wjpmr, 2024, 10(4), 222-227

SJIF Impact Factor: 6.842

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Research Article

ISSN 2455-3301

WJPMR

PREPARATION AND EVALUATION OF FAST DISSOLVING TABLETS OF ANTI-HYPERTENSIVE DRUG

Jyoti Narvariya*[1], Shonu Jain[2], Anjali Singh[3] and Rashmi Haldkar[4]

[*1]Truba Institute of Pharmacy, Karond Gandhi Nagar, Bypass Road, Bhopal, MP, 462038.
[2]NRI Institute of Pharmacy, Sajjan Singh Nagar, Raisen Road, Bhopal, MP, 462022
[3]Aryan College of Pharmacy, Ghaziabad, UP, 201002.
[4]Sir Atma Ram Institute of Pharmacy and Technology, Saript, Khasra no 69/1, PHN 30, Tilwara-Nagpur Road, Manegaon, Jabalpur, MP, 482051.

***Corresponding Author: Jyoti Narvariya**

Truba Institute of Pharmacy, Karond Gandhi Nagar, Bypass Road, Bhopal, MP, 462038.

Article Received on 21/02/2024 **Article Revised on 11/03/2024** **Article Accepted on 01/04/2024**

ABSTRACT

The patients with sudden increase blood pressure have markedly reduced function ability and extremely restless, in such cases rapid onset of action is of prime importance. So the patients would be benefited from acute treatment by using fast dissolving drug delivery system. Trandolapril (TD) is an anti-hypertensive drug which is insoluble in water; hence the drug may be slowly or incompletely dissolves in the gastro-intestinal tract. So the rate of dissolution and therefore its bioavailability is less (bioavailability 4-14%). The aim of the present work is to develop fast dissolving tablets from the solid dispersion of TD for enhancement of solubility. The solid dispersions of TD were prepared with PEG 4000, PVP K-90 in 1:1, 1:2 and 1:3 by using conventional method. The prepared solid dispersions were analyzed for all the physical parameters, drug: carrier interactions like FTIR. Solid dispersions showed a better dissolution compared to the pure drugs and among all the other formulations F3 shows high percentage drug release i.e. 39.98 % for 240 min and selected as an optimized formulation for the preparation of fast dissolving tablets of TD. Sodium starch glycolate, croscarmellose sodium used in the preparation of fast dissolving tablets prepared by direct compression method. The post compression parameters of all the prepared tablets were within the limits. F4 was selected as optimized formulation based on its highest disintegration time 60sec and drug release 89.98% for 15 min. Drug-excipients characterization also revealed that there is no interaction. Hence it concluded that solid dispersions incorporated fast dissolving tablets is very useful approach for immediate release of TD in the efficient management of hypertension.

KEYWORDS: Fast dissolving tablets, Trandolapril, Superdisintegrants, Anti-hypertensive drug, Post compression.

INTRODUCTION

Oral route is the most frequently used route of drug administration with convenient and cost-effective.[1] Tablet is one of the most popular among all the oral dosage forms existing today because of its convenience of self-administration, compactness and easy manufacturing. Fast dissolving dosage forms can be disintegrated, dissolved, or suspended by saliva in the mouth.[2] But the oral formulation with poor solubility is a greater limitation for the formulation scientists, solubility enhancement should be the prime concern for a dosage form to get ideal bioavailability.[3] Although salt formation, solubilization, particle size reduction has commonly used to increase dissolution rate and thereby oral absorption and bioavailability of low water-soluble drugs 2-4, there is practical limitation to these techniques.[4] Among all the techniques solid dispersions is one of the promising techniques.[5] Solid dispersions (SDs) have traditionally been used as an effective method to improve the dissolution properties and bioavailability of poorly water-soluble drugs.[6] Fast dissolving tablets are useful for patients with difficulties swallowing conventional tablets, for example pediatric patients and patients under chemotherapy treatment.[7] To allow fast dissolving of dosage forms in the mouth, these delivery systems comprise either very porous and soft-molded matrices or compression into tablets with very low compression force.[8]

Trandolapril is an angiotensin converting enzyme inhibitor, orally active and undergoes substantial fi rst-pass metabolism by cytochrome P450 enzymes. The terminal half-life of trandolapril is about 0.8 to 1 hour.[9] Following oral administration, Trandolapril is well-absorbed and undergoes substantial first-pass metabolism; the systemic bioavailability of trandolapril

is about 4–14%.[10] In view of these facts, this drug can be considered as a suitable candidate for fast dissolving tablet.

MATERIALS AND METHODS

Materials

Trandolapril was a gift from Hetero Drugs Ltd., (Hyderabad, India). Crospovidone, sodium starch glycolate and sodium starch glycolate was obtained from Hi-Media Laboratories Pvt. Ltd., Mumbai, India. Micro crystalline cellulose, talc and magnesium stearate was procured from Central Drug House (P) Ltd. New Delhi. All other solvents and chemicals used were of analytical grade.

Methods

Preformulation studies

Standardization of TD by UV-Visible spectrophotometry

Accurately weighed 10 mg of drug was dissolved in 10 ml of phosphate buffer pH 6.8 solutions in 10 ml of volumetric flask. The resulted solution 1000µg/ml and from this solution 1 ml pipette out and transfer into 10 ml volumetric flask and volume make up with phosphate buffer pH 6.8 solution prepare suitable dilution to make it to a concentration range of 5-25µg/ml. The spectrum of this solution was run in 200-400 nm range in U.V. spectrophotometer (Labindia-3000+).

Drug-excipient compatibility study

FTIR spectra of pure drugs, polymers used and blends were recorded on KBr disk method using Brukers Alpha Spectrophotometer with IR solution software to confirm the compatibility between drug and excipients. Sample powder was thoroughly mixed by triturating with potassium bromide in a glass mortar with pestle and compressed into disks in a hydraulic press (Techno search Instruments, India). FTIR spectra of all the samples were recorded over a spectral region from 4700 to 400 cm-1 using 20 scans with 4 cm-1 resolution.

Preparation of solid dispersion of TD

For the preparation of Trandolapril-PEG 4000 solid dispersion by conventional method, PVP K-90 was weighed and melted at 58°C (± 1°C) and a measured amount of Trandolapril was added and stirred. After solidification at room temperature, sample was pulverized with use of a pestle and mortar and sieved through a 400-mm mesh. 6mg of Trandolapril- PEG 4000 powder (containing 6mg of Trandolapril and 2 mg of PEG 4000) was used for further investigations.

Preparation of physical mixture

For the preparation of Trandolapril-PEG 4000 physical mixture were weighed and mixed for 5 min with use of a pestle and mortar and sieved through a 400mm mesh. Trandolapril-PEG 4000 powder mixture was used for further tablet preparation. Percentage cumulative drug release of physical mixture given in Table 1.

Table 1: Percentage cumulative drug release of physical mixture.

F. Code	Time interval (min.)	Percentage cumulative drug release of physical mixture*			
		Drug: PEG 4000			
		F1	F2	F3	
1	0	1:1	1:2	1:3	Pure Drug
2	30	8.98	13.32	15.56	1.12
3	60	11.25	25.65	29.98	3.32
4	120	16.65	32.12	34.45	5.65
5	240	25.56	35.69	39.98	8.12

Preparation of tablets of TD

Fast dissolving tablets of TD were prepared by direct compression[11] according to the formulae given in Table 1. All the ingredients were passed through # 60 mesh separately. Then the ingredients were weighed and mixed in geometrical order and compressed into tablets of 100 mg using 8 mm round flat punches on 10-station rotary tablet machine.

Table 2: Composition of Trandolapril fast dissolving tablets.

Ingredients (mg)	Formulation code					
	F1	F2	F3	F4	F5	F6
Equivalent to 2 mg Trandolapril	2	2	2	2	2	2
Sodium Starch glycolate	10	15	20	-	-	-
Croscarmellose sodium	_	_	_	10	15	20
Microcrystalline cellulose	77	72	67	77	72	67
Talc	5	5	5	5	5	5
Magnesium stearate	6	6	6	6	6	6
Total weight	100	100	100	100	100	100

Evaluation of fast dissolving tablets of TD

Precompression parameters

Angle of repose (θ)

The frictional forces in a loose powder or granules can be measured by the angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane.

$\tan \theta = h/r$

$\theta = \tan^{-1}(h/r)$

Where, θ is the angle of repose, h is the height, r is the radius.

The granules were allowed to flow through the funnel fixed to a stand at definite height. The angle of repose was then calculated by measuring the height and radius of the heap of granules formed.

Bulk density

Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. Accurately weighed amount of granules taken in a 50 ml capacity measuring cylinder was tapped for 100 times on a plane hard wooden surface and estimated the LBD and TBD, calculated by using following formulas.

LBD (Loose Bulk Density) = Mass of Powder/Volume of Packing

TBD (Tapped Bulk Density) = Mass of Powder/Tapped Volume of Packing.

Compressibility index

The compressibility index of the granules was determined by Carr's compressibility index**.**

Carr's index (%) = [(TBD – LBD)/TBD] × 100.

Hausner's ratio

Hausner's ratio is an indirect index of ease of measuring the powder flow. It was calculated by the following formula.[12]

Hausner's ratio = Tapped density/Bulk density.

Evaluation of Tablets

Thickness

Twenty tablets from the representative sample were randomly taken and individual tablet thickness was measured by using digital vernier caliper.[13]

Hardness

Tablet hardness was measured by using Monsanto hardness tester. From each batch six tablets were measured for the hardness and average of six values was noted along with standard deviations.

Friability Test

From each batch, ten tablets were accurately weighed and placed in the friability test apparatus (Roche friabilator). Apparatus was operated at 25 rpm for 4 minutes and tablets were observed while rotating. The tablets were then taken after 100 rotations, de dusted and reweighed. The friability was calculated as the percentage weight loss.

% friability was calculated as follows

% Friability = (W1 – W2) x 100/W1

Where W1 = Initial weight of the 10 tablets, W2 = Final weight of the 10 tablets after testing.

Friability values below 0.5-1% are generally acceptable.

Weight variation test

To study weight variation individual weights (WI) of 20 tablets from each formulation were noted using electronic balance. Their average weight (WA) was calculated. Percent weight variation was calculated as follows. Average weights of the tablets along with standard deviation values were calculated.

Drug content

The test is mandatory for tablets with 10 mg or less weight of active ingredient. Ten randomly selected tablets from each formulation (F1 to F6) were finely powdered and Drug equivalent to 2 mg of drug dissolved in 10 ml phosphate buffer pH 6.8 sonicate it for 20 minutes, till the entire drug leached out from complex, then the solution was filtered through whatman filter paper No. 41. From this solution take 1 ml and diluted up to 100 ml with phosphate buffer pH 6.8 and the drug content was determined spectrophotometrically at 220 nm.

In vitro disintegration time

The disintegration test was performed using an USP disintegration apparatus, with distilled water at 24±0.50C. The time reported to obtain complete disintegration of six tablets were recorded and average was reported.

Dissolution Rate Studies

The prepared tablets were evaluated for *in vitro* drug release. The drug release studies were carried out using USP XXII paddle type Dissolution test apparatus. A tablet placed in dissolution media (900 ml) which was stirred at 75 rpm maintained at 37±0.2°C. Samples were withdrawn at different time interval and compensated with same amount of fresh dissolution medium. Volume of sample withdrawn was made up to 10ml Phosphate buffer pH 6.8. The samples withdrawn were assayed spectrophotometrically at 220 nm using UV visible spectrophotometer. The release of drug was calculated with the help of standard curve of TD.[14, 15]

RESULTS AND DISCUSSION

The λ_{max} of TD was found to be 220 nm by using U.V. spectrophotometer (Labindia-3000+) in linearity range 5-25 µg/ml Fig.1& 2. Tablet powder blend was subjected to various pre-compression parameters Table 3. The angle of repose values indicates that the powder blend has good flow properties. The bulk density, tapped density, compressibility index and Hauser's ratio of all the formulations was found to be within the range and showing that the powder has well flow properties. The results of post-compression parameters such as the uniformity of weight, hardness, thickness, friability and

drug content of the tablets are given in Table 4. All the tablets of different batches complied with the official requirements of uniformity of weight. The hardness of the tablets ranged from 2.36 to 2.46kg/cm^2 and the friability values were less than 0.9% indicating that the tablets were compact and hard. The thickness of the tablets ranged from 1.12 to 1.16 mm. All the formulations satisfied the content of the drug as they contained 97.89 to 99.21 % of TD and good uniformity in drug content was observed. Thus all the physical attributes of the prepared tablets were found be practically within control. The result in vitro disintegration were within the prescribe limit and comply with the criteria for orally disintegrating tablets. The tablets were evaluated for in vitro dissolution studies in phosphate buffer pH 6.8 for 15 min. The results of the optimized formulation F4 showed maximum drug release i.e. 89. 98% at the end of 15 min. The results of release studies of formulations F4 was shown in Table 5. The *in vitro* drug release data of the optimized formulation F4 was subjected to goodness of fit test by linear regression analysis according to zero order, first order kinetic equation, Higuchi's and Korsmeyer's models in order to determine the mechanism of drug release. When the regression coefficient values of were compared, it was observed that 'r' values of first order was maximum i.e. 0983 hence indicating drug release from formulations was found to follow first order kinetics Table 6 & Fig. 3, 4.

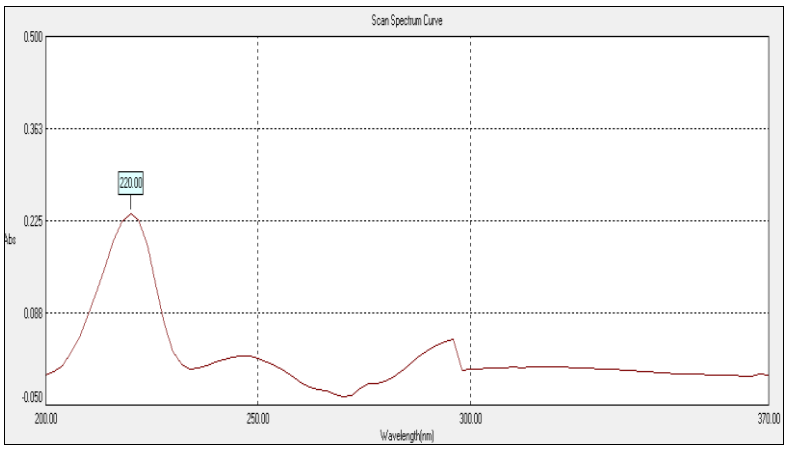

Figure 1: Determination of λ_{max} of TD.

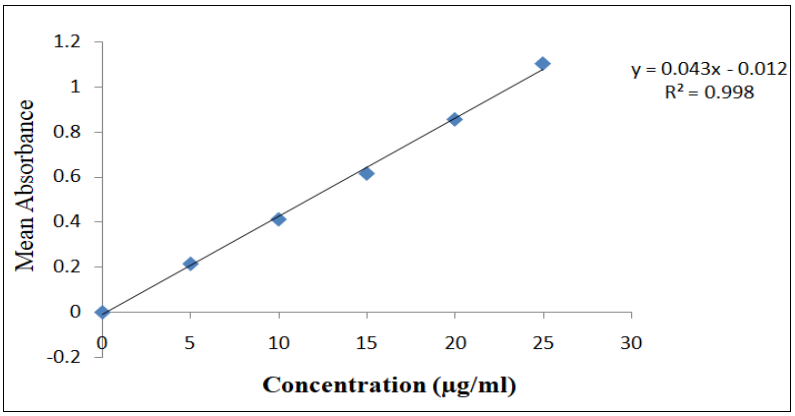

Figure 2: Calibration Curve of TD in Phosphate buffer pH 6.8 at 220 nm.

Table 3: Results of pre-compressional parameters of Trandolapril.

Formulation code	Parameters			
	Loose Bulk density(gm/ml)	Tapped bulk density(gm/ml)	Carr's Index (%)	Hausner's Ratio
F1	0.38	0.49	22.449	1.289
F2	0.39	0.48	18.750	1.231
F3	0.36	0.46	21.739	1.278
F4	0.35	0.48	27.083	1.371
F5	0.34	0.45	24.444	1.324
F6	0.36	0.47	23.404	1.306

Table 4: Results of Post-Compression parameters of all formulations.

F. Code	Hardness test (kg/cm^2)	Friability (%)	Weight variation (%)	Thickness (mm)	Drug content (%)	Disintegration Time (sec.) (n=3) Mean ± SD
F1	2.46	0.689	Passes	1.12	98.85	85±5
F2	2.45	0.652	Passes	1.14	98.81	82±3
F3	2.36	0.587	Passes	1.16	99.21	80±2
F4	2.41	0.652	Passes	1.15	97.89	60±4
F5	2.42	0.654	Passes	1.13	99.10	89±2
F6	2.43	0.521	Passes	1.12	97.89	92±3

Table 5: *In-vitro* drug release data for optimized formulation F4.

Time (min)	Square Root of Time(h)$^{1/2}$	Log Time	Cumulative*% Drug Release	Log Cumulative % Drug Release	Cumulative % Drug Remaining	Log Cumulative % Drug Remaining
1	1	0	33.45	1.524	66.55	1.823
5	2.24	0.698	55.65	1.745	44.35	1.647
10	3.16	1	75.56	1.878	24.44	1.388
15	3.87	1.176	89.98	1.954	10.02	1.001

Table 6: Regression analysis data.

Batch	Zero Order	First Order
	R^2	R^2
F4	0.980	0.983

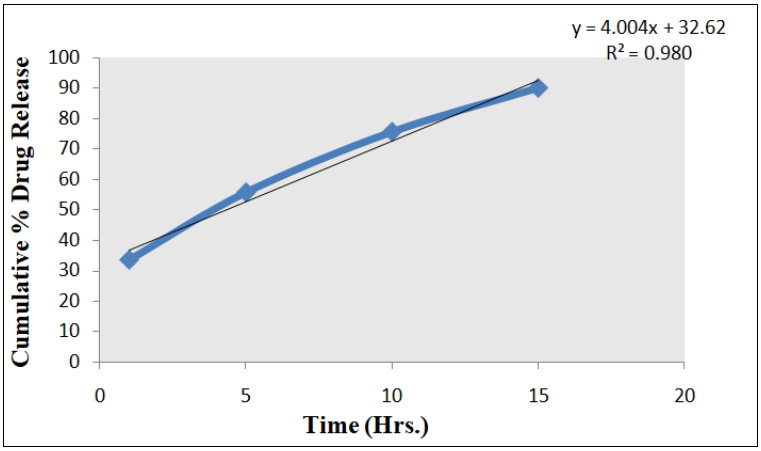

Figure 3: Zero order release Kinetics.

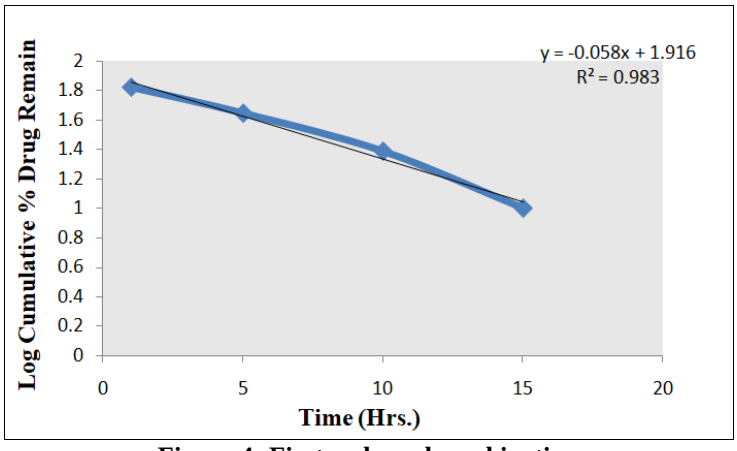

Figure 4: First order release kinetics.

CONCLUSION

In accordance with present study it was concluded that, the present investigated TD solid dispersion fast dissolving tablets can be an alternative dosage form for TD tablets and the rate of drug release increased from dosage form due to which there is increase in the dissolution rate. In addition there is increase in the bioavailability of TD. Method of preparation is simple, cost effective and scalable.

REFERENCES

1. Benet LZ. Effect of route of administration and distribution on drug action. Journal of pharmacokinetics and biopharmaceutics, 1978 Dec 1; 6(6): 559-85.
2. Das PS, Verma S, Saha P. Fast dissolving tablet using solid dispersion technique: a review. Int J Curr Pharm Res, 2017; 9(6): 1-4.
3. Rramaswamy R, Mani G, Ranganathan H, Hyun TJ. Preparation of immediate release tablets of Repaglinide by a solubility enhancer and hot-melt extrusion method. Int J Res Ayurveda Pharma, 2016; 7(5): 85-90.
4. Arunprasad K, Narayanan N, Rajalakshmi G. Preparation and evaluation of solid dispersion of terbinafine hydrochloride. Int J Pharm Sci Rev Res, 2010; 3(1): 130-4.
5. Brahmankar DM, Jaiswal SB. Bioavailability and Bioequivalence, Biopharmaceutics and pharmacokinetics A treatise. Edn II, Vallabh prakashan, 2009; 349-357.
6. Varalakshmi TS, Ramesh CS, Jyothi I, Jyothi Y, Bharathi G, Babu PC. Formulation and evaluation of solid dispersions of valsartan for dissolution rate enhancement. Journal of Pharmacy Research, 2015 Feb; 9(2): 139-44.
7. Satpute MM, Tour NS. Formulation and *in vitro* evaluation of fast dissolving tablets of metoprolol tartrate. Brazilian Journal of Pharmaceutical Sciences, 2013; 49(4): 783-792.
8. Armando YP, Schramm SG, de Freitas Silva M, Kano EK, Koono EE, Porta V, dos Reis Serra CH. Bioequivalence assay between orally disintegrating and conventional tablet formulations in healthy volunteers. International journal of pharmaceutics, 2009 Jan 21; 366(1-2): 149-53.
9. Guay DR. Trandolapil: a newer angiotensin-converting enzyme inhibitor. Clin Ther, 2003; 25: 713–75.
10. Wiseman LR, McTavish D. Trandolapril: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic use in essential hypertension. Drugs, 1994; 48: 71–90.
11. Kuchekar BS, Badhan AC, Mahajan HS. Mouth dissolving tablets of salbutamol sulphate: A novel drug delivery system. Indian Drugs, 2004; 41: 592-8.
12. Subramanyam CVS. Textbook of Physical Pharmaceutics. 3rd ed. Vallabh Prakashan: Delhi, 2001; 181-234.
13. T. Salsa, F. Veiga, M.E. Pina. Oral controlled-release dosage forms. i. cellulose ether polymers in hydrophilic matrices Drug Dev Ind Pharm, 1997; 23: 929-938.
14. Mohd. Adil Khan, Girijesh Kumar Pandey, Amit Joshi, B.K. Dubey, Amit Kumar Jain, Prabhat Jain. Formulation development and evaluation of fast dissolving oral film of a lipid-lowering drug. Asian Journal of Pharmaceutical Education and Research, 2019; 8(1): 12-22.
15. Surya Prakash Gautam, Janki Prasad Rai, Uma Billshaiya, Nilesh Jain, Pradeep Vikram and Deepak Kumar Jain. Formulation and evaluation of mouth dissolving tablet of loperamide. International Journal of Pharmaceutical Sciences and Research, 2013; 4(5): 1782-1788.