FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS FOR THE TREATMENT OF HYPERTENSION

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Abstract: In this research paper we focus on the preparation of orodispersible tablets of telmisartan because sometimes patients have a remarkable increase in blood pressure and the instantly increase blood pressure may cause inactiveness, restless and anxious. To tackle such complications orodispersible tablets of telmisartan were formulated by direct compression techniques so that rapid onset of action can be produced to lower down the blood pressure in the normal range. Telmisartan belongs to an antihypertensive class of drug which is soluble in phosphate buffer, and other solvents. The bioavailability of telmisartan is about 42-99% which is better than other drugs that belong to the same class. Here we used several superdisintegrants such as treated agar, avicel-101, magnesium stearate, etc. Which increases the rate of dissolution and bioavailability of drugs up to optimum level.

Keywords: Telmisartan, Orodispersible tablets, Direct compression technique, Superdisintegrants

Introduction

Hypertension is a common arterial disease in which blood pressure increase instantly. Increased blood pressure is characterized by several health complications such as coronary heart attack, stroke, myocardial infarction, chronic kidney disease, and sometimes causes death. A few attributes of cardiovascular disease, including increased blood pressure and pulse, are described by unsurprising changes during the 24 h, generally in synchrony with the rest-movement cycle[1].BP is commonly expressed as the proportion of the systolic BP (that is, the pressing factor that the blood applies on the blood vessel dividers when the heart contracts) and the diastolic BP (the pressing factor when the heart relaxes). The greater part (90–95%) of patients have an exceptionally heterogeneous 'fundamental' or essential hypertension with a multifactorial quality climate etiology[2]. A positive family ancestry is an incessant event in patients with hypertension, with the heritability (a proportion of the amount of the variety in a characteristic is because of variety in hereditary variables) assessed somewhere in the range of 35% and half in most studies[3].

Stream of blood is based on the heartbeat and the blood pump through the heart. The pressing factor of the heart doesn't remain at a similar level consistently. It differs dependent on exercises at a specific point on the schedule. Hypertension happens due to the long duration of abnormal pressure applied in artries[4].

Hypertension is divided into two main classes. These incorporate primary and secondary hypertension. Primary hypertension is also called fundamental hypertension and it influences 95% of people experiencing the sickness. Reasons for hypertension are not yet referred to, notwithstanding, factors as age, high salt intake, low potassium diet, inactive way of life, stress just as qualities have been found as adding to hypertension. Hypertension happening as an outcome to a result of another problem or a symptom of the drug is referred to as secondary hypertension. Such problems may incorporate renal disappointment or renovascular infection. This kind of circulatory strain is clear in around five to 10% of cases[5].

Telmisartan is an antihypertensive drug that belongs to the class of ACE inhibitors. It is used for the treatment of moderate to severe cases of hypertension, heart diseases, heart attack. Telmisartan is available in the market under the class of antihypertensive drugs. Telmisartan drugs interact with renin and are used to regulate the central regulator of blood pressure as well as electrolyte homeostesis[6].

Orodispersible tablets

Oral administration is considered the most broadly acknowledged course because it accommodates self-administration, simple manufacturing, patient compliance, and painless treatment. But the most obvious disadvantage of the generally utilized oral measurement like

tablets and capsules is trouble in swallowing, prompting patients in In-compliance especially if there should be an occurrence of pediatric and geriatric patients[7].

Tablets and capsules comprise a significant segment of medication that are at present available. In any case like pediatric and geriatric patients who are intellectually hindered, uncooperative, sickened, or on decreased fluid intake have troubles have to swallow these dosage forms[8]. The individuals who are traveling or have little admittance to water are comparably affected. To satisfy these clinical requirements, drug technologists have built up novel drug delivery systems known as Orodispersible Tablets (ODTs) which break down quickly in saliva, typically in seconds, without the need for water.

Drug disintegration, dissolution as well as the onset of action impact, and medication bioavailability might be fundamentally more significant than those seen from traditional dosage forms When such tablets are set in the oral cavity, salivation rapidly enters into the pores to cause fast tablet disintegration[9].

Materials and methods

Materials: Drug telmisartan was obtained as a gift sample from Psychotropic India Ltd., Agar was obtained from Himedia Pvt.Ltd., Avicel-101 was obtained from Loba Chemie Pvt. Ltd., Mannitol, Magnesium Stearate, and Talc were obtained from CDH Laboratory agent.

methods

Pre-formulation parameters

Precompression studies

Drug excipients interactions

FTIR: IR spectra with pure drug (telmisartan) were taken alone and a peak was determined. Later pure drug with excipients was taken and spectra were determined for stability studies.FTIR used in this research work was labtronics India with KBr pellets[10].

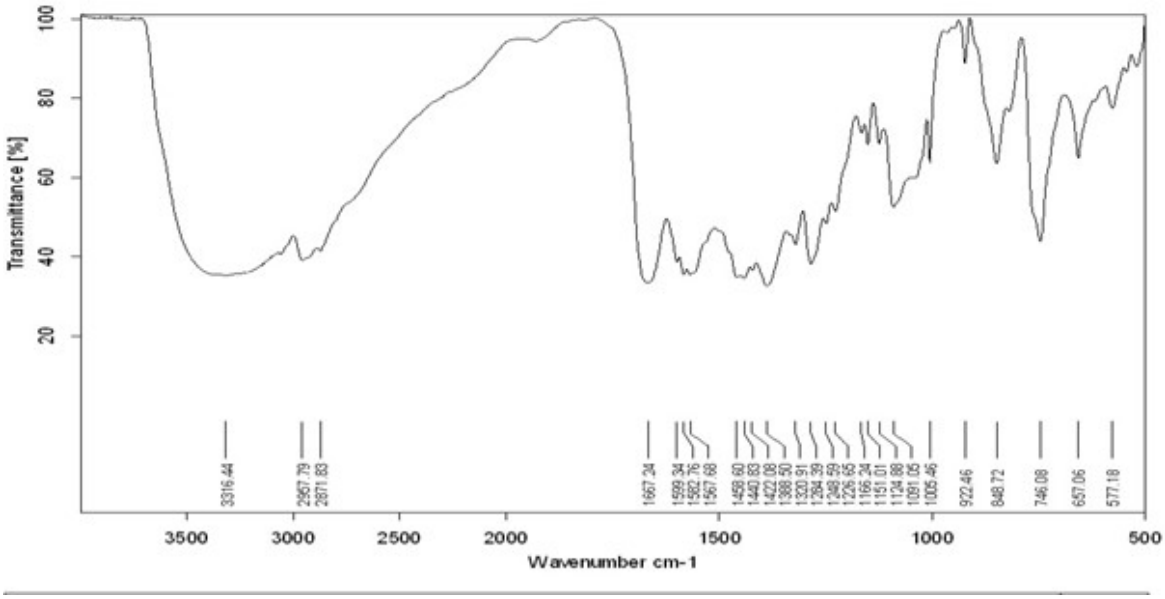

Figure 6: IR spectrum of the pure drug (Telmisartan)

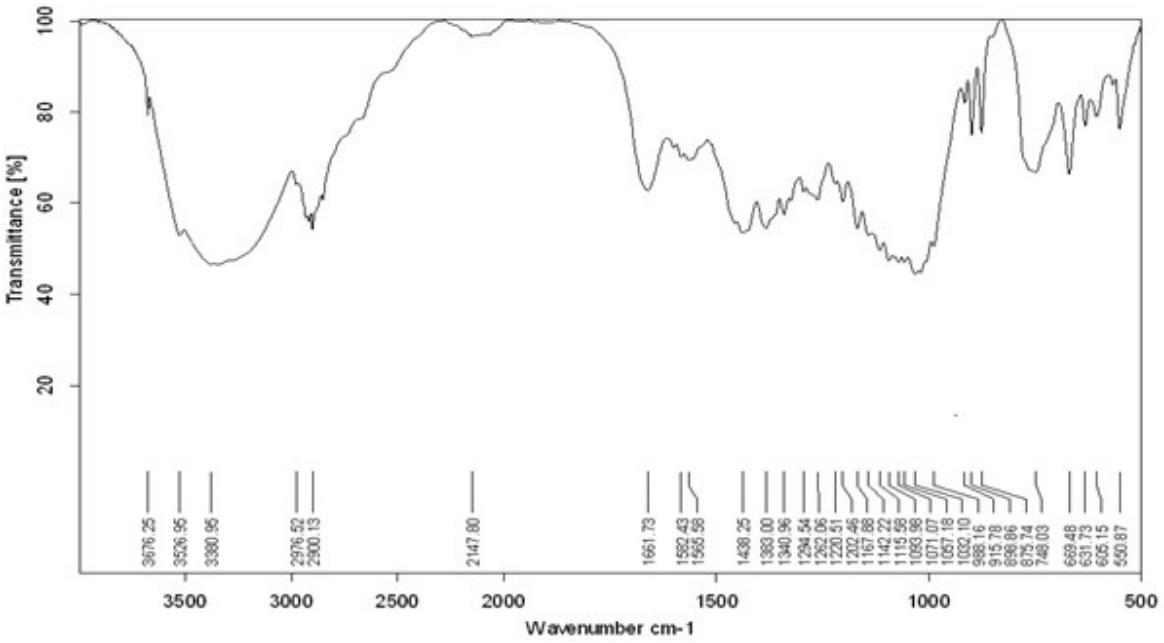

Figure 7: IR spectrum of formulation F9

The angle of repose (θ): It is defined as the maximum angle possible between the surface of the pile of the powder to the horizontal plane. The angle of repose is the indication of the flow properties of the materials. It depends upon the type of excipients used in the formulation. the angle of repose is good in free-flowing powders[11].

$\tan(\theta)=h/r$,

$\theta= \tan^{-1}(h/r)$, where θ is the angle of repose

h is the height of pile and,

r is the radius of the pile

Table 5: Angle of repose with different ranges of flow properties

The angle of repose θ	Flow property
<25	Excellent
25=30	Good
30-40	Passable
>40	Very poor

Method: A funnel was taken and filled to the brim and the test sample was allowed to pass through the end under gravity. A graph paper sheet was taken to measure the area of the pile thereby, evaluating the flow property. The distance between the funnel and the paper sheet was just 2cm[12].

Bulk density: Bulk density is defined as the total mass of the powder divided by the total volume of powder taken. Bulk density mainly depends upon particle shape and particle size distribution.

Method: Both bulk density and tapped density are measured by tapped density tester. In this process accurately weighed amount of powder is taken and fill in a 25ml measuring cylinder, initial volume is measured. After that cylinder was allowed to fall from 2cm height with a 2 sec time interval. Taping is continued till there is no change in powder volume[13].

Bulk and tapped density can be calculated as:

Bulk density= weight of powder/ Volume of packing (a)

Tapped density=weight of powder/ volume of packing (b)

Carr's compressibility index: The compressibility index is the property of powder to be compressed. It's the measure of powder's ability to settle[14]. Grading of compressibility index of powder according to carr's index.

Table 6: Carr's compressibility parameters according to flow properties

Carr's index(compressibility %)	Flow
5-15	Excellent
12-16	Good
18-21	Fair
23-28	Slightly poor
28-35	Poor
35-38	Very poor
>40	Extremely poor

Carr's index compressibility can be calculated as:

CI %=tapped density-bulk density/tapped density X 100 ...(c)

Hausner's ratio: Hausner's ratio is the collectively flow properties of powder and granules. Hausner's ratio is the ratio of tapped density and bulk density[15].

Hausner's ratio= Tapped density/ Bulk density

Table 7: Grading of Hausner's ratio in flow properties

Hausner's ratio	Flow
<1.2	Free-flowing
>1.6	Less free-flowing

Formulation of orodispersible tablets:

Mouth dissolving tablets of telmisartan from batch number 1 to batch number 9 were prepared by direct compression method and the details were assigned in the table-. In each batch, 60 tablets were prepared and analyzed.

Method of preparation:

- All the ingredients were collected from different sources.
- Excipients were passed through sieve number 60 separately.
- All the excipients mix in a mortar pestle and uniform mixing is done.
- The drug is added to the excipients and mixed uniformly.
- The mixture of drug and excipient is taken and punched by direct compression

machine to get 90mg of tablet.

Table 8: Formulation of Orodispersible tablets of telmisartan by direct compression method

Sl.No.	Ingredients	The quantity used in mg								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
1.	**Telmisartan**	40	40	40	40	40	40	40	40	40
2.	**Treated Agar**	2	3	4	5	6	7	8	9	10
3.	**Avicel-101**	36	35	34	33	32	31	30	29	28
4	**Mg. Stearate**	1	1	1	1	1	1	1	1	1
5.	**Talc**	1	1	1	1	1	1	1	1	1
6.	**Mannitol**	10	10	10	10	10	10	10	10	10
7.	**Total**	90	90	90	90	90	90	90	90	90

Post compression parameters

The prepared formulation was evaluated for physical and chemical parameters.

- **Physical parameters**

1. **Color:** Telmisartan fast dissolving tablet is white.
2. **Shape:** Circular in shape.
3. **Size:** The size of the tablet is 6mm in diameter and 3mm in thickness.

Tablet properties:

Hardness: Tablets require a specific measure of solidarity, or hardness and protection from friability, to withstand the mechanical shock of production, bundling, and transportation. The hardness of the tablets was resolved to utilize the Monsanto Hardness analyzer. It is communicated in Kg/cm2. Three tablets were randomly picked from every batch and the mean and standard deviation were determined[16].

Friability test: The Friability of the tablet is determined by using Roche friabilator. It is the process in which tablet surfaces are damaged and additionally exposed to mechanical shock. In this method, ten tablets are initially moved into a friabilator. The tablets were worked at 25rpm for 4 mins or up to 10 rotations. Later tablets were weighed again and friability was determined[17].

Rate of friability was determined using:

F=W(initial) – W(final)/ W(initial) X 100

Less than 1% friability of tablets is accepted.

Weight variation test: The tablets were chosen randomly from every batch and gauged exclusively to check for weight variation. The U.S Pharmacopeia permits a little in the hardness of the tablet[18].

Table 11: Percentage deviation in weight variation

The average weight of the tablet	Percentage deviation
130mg or less	10
More than 130 mg or less than 324mg	7.5
324mg or more	5

Drug content uniformity: In the method, twenty tablets were weighed and transferred into the mortar. Tablets were crushed and a powder of tablet containing 100mg of equivalent drug transferred into 100ml of phosphate buffer pH 6.8.

It contains 1000mcg/ml of drug solution. From this 10ml of stock solution taken and diluted to 100ml of phosphate buffer pH6.8, it forms 100 µg/ml.out of this 0.1-0.6ml of stock solution was taken and diluted to 10ml of phosphate buffer. The absorbance was measured at 295nm[19].

In-vitro disintegration time: Disintegration is the process in which a tablet is broken down into fragments, this phenomenon is known as disintegration. In-vitro disintegration time is analyzed using various disintegration apparatus according to I.P specifications[20].

According to I.P specifications: place one tablet in each tube of the basket. Add a plate to each cylinder and run the mechanical assembly using phosphate buffer solution pH 6.8 and maintain temperature up to 37°C. The Time taken for complete disintegration of the tablet was recorded[21].

In-vitro dissolution studies: In-vitro dissolution studies were examined by USP type-2 apparatus using 900ml of phosphate buffer solution to maintain pH 6.8. in this process, the temperature was maintained up to 37°c. The aliquot solution was withdrawn in 5min intervals and then filtered using filter paper. The absorbance of the filtrate was measured at a maximum wavelength of 295nm. The concentration and absorbance were determined using the standard deviation curve[22].

Table 12: Details of In-vitro dissolution studies taken

Sl. No.	Parameter	Specification
1.	Apparatus used	Electrolab USP type-2
2.	Dissolution media	Phosphate buffer pH 6.8
3.	Dissolution media volume	Up to 900ml
4.	Temperature	37± 5°C
5.	Rotation speed	50rpm
6.	Sample withdraw time	5 min.
7.	Sample withdraw vol.	5ml
8.	Absorbance measured	295nm

The aim and objectives of this present study are to formulate and design mouth dissolving tablets of telmisartan. This novel approach is used for patient compliance, the onset of action, and greater bioavailability.

Telmisartan granule parameters

Table 13: Results of granule parameters

Formulation code	Bulk density gm/cc	Angle of repose	Hardness (Kg/cm^2)	Friability (%)
F1	0.54	29.08	3.25±0.15	0.54
F2	0.53	30.21	3.22±0.12	0.55
F3	0.54	28.32	3.23±0.15	0.56
F4	0.52	31.15	3.33±0.24	0.57
F5	0.53	30.38	3.31±0.13	0.61
F6	0.54	31.05	3.23±0.14	0.57
F7	0.53	29.56	3.25±0.16	0.55
F8	0.53	31.33	3.27±0.11	0.62
F9	0.52	30.13		0.55

Weight variation of tablets

Sl No.	Formulation code (F7) in mgs	Wt. Variation ±SD	Formulation code (F8) in mgs	Wt. Variation ±SD	Formulation code(F9) in mgs	Wt. Variation ±SD

	90	o.3±o.33	90	0.2±0.22	90	0.2±0.22
2.	91	1.3±1.44	90	0.2±0.22	89	0.8±0.89
3.	90	0.3±0.33	89	0.8±0.89	90	0.2±0.22
4.	88	1.7±1.89	89	0.8±0.89	90	0.2±0.22
5.	90	0.3±0.33	90	0.2±0.22	89	0.8±0.89
6.	91	1.3±1.44	88	1.8±2.00	91	1.2±1.33
7.	88	1.7±1.89	90	0.2±0.22	90	0.2±0.22
8.	90	0.3±0.33	91	1.2±1.33	90	0.2±0.22
9.	90	0.3±0.33	91	1.2±1.33	89	0.8±0.89
10.	89	0.7±0.78	90	0.2±0.22	90	0.2±0.22

Drug content of telmisartan tablets

Table 19: Drug content of telmisartan mouth dissolving tablets

Sl No.	Formulation Code	Absorbance	Concentration	Average drug content ±SD
1.	F1	0.996	17.2	73±0.0116
2.	F2	0.953	17.0	73±0.106
3.	F3	0.932	16.9	69±0.102
4.	F4	0.998	17.3	79±0.119
5.	F5	1.001	18.3	81±0.121
6.	F6	1.0123	18.7	87±0.125
7.	F7	1.153	19.1	94± 0.263
8.	F8	1.198	19.0	97±0.163
9.	F9	1.201	19.8	99± 0.173

In-vitro dispersion time

Table 20: In-vitro dispersion time of telmisartan tablet

Formulation code	Dispersion time±SD
F1	44.08±1.5
F2	41.01±1.7
F3	37.02±1.7
F4	35.07±1.2
F5	16.13±1.23
F6	16.0±1.2
F7	9.87±1.2
F8	7.77±1.0

F9	5.13±1.1

Conclusion: According to this research study it was concluded that the drug telmisartan and its formulation has very good solubility among the solvents and it is very helpful for the treatment of hypertension as well as in kidney diseases. The model drug has optimum solubility, bioavailability, and dissolution.

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Conflict of interest: Nil

References

1. Sanjeev Kumar et al, Efficient and improved synthesis of Telmisartan, Journal of Organic Chemistry, Jan-2019.
2. Ramón C. Hermid et al, Influence of Circadian Time of Hypertension Treatment on Cardiovascular Risk, Journal of Biological and Medical Rhythm Science, Vol-27, Issue-8, 2019.
3. S. Yang et al, Association between hypertension and fragility fracture: a longitudinal study, Osteoporosis International, July-2016.
4. Rubin M. Tuder, Pulmonary vascular remodeling in pulmonary hypertension, Cell and Tissue Research, Dec-2016.
5. Suzanne Oparil et al, Hypertension, Nature reviews disease primers, Mar-2018.
6. Kapil Chauhan et al, Formulation and Evaluation of Fast Dissolving Tablets of Telmisartan, International Journal of Pharmaceutical Science and Research, Vol-4, Issue-4, 2018, Pages 1514-1520.
7. Poonam Chaudhari et al, Formulation and Evaluation of Fast Disintegrating Tablet of Telmisartan, International Journal of Pharmaceutical Technology, 2014.
8. Bandameedi Ramu et al, International Journal of Pharmacy Research and Technology, August 2015,8(3):974-4304.
9. Ved Prakash et al, Fast disintegrating tablets: Opportunity in drug delivery system, Journal of Advanced Pharmaceutical Technology and Research, 2014 Oct-Dec; 2(4): 223–235.
10. SamixaDesai et al, Formulation of cyclodextrin inclusion complex-based orally disintegrating tablet of eslicarbazepine acetate for improved oral bioavailability, Materials Science and Engineering, Volume 58, 1 January 2016, Pages 826-834.
11. B. P. Patel et al, Formulation and Evaluation of Mouth Dissolving Tablets of Cinnarizine, Indian Journal of Pharmaceutical Sciences, 2019 Jul-Aug; 72(4): 522–525.
12. R. M. Sarfraz et al, Formulation and Evaluation of Mouth Disintegrating Tablets of Atenolol and Atorvastatin, Indian Journal of Pharmaceutical Science, 2015 Jan-Feb; 77(1): 83–90.
13. R. M. Sarfraz et al, Formulation and Evaluation of Mouth Disintegrating Tablets of Atenolol and Atorvastatin, Indian Journal of Pharmaceutical Sciences,2015 Jan-Feb; 77(1): 83–90.
14. Rebecca et al, Formulation and In-vitro Evaluation of Mouth Dissolving Tablets of Labetalol HCL by Sublimation method, Asian Journal of Pharmacy and Technology, Vol-6, Issue-2, 2016, Pages 60-70.
15. YagmurAkdag et al, Characterization and comparison of deferasirox fast disintegrating tablets prepared by direct compression and lyophilization methods, Journal of Drug Delivery Science and Technology, Volume 57, June 2020, 1017-60.
16. Jaya Malladi et al, Novel platens to measure the hardness of a pentagonal shaped tablet, National Library of Medicines, 2017 Mar;22(2):246-255.
17. Emma Hellberg et al, Evaluation of dissolution techniques for orally disintegrating mini-tablets, Journal of Drug Delivery Science and Technology, Volume 61, February 2021.

18. Santosh Kumar Rada, Fast dissolving tablets: waterless patient compliance dosage forms, Journal of Drug Delivery and Therapeutics, Vol-9, Issue- 1, Jan-Feb 2019.
19. VivekDave et al, Formulation design and optimization of novel fast dissolving tablet of chlorpheniramine maleate by using lyophilization techniques, Bulletin of Faculty of Pharmacy, Volume 55, Issue 1, June 2017, Pages 31-39.
20. Muhammad Irfan et al, Orally disintegrating films: A modern expansion in drug delivery system, Saudi Pharmaceutical Journal, Volume 24, Issue 5, September 2016, Pages 537-546.
21. Arti Mohan et al, In vitro and in vivo evaluation of fast-dissolving tablets containing solid dispersion of lamotrigine, International Journal of Pharmaceutical Investigation, 2015 Jan-Mar; 5(1): 57–64.
22. Mangesh Machhindranath Satpute et al, Formulation and in vitro evaluation of fast dissolving tablets of metoprolol tartrate, Brazilian Journal of Pharmaceutical Sciences, vol. 21, n. 4, oct./dec, 2017.