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Research Article

Formulation and Evalution of Telmisartan Solid Dispersion of Encapsulation Using Different Polymer

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Abstract

The aim of the present study was to improve the solubility and dissolution rate of a poorly water soluble drug, telmisartan by solid dispersion technique. The objective of the study is to prepare telmisartan solid dispersion and encapsulation using different polymers to achieve the enhanced solubility and to determine the Kinetic Modeling of Drug Release and Stability studies. Telmisartan has PH dependent solubility. Due to this reason only the % release for the prepared solid dispersions was higher in PH 4.5 acetate buffer when compared with other mediums. Based on mathematical data revealed from models, it was concluded that the release data was best fitted with First order kinetics. Stability studies showed that there were no significant changes in physical and chemical properties of capsule of formulation after 3 months.

Keywords: *Solid dispersion; Telmisartan; PEG6000; PEG20000; HPMC E15; HPC LH21; β-Cyclodextrin*

Introduction

Telmisartan is a member of a family of drugs called angiotensin receptor blockers (ARBs). Angiotensin, formed in the blood by the action of angiotensin converting enzyme (ACE), is a powerful chemical that attaches to angiotensin receptors found in many tissues but primarily on muscle cells of blood vessels. Angiotensin's attachment to the receptors causes muscle cells to shorten and narrow the blood vessels (vasoconstrict), which leads to an increase in blood pressure (hypertension). Telmisartan blocks the angiotensin receptor. By blocking the action of angiotensin, telmisartan widens blood vessels (vasodilate) and reduces blood pressure. Telmisartan belongs to class II drug in BCS classification i.e. low solubility and high permeability. One of the major problems with this drug is its low solubility in biological fluids, which results into poor bioavailability after oral administration. The solubility of Telmisartan in aqueous medium was very low i.e. 0.078 mg/ml in water. Absolute bioavailability of the Telmisartan was 42 - 58% and biological half-life is only 24 hours that results into poor bioavailability after oral administration. Poor solubility of Telmisartan leads to poor dissolution and hence variation in bioavailability. Thus increasing aqueous solubility and dissolution of Telmisartan is of therapeutic importance.

The approaches in overcoming the bioavailability problems due to such causes are: 1. The pharmaceutics approach which involves modification of formulation, manufacturing process, or the physiochemical properties of the drug without changing the chemical structure. 2. The pharmacokinetic approaches in which the pharmacokinetics of the drug is altered by the modifying its chemical structure. 3. The biological approach whereby the route of the drug administration may be changed such as changing from oral to parental route.

Materials and Methods

Materials

The materials used for the formulation are Telmisartan, gifted by SERDIA Pharma Ltd, Hyderabad, PEG6000, PEG20000, HPMCE15, HPC LH21- S D Fine chem. Ltd. Mumbai, β-Cyclodextrin- Himedia laboratoty pvt. Mumbai, Lactose, Aerosil, Magnesium Stearate, Isopropyl Alcohol. All the materials used in study were of analytical grade.

Instruments

UV/VIS spectrophotometer, Electronic balance, PH meter, Dissolution apparatus, Tapped density apparatus USP.

Methods

Formulation of solid dispersions

In the present investigation Solid scatterings were set up by Physical strategy.

Physical method

The physical blend were readied utilizing Telmisartan as medication and Polyethylene glycol 6000, Polyethylene glycol 20000, HPMC E15, HPC LH21, SOLUPLUS, β-Cyclodextrin as bearers in the proportion of 1:1 individually given in plan table. The required amount of bearers was said something electronic computerized balance, taken in a mortar and it was blended with measured amount of medication mind geometric weakening technique to shape a homogenous physical blend. The physical blend was dried legitimately utilizing hot air broiler at 45ºC for 60 minutes. The dried blend was gone through sifter no 80 and put away in desiccators for additionally contemplate.

Encapsulation

The readied strong scattering were blended with lactose, magnesium Stearate and Aerosil and filled into containers.

Preparation of standard curve for telmisartan in 0.1N HCL

The absorption maxima for Telmisartan in 0.1N HCl was established at 229 nm.

Standard solution of telmisartan

100 mg of Telmisartan pure drug was accurately weighed and transferred into a 100 ml volumetric flask, dissolved in little quantities of methanol, then made up to 100ml with methanol (1000 µg/ml). From this solution, 10ml of solution was withdrawn into a 100ml volumetric flask and made up to 100 ml with 0.1N HCL buffer to get a concentration of 100 µg/ml. From this 10, 12, 14, 16, 18 ml pipetted and diluted to 100 ml with 0.1N HCL to get a concentration of 10, 12,14,16,18 µg/ml. Absorbance of the solution was measured at 229 nm using UV/VIS spectrophotometer against blank (0.1N HCL buffer).

Preparation of standard curve for telmisartan in 4.5 acetate buffer

The absorption maxima for Telmisartan in Acetate Buffer were established at 230 nm.

Standard solution of telmisartan

100 mg of Telmisartan pure drug was accurately weighed and transferred into a 100 ml volumetric flask, dissolved in little quantities of methanol, then made up to 100 ml with methanol (1000 µg/ml). From this solution, 10ml of solution was withdrawn into a 100 ml volumetric flask and made up to 100ml with 4.5 Acetate buffer to get a concentration of 100 µg/ml. From this 30, 40, 50, 60, 70 pipetted and diluted to 100 ml with 4.5 Acetate buffer to get a concentration of 30, 40, 50, 60, 70 µg/ml. Absorbance of this was measured at 230 nm using UV/VIS spectrophotometer against blank (4.5 Acetate buffer).

Formulation table

	Ingredients	mg/tab											
		F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	Telmisartan	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg	20 mg
2	PEG6000	30 mg	30 mg	-	-	-	-	-	-	-	-	-	-
3	PEG20000	-	-	30 mg	30 mg	-	-	-	-	-	-	-	-
4	HPMC E15	-	-	-	-	30 mg	30 mg	-	-	-	-	-	-
5	HPC LH21	-	-	-	-	-	-	30 mg	30 mg	-	-	-	-
6	β- CYCLODEXT RIN	-	-	-	-	-	-	-	-	30 mg	30 mg	-	-
7	Soluplus	-	-	-	-	-	-	-	-	-	-	30 mg	30 mg
8	Lactose	38 mg	38 mg	38 mg	38 mg	38 mg	38 mg	38 mg	38 mg	38 mg	38 mg	38 mg	38 mg
9	Aerosil	1 mg	1 mg	1 mg	1 mg	1 mg	1 mg	1 mg	1 mg	1 mg	1 mg	1 mg	1 mg
10	mg Sterate	1 mg	1 mg	1 mg	1 mg	1 mg	1 mg	1 mg	1 mg	1 mg	1 mg	1 mg	1 mg
11	ISO Propyl Alcohol	-	0.2 ml	-	0.2 ml	-	0.2 ml	-	0.2 ml	-	0.2 ml	-	0.2 ml
12	Wt of Ingredients	100	100	100	100	100	100	100	100	100	100	100	100
13	Method of Preparation	Physical Method	Kneading Method	Physical Method	Kneading Method	Physical Method	Kneading Method	Physical Method	Kneading Method	Physical Method	Kneading Method	Physical Method	Kneading Method
14	Mfg Process	Capsule	Capsule	Capsule	Capsule	Capsule	Capsule	Capsule	Capsule	Capsule	Capsule	Capsule	Capsule

Table 1: Table for formulation of F1-F12.

Drug content estimation

Weigh and powder 20 capsules. Weigh accurately a quantity of powder containing equivalent weight of 5 capsules weight of Telmisartan into a 100 ml volumetric flask. Dissolve with the aid of small quantities of methanol, make up to 100 ml with methanol and filter. Dilute 10 ml of filtrate to 100 ml with 6.8 phosphate buffer, 0.1N HCL, 4.5 Acetate buffer and mix. Pipette out 10 ml of solution into a 100 ml volumetric flask and make up to 100 ml with 7.2 phosphate buffer and mix. Measure the absorbance of the resulting solution at 226, 229 and 230 nm in UV.

Results and Discussion

Calibration curve of telmisartan

A calibration curve for Telmisartan was constructed in phosphate buffer pH 6.8, Acetate buffer pH 4.5, 0.1N HCL by scanning the drug solution at 226, 229 and 230 nm using UV spectrophotometer. The linearity of the calibration curve was found to be in the range of 1 - 10 µg/ml. A regression coefficient value of 0.999 was noticed for Telmisartan.

Concentration (µg/ml)	Absorbance (nm)
0	0
10	0.192
12	0.242
14	0.291
16	0.356
18	0.412

Table 2: Standard Curve for Telmisartan in 0.1N HCL at 229 nm.

Figure 1: Standard calibration curve for telmisartan.

Concentration (µg/ml)	Absorbance (nm)
0	0
30	0.169
40	0.246
50	0.377
60	0.455
70	0.534

Table 3: Standard curve for telmisartan in 4.5 acetate buffer at 230 nm.

Figure 2: Standard calibration curve for telmisartan.

Melting point

The melting point of Telmisartan was found to be 165˚C, which complied with BP standards thus indicating purity of obtained drug sample.

Results for pre-formulation studies

Formulation	Bulk density	Tapped density	Carr's Index	Hausner's Ratio	Angle of Repose
Prepared Conventional	0.371	0.457	18.81	1.231	28.86
F1	0.318	0.389	18.25	1.223	24.93
F2	0.331	0.399	17.04	1.205	24.25
F3	0.329	0.396	16.91	1.203	25.05
F4	0.345	0.409	15.64	1.185	26.4
F5	0.356	0.411	13.38	1.154	25.79
F6	0.389	0.444	12.38	1.141	27.56
F7	0.362	0.41	11.7	1.132	27.66
F8	0.338	0.378	10.58	1.118	28.67
F9	0.337	0.403	16.31	1.195	25.06
F10	0.35	0.414	15.45	1.182	26.71
F11	0.343	0.402	14.67	1.172	26.94
F12	0.367	0.422	13.03	1.149	27.1

Table 4: Pre compression studies.

The prepared Telmisartan solid dispersion systems can be arranged in ascending order, regarding the angle of repose measurements as follows: F2 < F1 < F3 < F9 < F5 < F4 < F10 < F11 < F12 < F6 < F7 < F8.

Compatibility studies by FTIR

The spectrum obtained after the analysis is shown in figure 3 and 4. The spectrum of the standard and the samples were then superimposed to find out any possible interactions between the drug and the polymers. The results suggest that the drug is intact in the formulations and there is no interaction found between the drug and the excipients.

Figure 3: FTIR spectra of pure drug telmisartan.

Figure 4: FTIR spectra of physical mixture of telmisartan.

Evaluation of post compression parameters

The liquisolid capsules were prepared by encapsulation technique. Similarly, Conventional capsule of pure drug was also prepared by encapsulation technique.

Drug content estimation

Formulation	Drug content (%)	Formulation	Drug content (%)
F1	95.69	F7	95.18
F2	94.67	F8	98.73
F3	96.19	F9	96.2
F4	93.67	F10	96.7
F5	93.15	F11	93.16
F6	94.17	F12	97.21

Table 5: % of Drug content in different formulation.

F8 showing maximum drug content and F5 shows least content. Results showed in table 5 it was clear from table 5 that all the investigated solid dispersion capsules complied with the pharmacopoeial requirements with regard to their content uniformity, which was found to lie within the range of 93.15% to 98.73%.

In vitro dissolution study

Dissolution conditions: Apparatus: I.

Solvent: (0.1N HCL, 6.8 Phosphate buffer, 4.5 Acetate buffer), Volume: 900 ml.

Rpm: 50, Temperature: 37 ± 5˚C, λmax: 226, 229, 230 nm.

For pure drug % release			
Time	**0.1N HCL**	**pH 6.8**	**pH 4.5**
5	8.794	0.209	15.448
10	10.408	0.21	16.588
15	10.63	0.214	20.481
30	14.841	0.229	21.526
45	16.392	0.398	21.621
60	16.741	0.596	22.38

Table 6: Dissolution profile of prepared conventional formulation.

Figure 5: *In vitro* release of prepared conventional formulation.

Dissolution profile of solid dispersions

Dissolution media 0.1N HCl

Sl No	Time	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	5 min	18.963	27.48	15.14	15.9	9.47	8.11	19.06	27.16	10.86	8.304	26.60	18.9
2	10 min	27.079	36.504	31.346	32.003	14.75	12.05	24.13	31.96	16.39	14.55	37.30	36.63
3	15 min	38.458	41.702	36.681	37.735	18.48	16.49	27.83	35.16	22.34	18.95	39.91	38.56
4	30 min	39.106	44.295	42.494	42.781	25.94	23.93	32.38	41.80	34.99	32.51	41.74	39.50
5	45 min	42.77	44.904	44.025	45.157	45.50	32.91	37.13	45.98	48.07	46.50	46.92	43.98
6	60 min	57.389	47.97	47.28	47.101	51.64	45.48	41.13	47.57	51.22	55.53	47.56	45.58

Table 7: Dissolution profile of solid dispersions in 0.1N HCl

Figure 6: Dissolution profile comparison of formulations F1-F5 in 0.1N HCL.

Figure 7: Dissolution profile comparison of formulations F6-F10 in 0.1N HCl.

Dissolution media 4.5pH Phosphate buffer

When dissolution carried out with 0.1NHcl, the formulation prepared with PEG6000 (P.M) releases the drug faster than with other.

When dissolution carried out with PH 4.5 acetate buffer, the formulation prepared with HPC LH21 (P.M) releases the drug faster than with other.

Drug content estimation

It was clear from table 9 that all the investigated solid dispersion capsules complied with the pharmacopoeial requirements with regard to their content uniformity, which was found to lie within the range of 93.15% to 98.73%.

F8 showing maximum drug content and F5 shows least content. Results showed in table 9.

S. No	%drug release-pH4.5 acetate buffer												
	Time	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1	5 min	46.3	43.5	44.3	36.8	24.4	22.6	48.0	73.0	33.7	28.4	36.4	52.1
2	10 min	62.0	64.1	62.2	63.2	32.4	30.6	57.8	84.0	42.7	34.9	71.3	74.2
3	15 min	64.6	67.5	71.3	68.3	39.2	38.5	63.8	91.1	53.1	49.3	78.6	78.2
4	30 min	70.0	73.5	75.1	71.5	52.6	49.0	85.1	95.7	72.8	63.7	87.7	88.4
5	45 min	72.9	76.0	79.1	76.5	53.5	52.5	98.1	97.8	86.6	77.5	98.3	92.2
6	60 min	82.2	85.2	89.7	89.0	61.1	58.3	99.7	99.6	98.1	94.4	99.5	98.8

Table 8: Dissolution profile of solid dispersions in pH 4.5 buffer.

Figure 8: Dissolution profile comparison of formulations F1-F5 in pH 4.5 buffer.

Figure 9: Dissolution profile comparison of formulations F6-F10 in pH 4.5 buffer.

Formulation	Drug content (%)	Formulation	Drug content (%)
F1	95.69	F7	95.18
F2	94.67	F8	98.73
F3	96.19	F9	96.20
F4	93.67	F10	96.70
F5	93.15	F11	93.16
F6	94.17	F12	97.21

Table 9: % drug content.

Release kinetics

Release kinetics	R^2	Intercept	Slope
Zero order	0.412	-4.568	1.011
First order	0.903	53.15	1.626

Table 10: Kinetic studies of solid dispersion.

The cumulative percentage drug release data obtained were fitted to Zero order, first order. The slopes and the regression coefficient of determinations (r^2) were listed in table 10. The coefficient of determination indicated that the release data was best fitted with first order kinetics.

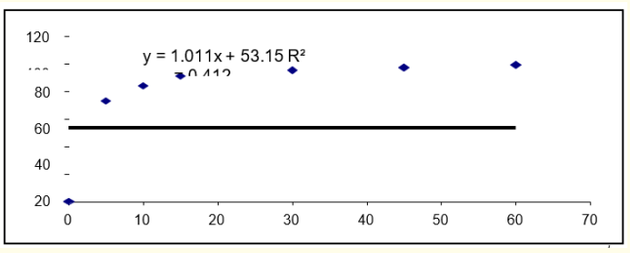

Figure 10: Release profile of telmisartan solid dispersion according to zero order.

Figure 11: Release profile of telmisartan solid dispersion according to first order.

Summary

Telmisartan showed a maximum solubility of 2.392 mg/ml in HPC LH21 followed by 0.812 mg/ml in PEG 20000, 0.544 mg/ml in PEG 6000, 0.231 mg/ml in SOLOPLUS, 0.129 mg/ml in HPMC E15, 0.101 mg/ml in 4.5 Phosphate buffer, 0.0253mg/ml in 0.1N HCL, 0.008 mg/ml in 6.8 Phosphate buffer and 0.005 mg/ml in water. Hence we can conclude the Telmisartan has P^H dependent solubility. Due to this reason only the % release for the prepared solid dispersions was higher in P^H 4.5 acetate buffer when compared with other mediums.

F8 showed higher release rate (99.645% at the end of the 60^{th} minute. Conventional showed only 22.38% cumulative release. It was confirmed that at 10^{th} minute F8 had the highest drug release 84.062% compared with 16.588% for the conventional capsule. Since for solid dispersions, the drug surface available for the dissolution is tremendously increased. Based on mathematical data revealed from models, it was concluded that the release data was best fitted with First order kinetics.

Conclusion

This research work has produced encouraging results in terms of increasing the *in vitro* dissolution of poorly soluble drugs such as Telmisartan using solid dispersion technology and we expect a good correlation between the *in vitro* and *in vivo* performance of the formulations. The technique being simple and effective can also be extended to other poorly soluble drugs. The FTIR spectra revealed that, there was no interaction between polymer and drug. (F8) was showing best release. Based on mathematical data revealed from models, it was concluded that the release data was best fitteds with First order kinetics [1-11].

Conflict of Interest

This article has not published before and it is not under consideration for publication in any other journal.

Bibliography

1. Alfred Martin. "Physical pharmacy, fifth edition, Lippincott, Williams and Wilking, New York (2007): 230-245, 337-345.
2. Michael E Aulton. "Pharmaceutics the science of dosage form design". Second edition, Churchill Living stone, New York (2002): 15-32.
3. James Swarbrick and James Boylan. "Encyclopedia of pharmaceutical technology second edition". Marcel Dakker, Ic, Volume 1 (2002): 717-727.
4. DM Brahmankar and Sunil B Jaiswal. "Biopharmaceutics and pharmacokinetics A treatise". First edition, Vallabh Prakashan, Delhi (1995): 19-25.
5. Gong Y., *et al*. "Principles of Solubility". In: P Augustijns, ME Brewster (Eds.), Solvent Systems and Their Selection in Pharmaceutics and Biopharmaceutics, Springer Science + Business Media, LLC, New York (2007): 1-27.
6. USP 28-NF 23. The United States Pharmacopoeial Convention, Rockville (2005): 2875.
7. Vasconcelos T., *et al*. "Solid dispersions as strategy to improve oral bioavailability of poor water soluble drugs". *Drug Discovery Today* 12.23-24 (2007): 1068-1075.
8. Serajuddin ATM. "Solid dispersion of poorly water-soluble drugs: Early promises, subsequent problems, and recent breakthroughs". *Journal of Pharmaceutical Sciences* 88 (1999): 1058-1066.
9. "Indomethacin using gelucire 50/13 and PEG 4000". *Saudhi Pharmaceutical Journal* 17: 217-225.
10. Rahul Gaste. "An overview on solid dispersions" (2009).
11. Newa M., *et al*. "Enhancement of Solubility, Dissolution and Bioavailability of Ibuprofen in Solid Dispersion Systems". *Chemical and Pharmaceutical Bulletin* 56.4 (2008): 569-574.