPaeratakul, Andrei Dashevsky, Roland Bodmeier. Development of pulsatile release tablets with swelling and rupturable layers. J Control Rel 2004:147 159.

DOI: 10.21276/IJIPSR.2018.06.04.685

8. Qureshi J, Amir M, Ahuja A, Baboota S, Ali J: Chronomodulated Drug Delivery System Of Salbutamol Sulphate For Treatment Of Nocturnal Asthma. Indian J Pharm Sci. 2008. May/Jun;70(3): 351-56.

9. Sadaphal K.P, Thakar V.M, Gandhi B.R, TekadeB.W **:** Formulation And Evaluation Of Pulsatile Drug Delivery System For Chronobiological Disorder: Asthma. IJDD.2011; 3: 348-56.

10. Chaudhari S.P, Kabra S.B, Ratnaparkhi M.P**:** Formulation And Evaluation Of Optimised Chrono Release Of Anti-Hypertensive Drug. Journal Of Drugs Delivery & Therapeutics; 2013; 3(4): 1-7.

11. Janugade B.U, Patil S.S, Patil S.V, Lade P.D**:**Formulation And Evaluation Of Press-Coated Montelukast Sodium Tablets For Pulsatile Drug Delivery System. IJCRGG.2009 Jul/Sep ;1(3):690-91.

12. K.Surendra, Kotaiah M.R, Rao M.P:Formulation And Evaluation Of Pulsatile Drug Delivery System Of Metoprolol Tartrate. IJPRNK. 2013;2(5):246-57.

13. Krishnaveni G, Muthukumaran M, Krishnamoorthy B:Development And Evaluation Of Pulsatile Drug Delivery System Containing Montelukast Sodium By Press Coated Tablets. Int J Adv Pharm Gen Res. 2013; 1(2):41-51.

14. M. Efentakis, Koligliati S, Vlachou M:Design And Evaluation Of A Dry Coated Drug Delivery System With An Impermeable Cup, Swellable Top Layer And Pulsatile Release. International Journal of Pharmaceutics. 2006;3(11):147-56.

15. Ratnaparkhi M.P, Khade R.B, Chaudhari S.P:Formulation And Evaluation Of Chronotherapeutic Drug Delivery System Of Meloxicam. Journal Of Drug Delivery And Therapeutics.2013;3(4):229-36.

16. Shivhare U.D, KakadeV.N :Formulation And Evaluation Of A Pulsatile Delivery System Of Losartan Potassium By Factorial Design. IJPSN.2013 Jan/Mar;5(4):1895-1901.

17. Kamat A.R, Shabaraya A.R, Mohd A, KamathK.K:Formulation And Evaluation Of Pulsatile Drug Delivery System Containing Indomethacin Using Natural Polymers. IRJP. 2013 Feb 11;4(2):111-14.

18. Bălan H. Chronotherapy of hypertension: when can be as important as with what. Rom. J Intern Med. 2008;46(4):269–274.

19. Takeda N, Maemura K. Circadian clock and cardiovascular disease. J Cardiol. 2011;57:259–256.

DOI: 10.21276/IJIPSR.2018.06.04.685

20. Smith DHG. Pharmacology of cardiovascular chronotherapeutic agents. Am J Hypertens. 2001;14:296S–301S.

21. Shigehiro O. Chronotherapeutic strategy: rhythm monitoring manipulation and disruption. Adv Drug Deliv Rev. 2010;62:859–875.

22. Smith D, Neutel JM, Weber MA. A new chronotherapeutic oral drug absorption system for verapamil (CODAS-Verapamil) designed for once daily bedtime dosing optimizes blood pressure control in the morning. Am J Hypertens.2001;14:14–19.

23. White WB, Mehrotra DV, Black HR, Fakouhi TD. Effects of controlled on setextended-release Verapamil on nocturnal blood pressure (dippers versus nondippers). COER Verapamil Study Group. Am JCardiol. 1997;80:469– 474.

24. Ruffolo RR, Feuerstein GZ, Ohlstein EH. Recent observations with β-adrenoceptor blockade beneficial effects in hypertension and heart failure. Am J Hypertens. 1998,11(1 Pt 2):9S–14S.

25. Ding X, Alani AWG, Robinson JR. Extended release and targeted drug delivery systems. In: Gennaro AR, editor, Remington: The Science and Practice of Industrial Pharmacy. 21st ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2006:993– 940.

26. Collett J, Moreton C. Modified releaseperoral dosage forms. In: Aulton ME,editor. Pharmaceutics: The Science of Dosage Form Design. 2nd ed. London, UK: Churchill Livingstone; 2002:289–306.