International Journal of Chemistry and Pharmaceutical Sciences

Journal Home Page: www.pharmaresearchlibrary.com/ijcps

Research Article Open Access

Comparative Study on Effect of Natural and Synthetic Superdisintegrants in fast Dissolving Tablets of Metoprolol Tartrate

P. Mohan Vikas*, CH. Murali, P. Nagasri, Y. Bhargav

Department of Pharmaceutics, Mother Teresa Pharmacy College, Sathupally, Khammam -507303, India.

A B S T R A C T

Metoprolol Tartrate (MT) is used as an anti-hypertensive and also as an adjunct in the treatment of hyperthyroidism. Adult dose as conventional preparations is 25-100 mg daily in single or divided doses, as extended release 100-200 mg once daily. The bioavailability of the drug when formulated as conventional tablets is 40 %. The aim of the study is to prepare and evaluate Oral Disintigrating Tablets (ODT) of metoprolol Tartrate using super disintegrants- sodium starch glycolate, cross povidone and Treated Agar to observe the effect of various concentrations of super disintegrants on the release profile of tablets. The main objective of the study is to formulate and evaluate or dispersible tablets of metoprolol tartrate with natural and synthetic, semisynthetic superdisintegrants. Various formulations of metoprolol tartrate were prepared by direct compression method using different ratios of natural super disintegrant (Treated Agar,) and synthetic, semi synthetic superdisintegrants (Poly plasdone (Crospovidone), sodium starch glycolate) at the concentrations ranging from 6%-12%. The drug and excipients compatibility study was performed by Stability studies at room temprerature to study the interaction between drug and excipients. The blend of all formulations were evaluated for various precompressional parameters such as angle of repose, bulk, tapped densities, compressibility index, Hausner's ratio and the prepared tablets were evaluated for various parameters like weight variation, thickness, hardness, friability, wetting time, water absorption ratio, disintegration time, content uniformity and in vitro drug release. Formulations with treated agar have shown promising results compared to other formulations with semi synthetic superdisintegrants.

Keywords: Orodispersible tablets, Superdisintegrants, Treated Agar

A R T I C L E I N F O

CONTENTS

Article History: Received 13 April 2015, **Accepted** 24 May 2015, **Available Online** 27 June 2015

***Corresponding Author**
P. Mohan Vikas
Department of Pharmaceutics,
Mother Teresa Pharmacy College,
Sathupally, Khammam-507303, India.
Manuscript ID: IJCPS2551

PAPER-QR CODE

Citation: P. Mohan Vikas, et al. Comparative Study on Effect of Natural and Synthetic Superdisintegrants in fast Dissolving Tablets of Metoprolol Tartrate. *Int. J. Chem, Pharm, Sci*., 2015, 3(6): 1747-1752.

1. Introduction

Oral disintegrating tablets (ODTs) have received ever-increasing demand during the last decade, and the field has become a rapidly growing area in the pharmaceutical industry. Upon introduction into the mouth, these tablets dissolve or disintegrate in the mouth in the absence of additional water for easy administration of active pharmaceutical ingredients. Most commonly used methods to prepare fast disintegrating tablets are; freeze-drying / Lyophilization tablet molding and direct-compression methods.

Advantages

a. The advantages of sublingual drug delivery over other delivery modalities are as follows:
b. Avoidance of 'first-pass'metabolism of drugs.
c. Ease of administration and termination of therapy in emergency.
d. Can be administered to unconscious and trauma patients.
e. Excellent accessibility.
f. Rapid absorption because of enormous blood supply and good blood flow rates increase.
g. Drug is protected from degradation in the acidic environment in the GIT.
h. Improved patient compliance- ease of drug administration.
i. Faster onset of action is achieved due to mucosal surface.

Limitations

a. Drugs with large dose are difficult to be administered.
b. Eating and drinking may be restricted.
c. This route cannot administer the drugs, which are unstable at sublingual pH.
d. This route cannot administer drugs, which irritate the mucosa or have a bitter or unpleasant taste or an obnoxious odour.
e. Small surface area is available for absorption.

Metoprolol tartrate (MT) is a selective beta1-adrenoreceptor blocking agent. Metoprolol tartrateis (±)-1-(isopropyl amino)-3-[p-(2-methoxyethyl) phenoxy]-2-propanol (2:1) dextro-tartrate salt used in Essential hypertension, prevention after a myocardial infarction, tachycardia, coronary heart disease (prevention of angina attacks), treatment of heart failure. Oral bioavailability of metoprolol tartrate is around 40 % 12.

The concept of formulating orally disintegrating tablets of Metoprolol tartrate using different concentrations of superdisintegrants which increase the water uptake with shortest wetting time and there by decrease the disintegration time of the tablets by simple and cost effective direct compression technique. Another objective includes observing the effect of Super disintigrants on drug release profile from optimized formulations.

2. Materials and Methods

Preparation of ODT's:

Metoprolol tartrate ODT's were prepared by the direct compression method using different excipients. The excipients used were Mannitol (diluents), Crospovidone [Polyplasdone xl-10] (super disintegrant), Sodium Starch Glycolate [Promojel] (superdisintegrant) Treated Agar (superdisintegrant), Starch 1500 (diluents), Aspartame (sweetening agent), Magnesium stearate. Different concentration of excipients was used to prepare different group of Oral Disintegrating tablets.

Preformulation studies

Melting Point Determination

Melting point of the drug was determined by taking small amount of drug in a capillary tube closed at one end and placed in a melting point apparatus and the temperature at which drug melts was recorded. This was performed in triplicates and average value was noted [5].

Drug–Excepients Interaction Study

The infrared (IR) spectra were recorded using an FTIR spectrophotometer (Perkin Elmer Spectrum GX) by the KBr pellet method in the wavelength region between 4000 and 400 cm^{-1}. The spectra obtained for Metoprolol Tartrate and physical mixtures of Metoprolol Tartrate with polymers were compared to check compatibility of drug with polymers [6].

Angle of repose

The angle of repose a powder blend was determined by funnel method. The accurately weighed powder blend was taken into the funnel. The height of the funnel was adjusted in such a way the tip of the funnel just touched to the apex of the powder blend. The powder blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using formula [7].

$$\mathbf{Tan\ \theta = \frac{h}{R}}$$

Table 1

Comparison between angle of repose and flow property	
Angle of repose (θ)	**Flow**
< 25	Excellent
25- 30	Good
30- 40	Moderate
>40	Poor

Bulk density

Both bulk density and tapped density were determined. a quantity of 20 gms of powder blend from each formula, previously shaken to break agglomerates formed, was introduced in to 50 ml measuring cylinder was allowed to fall under its own weight on to a hard surface from the height of 2.5 cm at second intervals. Tapping was continued until no further change in volume was noted. Bulk density

and tapped density were calculated by using following equation [8].

Bulk density = Weight of the powder blend / Untapped volume of the packing

Tapped density = Weight of the powder blend / Tapped volume of the packing

Hausner's ratio: It indicates the flow property, measured by the ratio of tapped density to the bulk density [8].

Table 2

Hausner's ratio	Property
0 - 1.2	Free flowing
1.2- 1.6	Cohesive powder

Development of Fast Dissolving tablets of Metoprolol Tartrate

Metoprolol Tartrate, polymers like Treated Agar, SSG and Poly Plasadone Diluents like Starch1500, Mannitol. Lubricants like magnesium stearate, Talc were added by blending and sieve the drug and polymers mixture to get uniform and homogeneous mixture. Tablets were prepared by direct compression using 8mm diameter punch at 3kg/cm^2 pressure.

Evaluation of formulated Oral Disintegrating Tablets of Metoprolol Tartrate: The evaluations of physicochemical parameters of tablets were done as per standard procedures .The following parameters were evaluation**.**

Hardness

The test was done as per the standard methods. The hardness of three randomly selected tablets from each formulation (FA1 to FP3) was determined by placing each tablet diagonally between the two plungers of tablet hardness tester (Monsanto) and applying pressure until the tablet broke down into two parts completely and the reading on the scale was noted down in Kg/cm^2.

Thickness

The thickness of three randomly selected tablets from each formulation was determined in mm using vernier calipers (Pico India). The average values were calculated.

Uniformity of Weight

Weight variation test was done as per standard procedure. Ten tablets from each formulation (FA1 to FP3) were weighed using an electronic balance and the average weight was calculated. The results are shown in Table 2.

Friability

The friability of tablets using 10 tablets as a sample was measured using a Roche Friabilator. Tablets were rotated at 25 rpm for 4 minutes or up to 100 revolutions. The tablets were taken out, dedusted and reweighted. The percentage friability was calculated from the loss in weight as given in equation below. The weight loss should not more than 1%.

$$\textbf{\% Friability} = \frac{\text{(Initial weight- final weight) x 100}}{\text{(Initial weight)}}$$

Wetting Time

The tablet was placed at the centre of two layers of absorbent paper fitted into a dish .After the paper was thoroughly wetted with distilled water, excess water was completely drained out of the dish. The time required for the water to diffuse from the wetted absorbent paper throughout the entire tablet was then recorded using a stopwatch.

Dissolution study of Metoprolol Tartrate tablets

Dissolution rate was studied by using USP type II apparatus at 50 rpm. 6.8 pH phosphate buffer (900mL) was used as dissolution medium. Temperature of dissolution medium was maintained at 37±0.5°c.Aliquot of dissolution medium was withdrawn at specific time interval and it was filtered. Absorption of filtered solution was checked by UV spectroscopy at required wavelength (275nm) and drug content was determined from standard calibration curve. Dissolution rate was studied for all designed formulations.

Table 3

Formula Code	Drug (mg)	Agar (mg)	SSG (mg)	Poly plasdone (mg)	Mannitol (mg)	Starch 1500 (mg)	Aspartame (mg)	Mg Stearate (mg)	Talc (mg)	Total wt (mg)
FA1	25	12	--	--	80	64	15	2	2	200
FA2	25	18	--	--	80	58	15	2	2	200
FA3	25	24	--	--	80	52	15	2	2	200
FS1	25	--	12	--	80	64	15	2	2	200
FS2	25	--	18	--	80	58	15	2	2	200
FS3	25	--	24	--	80	52	15	2	2	200
FP1	25	--	--	12	80	64	15	2	2	200
FP2	25	--	--	18	80	58	15	2	2	200
FP3	25	--	--	24	80	52	15	2	2	200

3. Results and Discussion

Preformulation studies

Melting Point

Melting point of riboflavin was determined by capillary tube method and it was found to be 278ºC (*n* = 3). This value is same as that of the literature citation.

Drug-Excipient compatibility studies

Figure 4: Drug – Excepients Compatibility Studies

Ingredient	Initial Description	Final Description
Metoprolo Tartrate (D)	White Crystalline Powder	No Change
D + Mannitol (1:10)	White Powder	No Change
D + Sodium Starch Glycolate (1:10)	Off- White Powder	No Change
D + Agar (1:10)	White Powder	No Change
D + Crosspovidone (1:10)	White Powder	No Change
D + Aspartame (1:10)	White Powder	No Change
D + Magnesium Stearate (1:1)	White Powder	No Change
D + Talc (1:1)	White Powder	No Change

As described in the methodology section the infrared spectroscopy studies were carried out for pure drug and along with polymers and there was no incompatibility found.

Table 5: Bulk density, Tapped density, Angle of repose, Hausner's ratio for FA1 to FP3

Formulation code	Bulk density g/cm^3	Tap density g/cm^3	Hauner's ratio	Angle of repose
FA_1	0.55	0.64	1.16	31.19
FA_2	0.55	0.64	1.16	31.27
FA_3	0.55	0.65	1.18	32.16
FS_1	0.520	0.62	1.190	33.03
FS_2	0.53	0.63	1.18	33.72
FS_3	0.51	0.62	1.21	32.85
FP_1	0.52	0.62	1.19	32.26
FP_2	0.52	0.63	1.21	33.52
FP_3	0.54	0.64	1.18	34.19

Table 6: Hardness and Friability of Different Formulations

Formulation Code	Hardness(kg/cm^2)*	Friability*(%)
F1	3	0.34
F2	3	0.15
F3	3	0.24
F4	3	0.43
F5	3	0.17
F6	3	0.57
F7	3	0.15
F8	3	0.14
F9	3	0.13

Table 7: Data of Various evaluation tests conducted on Formulations FA_1- FP_3

Product	Disintegration time USP(sec)	Disintegration time in spoon (sec)	Wetting time(sec)
FA_1	184	420	52
FA_2	197	550	55
FA_3	202	567	42
FS_1	224	657	69
FS_2	243	676	73
FS_3	232	646	71
FP_1	325	687	78
FP_2	345	787	83
FP_3	340	823	99

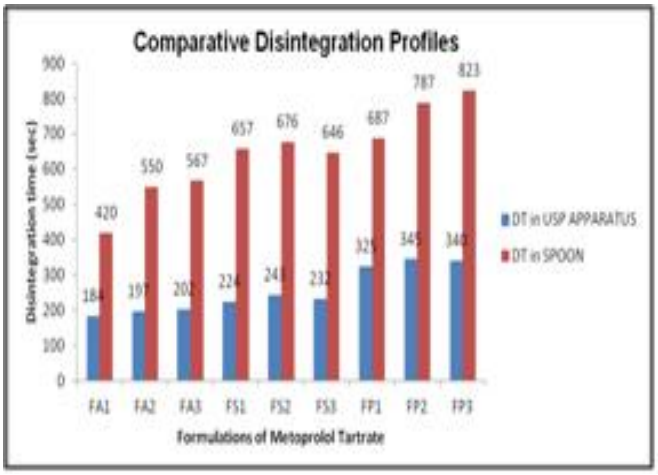

Figure 3: Comparative Disintegration profile of Formulations

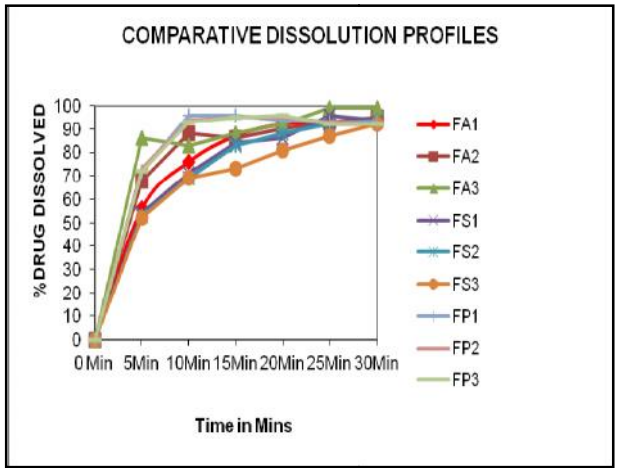

Figure 4: *In-Vitro* % Drug release of Metoprolol Tartrate in Formulations FA1- FP3

***In- vitro* dissolution study:**

USP rotating paddle method was used to study drug release from floating tablets of riboflavin 900 mL of 6.8P^{H} Buffer was used as dissolution medium the release study was performed at 37±0.5˚c at rotational speed of 50rpm. The maximum drug release was shown by formulation F5 was 96.108% after 6 hours. Because of the highly water soluble polymer PVP was used alone in the formulation.

Table 8

Time(min)	Cumulative % drug released								
	FA_1	**FA_2**	**FA_3**	**FS_1**	**FS_2**	**FS_3**	**FP_1**	**FP_2**	**FP_3**
0	0	0	0	0	0	0	0	0	0
5	56±4.1	68±3.1	86±3.1	54±3.1	53±3.1	52±8.6	72±0.6	73±3.1	72±3.1
10	76±3.1	88±3.3	83±3.3	71±3.3	69± 0.6	69± 0.6	96±0.6	94±3.3	93± 0.6
15	87±3.3	86±3.3	88±3.3	84±3.5	83±2.3	73±3.6	96±3.6	95±3.6	95±3.6
20	92±2.8	90±2.8	90±2.8	86±2.8	88± 0.9	81± 0.9	94±1.7	95±2.8	95± 0.9
25	92±2.8	93±2.8	99± 0.9	96±2.8	92±3.1	87±3.6	93±3.6	93±4.6	92±2.8
30	92±2.8	95±2.8	99± 1.2	94±2.8	94± 0.2	92± 1.2	93±1.7	92±2.8	92± 1.2

4. Conclusion

In the formulation of Metoprolol tartrate, initially superdisintegrant (6%) were added to the formulation by direct compression technique. Later trials were continued with 9% and 12% of super disintegrants. Six final formulations were prepared and evaluated. Formulation FA_3 showed rapid drug release profile i.e. it releases 85% drug in 5min whereas formulation FP2, FP3 releases 73% drug. All these tablets showed required hardness, limited % friability and good disintegration time as indicated in table 4 and 5. Various other tests such as wetting time, Disintegration in oral cavity, Disintegration in spoon were also conducted and good correlation was observed between these tests.

a. The major conclusions drawn from this work are as follows.
b. Superdisintegrant (12% Agar) showed better results rapid dissolution rate and almost all of the drug was released only in 30min.
c. Drug release profile of Orally Disintegrating Tablets followed first order release.
d. The above discussed results clearly indicated the usefulness of the ODT in the improvement of dissolution rate of poorly soluble drugs like Metoprolol tartrate whose bioavailability is dissolution rate limited. However further studies like, Preparation of ODT by other approaches Susing different excipients, characterization in term of its long term stability and in vivo absorption studies are necessary.

5. References

1. Kuchekar B S, Atulbadhan C, Mahajan H S, Mouth dissolving tablets: a novel drug delivery system, Pharma times, **2003**, 35: 7-9.
2. William.P.R., Tapas.K.G, Orally disintegrating tablets: Products, technologies and development issues, Pharm Technol, **2005**, 29: 136-150.
3. Jaysukh J Hirani, Dhaval A Rathod, Kantilal R Vadalia, Orally Disintegrating Tablets: A Review, Trop J Res, **2008**, 8: 161-172.
4. Indurwade N H, Rajyaguru T H, Indian drugs, **2002**, 39: 405-409.
5. Novel approach fast dissolving tablets – IJPS, Indurwade N.H., Rajyaguru T.H. and Nakhat P.D. April 2002 Vol-39.
6. www.Rx List.com.

7. Handbook of Pharmaceutical excipients, 5th Editionn, Raymond C Rowe and Paul. J. Sheskey (Pharmaceutical press, London) **2006**, 132-767.
8. D P Venkatesh, C G Geetha rao, Formulation of a taste masked oro dispersible tablets of Ambroxolol hydrochloride, Asian. J. Pharm, **2008**, 1: 261-264.