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Effect of Different Coating Level of Swellable Layer and Rupturable Layer on Drug Release of Time Controlled Release Tablet

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ABSTRACT:

Metoprolol Tartrate tablets consisting of core coated with two layers of swelling and rupturable coatings were prepared and evaluated as a time controlled release tablet. Cores containing the drug were prepared by direct compression using microcrystalline cellulose and Spray dried lactose (Ludipress) as hydrophilic excipients with the ratio of 1:1. Cores were then coated sequentially with an inner swelling layer of Swellable material such as Croscarmellose sodium in different coating level (10mg/cm2, 20mg/cm2 and 30mg/cm2)and an outer rupturable layer of different coating levels (1.5 mg/cm2 2.5 mg/cm2 3.5 mg/cm2) of ethylcellulose. The effect of the different coating level of swelling layer and the rupturable layer on the lag time and the water uptake were investigated. Drug release rate studies were performed using USP paddle method. Results showed the dependence of the lag time and water uptake prior to tablet rupture on the coating levels of the swelling layer and the rupturable layer. As the coating level of swellable layer increases the rate of drug release also increases. Increasing the level of ethylcellulose coating retarded the diffusion of the release medium to the swelling layer and the rupture of the coat, thus prolonging the lag time.

KEY WORDS: Metoprolol Tartrate , time controlled release, swelling layer, lag time, ethylcellulose

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INTRODUCTION:

Pulsatile drug delivery systems are characterized by two release phases. A first phase with no or little drug being released, followed by a second phase, during which the drug is released completely within a short period of time after a lag time.[1] Pulsatile delivery or time controlled release is desirable for drugs acting locally or having an absorption window in the gastrointestinal tract [2]; drugs that develop biological tolerance, where the constant presence of the drug at the site of action diminishes the therapeutic effect [3]; drugs with an extensive first pass metabolism, e.g., beta-blockers [4]; or for drugs with special pharmacokinetic features designed according to the circadian rhythm of humans [5]. Most pulsatile drug delivery systems are reservoir devices coated by a barrier polymeric coating [6,7].The coating prevents drug release from the core until the polymeric shell is completely dissolved, eroded[8,9] or ruptured[10] during/after a certain lag time, after which the drug is released rapidly from the inner reservoir core. The rupturing of the barriers are induced by an expanding core on water penetration through the barrier coating.1 The expansion can be caused by effervescent excipients [6] or swelling agents[11,12,13] .

Metoprolol Tartrate has short plasma elimination half-life i e., 3 to 4 hours and dose 50 to 100 mg, three to four times a day. During long-term therapy, the use of Metoprolol Tartrate may result in low patient compliance. This reason sometimes limits the usefulness of these agents mainly in the chronic treatment of hypertension.

This study is a trial to develop time–controlled, single-unit dosage form of Metoprolol Tartrate to overcome or diminish its limitation.

The proposed system consists of a directly compressed core tablet containing the drug and hydrophilic excipients namely, Ludipress and microcrystalline cellulose. The tablet core was then coated with two consecutive layers, an inner swelling layer and an outer rupturable coating layer. Superdisintegrants such as Croscarmellose sodium was chosen as swellable materials. Ethylcellulose (EC) was used as the rupturable coating. The effect of the level of the coating layer on the lag time, water uptake and drug release were investigated.

MATERIALS AND METHODS

Metoprolol Tartrate (Zim laboratories, Nagpur). microcrystalline cellulose (Avicel PH 102, USA), Ludipress (BASF, FRG), talc (Loba Chemie Pvt. Ltd., India), Croscarmellose sodium (Ac-Di-sol, FMC biopolymer, USA), polyvinylpyrrolidone (PVP 90 F, BASF, Germany), ethylcellulose (EC, FMC Corp., USA), were gift sample. All other reagents were of analytical grade.

Preparation of Core Tablets

The core tablets containing Metoprolol Tartrate (100 mg/tablet), Ludipress, and microcrystalline cellulose (in the ratio of 100:0, 70:30, 50:50, 30:70, 0:100 w/w.) were prepared by direct compression. All the excipient of the formulation firstly passes through the sieve no. 100. Then Metoprolol Tartrate, microcrystalline cellulose, spray dried lactose were simply mixed with each other followed by addition of magnesium stearate and talc. The core tablets (diameter, 7 mm; biconvex;; average tablet weight, 150 mg) were compressed using Pilot press tablet machine (Chamunda Pharma Machinery Pvt. Ltd., India).

Coating Core Tablets1

The core tablets were coated with two consecutive layers in a coating pan . The inner swelling layer was Croscarmellose sodium, whereas ethylcellulose was used as an outer rupturable coating layer. Croscarmellose sodium, was then dispersed in PVP alcoholic solution at a ratio of 6:1, w/w and then stirred for 30 min to obtain a homogenous dispersion prior to coating. The coating dispersion was then layered onto the core tablets in the coating pan to obtain swelling layer level 10mg/cm^2, 20mg/cm^2 and 30mg/cm^2.The coating conditions were spraying rate of 10 ml/min. using an atomizing nozzle, pan speed at 30 rpm, and inlet hot air at a temperature of 40◦C. The coated tablets were further dried in the pan for 10 min with the hot air after the coating process was finished. The tablets were then placed in an oven at 40◦C for 2 hr to remove the residual solvent. These tablets were then coated with 3.5% w/w ethanolic ethylcellulose solution, using triacetin as a plasticizer. The plasticized polymer solution was sprayed onto the tablets in the coating pan at 40◦C inlet air temperature and the same spraying rate to obtain coating levels of 1.5 mg/cm^2, 2.5 mg/cm^2 and 3.5 mg/cm^{2}of ethylcellulose.

Scanning Electron Microscopy (SEM)

The scanning of morphology of a cross-section of the time controlled release tablet of Metoprolol Tartrate was carried out by using Scanning Electron Microscopy (JSM-6360).The sample of tablet was mounted on stage and coated with gold under vacuum.

Rupture Test

The rupture test was carried out by using 900ml of phosphate buffer pH 6.8 in the dissolution apparatus USP TYPE-II at 50 rpm and temperature condition 37±0.5˚C.The sequence of rupturing of Time controlled release tablet was observed and photographs taken using a digital camera (Sony Ericsson).

Water Uptake Study

The water uptake study of time controlled release tablet of Metoprolol Tartrate was done using screw-caped container containing 100ml of phosphate buffer pH 6.8 .In this container tablet was added and placed in horizontal water bath shaker.(Remi equipments Pvt Ltd.) and temperature was maintained at 37±0.5˚C.The tablet was withdrawn at predetermined time intervals from dissolution media and weight of tablet was taken after removing the surface water by carefully blotting the tablet with tissue paper and tablet was again added to the medium. The same procedure was repeated until the rupturing of coat occurs.

$$\% \text{ water uptake} = \frac{Wt - Wo \times 100}{Wo}$$

Swelling Index

Swelling index of time controlled release tablet of Metoprolol Tartrate determined by weighing four tablets separately (m1) and each weighed tablet was placed into a beaker containing 6ml of phosphate buffer pH 6.8 at 37±0.5˚c. The tablets were removed from beaker at specified time interval and from the surface of tablet excess water was removed using tissue paper. Each swollen tablet was weighed (m2) and swelling index was calculated.

$$\text{Swelling index} = \frac{m2 - m1 \times 100}{m2}$$

Release Rate Study

In vitro dissolution studies of time Controlled release tablets of Metoprolol Tartrate were performed using USP paddle dissolution apparatus. The other conditions which were maintained throughout the test are paddle speed of 50 rpm at 37˚c using 900ml of Ph 6.8 phosphate buffer. Sample of 10 ml was withdrawn at regular interval of 60 minutes by using 10 ml of calibrated pipette upto 6hrs and then regular interval of 15min. The volume withdrawn was replaced by fresh volume of dissolution medium. The sample was analyzed spectrophotometrically at 274 nm.18 The amount of drug release was determined using calibration curve (PCP-Disso software)

RESULTS AND DISCUSSION

The scanning of morphology of a cross-section area of the time controlled release tablet of Metoprolol Tartrate was carried out by using Scanning Electron Microscopy. The photograph shows the three parts I) the dense tablet core, (microcrystalline cellulose, lactose and drug) (C), II)the more porous layer of the Ac-Di-Sol containing swelling layer (B), III) the homogeneous ethylcellulose coating as the outer rupturable coating (A).

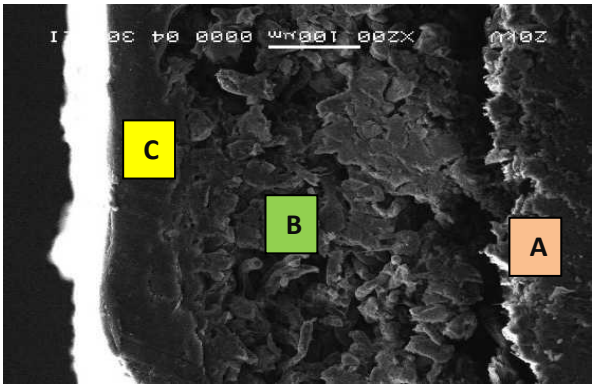


Fig No 1: The photograph shows the three parts of the tablet which are clearly visible, namely the dense tablet core, (microcrystalline cellulose, lactose and drug) (C), the more porous layer of the Ac-Di-Sol containing swelling layer (B), and the homogeneous ethylcellulose coating as the outer rupturable coating (A).

Ethylcellulose was use as outer rupturable layer because of its water insolubility, adjustable water permeability, and its mechanical properties. The swelling layer consisted of a crosscsrmellose as superdisintegrant and PolyVinyl Pyrolidine as a binder. The addition of PVP was necessary for the adherence of the swelling layer to the core surface, for the formation of continuous swelling layer. The fibrous structure of the superdisintegrant was retained during the layering process, resulting in a porous structure of the swelling layer. The rupture test was performed to follow up the rupture sequence of Metoprolol Tartrate tablet . The mechanism of membrane rupture consists of the following processes. Water is taken up by the tablet (Figure 2a) through the outer semipermeable ethylcellulose membrane and hydrates the swelling layer causing stress against the membrane (Figure 2b). As soon as stress exceeds membrane strength, the membrane destruction is initiated (Figure 2c). The drug is released through the destructive membrane to the dissolution medium (Figure 2d and 2e). Finally, the release of the drug was completed, leaving the evacuated coating membrane (Figure 2f). Ethylcellulose was reported to form a mechanically weak and semipermeable film that could rupture on exposure to the release medium and the resultant internal pressure developed within the tablet cores [6].

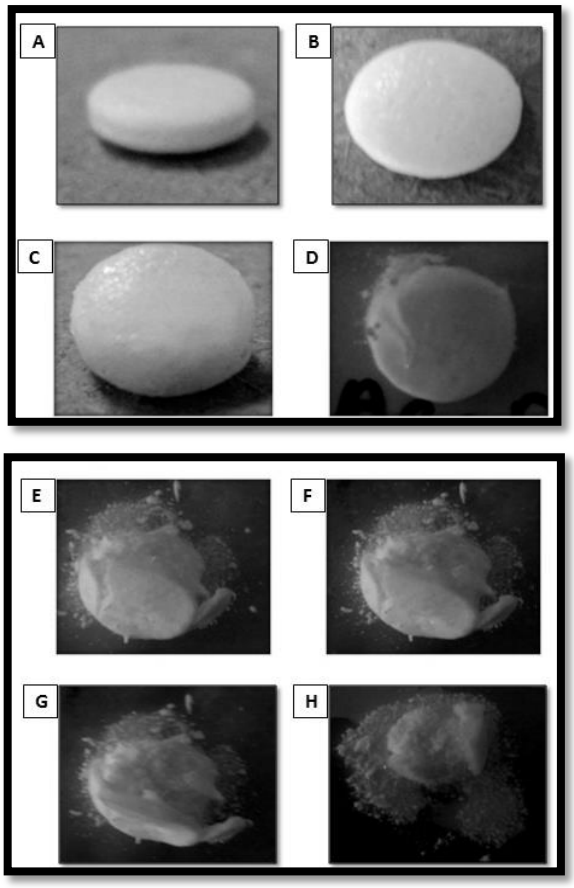
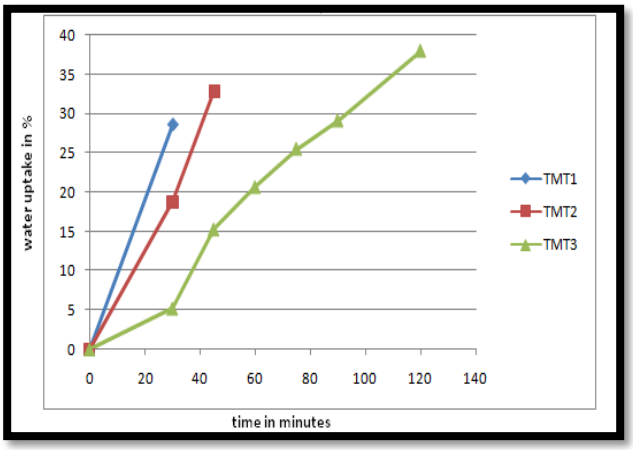


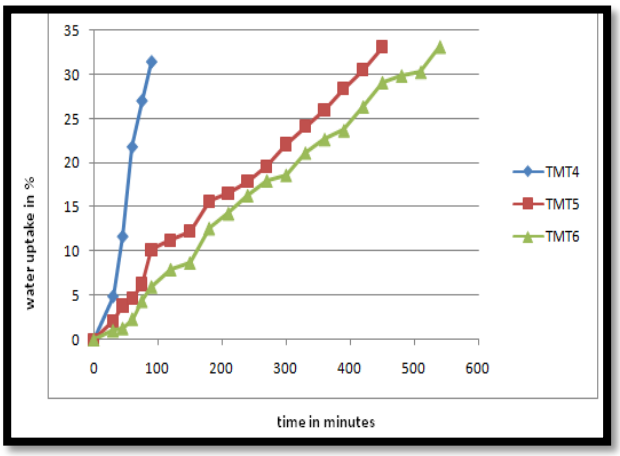
Figure No. 2: Rupturable sequence of time controlled tablets of Metoprolol Tartrate A to C- Water uptake studies, D- Rupture point, H- Total drug release

The core composition could affect the swelling and rupturing behavior of the coated tablets[6,7]. Microcrystalline cellulose possesses a good disintegration property, it increases the disintegrating force of the core which results in a shorter lag time. Ludipress(spray dried lactose) is highly soluble in water and has a high osmotic activity. According to this information, the core tablet was prepared using microcrystalline cellulose and Ludipress with the ratio of 50:50 w/w and showed reproducible results. Besides the core composition, the amount and the type of swelling layer were other variables affects the rupturing behavior. Table No 1 shows the swelling index of all formulations. Data from the table revealed that the swelling index of all formulations was higher at the lower level of ethylcellulose layer. As the coating level increased, the swelling index decreased.

water uptake study shows that higher ethyl cellulose levels retarded the water uptake. Interestingly, all curves showed an almost linear water uptake with time until critical water level, where the ethyl cellulose coating ruptured.

Sr. No.	Ethylcellulose coating level (mg/cm2)	Swelling index ± S.D. at Time (hrs)						
		1	**2**	**3**	**4.30**	**5**	**5.30**	**6**
1.	1.5	13.29.± 0.01	15.23 ± 0.02	17.63 ± 0.02	23.98 .68 ± 0.03	R		
2.	2.5	9.13 ± 0.02	11.63± 0.01	14.26± 0.02	22.38 ± 0.02	26.13 ± 0.01	R	
3.	3.5	4.23 ± 0.03	5.68 ± 0.03	10.21 ± 0.02	14.12 ± 0.02	18.21 ± 0.03	23.2± 0.03	R





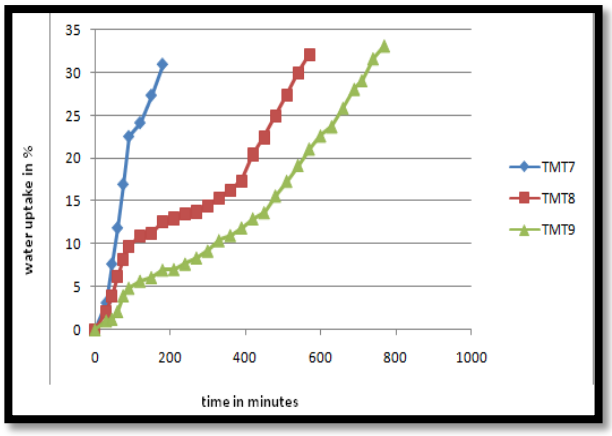


Fig No 3: Water Uptake Study

The critical water uptake level was slightly higher at the higher level of ethyl cellulose. This could be explained by the higher mechanical strength of the thicker coating requiring a higher degree of swelling (water uptake) for rupturing.

CONCLUSION

Metoprolol Tartrate as pulsatile release tablets with rapid release after a predetermined lag time were developed. The lag time could be adjusted and modified by varying the level of the coating layer and the type of the swelling materials.

REFERENCES

1. Hoda A, Maradny E. Modulation of a Pulsatile Release Drug Delivery System Using Different Swellable/Rupturable Materials. Drug Delivery 2007; 14:539-546.

2. Bussemer, T., and Bodmeier, R. 2001. A review of pulsatile drug delivery. Am.Pharm. Rev. 4(4):18–24.

3. Bussemer, T., Otto, L., and Bodmeier, R. 2001. Pulsatile-drug delivery systems.Crit. Rev. Ther. Drug Carrier Syst. 18(5):433–458.

4. Lemmer, B. 1999. Chronopharmacokinetic: implications for drug treatment.J. Pharm. Pharmacol. 51:887–890.

5. Karavas, E., Georgarakis, E., and Bikiaris, D. 2006b. Felodipine nanodispersions as active core for predictable pulsatile chronotherapeutics using PVP/HPMC blends as coating layer. Int. J. Pharm. 313(1-2):189–197.

6. Kr¨ogel, I., and Bodmeier, R. 1999a. Evaluation of an enzyme-containing capsular shaped pulsatile drug delivery system. Pharm. Res. 16(9):1424–1429.

7.Kr¨ogel, I., and Bodmeier, R. 1999b. Floating or pulsatile drug delivery systems based on coating effervescent cores. Int. J. Pharm. 187:175–184.

8. Karavas, E., Georgarakis, E., and Bikiaris, D. 2006a. Application of PVP/HPMC miscible blends with enhanced mucoadhesive properties for adjusting drug release in predictable pulsatile chronotherapeutics. Eur. J. Pharm. Biopharm. 64(1):115–126.

9. Freichel, O. L., and Lippold, B. C. 2000. A new oral erosion controlled drug delivery system with a late burst in the release profile. Eur. J. Pharm. Biopharm. 50:345–351.

10. Bussemer, T., Dashevsky, A., and Bodmeier, R. 2003. A pulsatile drug delivery system based on rupturable coated hard gelatin capsules. J. Control. Rel. 93:331–339.

11.Sangalli, M. E., Maroni, A., Zema, L., Busetti, C., Giordano, F., and Gazzaniga, A. 2001. In-vitro and in-vivo evaluation of an oral system for time and/or site-specific drug delivery. J. Control. Rel. 73:103–110.

12. Fan,T. Y.,Wei, S. L., Yan,W.W., Chen, D. B., and Li, J. 2001. An investigation of pulsatile release tablets with ethylcellulose and Eudragit L as film coatingmaterials and cross-linked polyvinylpyrrolidone in core tablets. J. Control. Rel. 77:245–251.

13. Morita, R., Honda, R., and Takahashi, Y. 2000. Development of oral controlled release preparations, a PVA swelling controlled release system (SCRS); I. Design of SCRS and its release controlling factor. J. Control. Rel. 63:297– 304