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INVESTIGATION OF THE EFFECT OF FORMULATION ADDITIVES ON TELMISARTAN DISSOLUTION RATE: DEVELOPMENT OF ORAL DISINTEGRATING TABLETS

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ABSTRACT

The aim of this work was to enhance solubility of telmisartan by the preparation of amorphous solid dispersion in presence and absence of pH modifying agent. This was achieved by preparing solid dispersion (SD) of telmisaratin with a hydrophilic polymer (polyethylene glycol 4000), in presence and absence of meglumine. The latter was used as alkanizer. Binary solid dispersion was prepared by solvent evaporation technique at different drug:polymer weight ratios. To selected formulation, meglumine was included as third component at different molar ratios to obtain ternary mixtures. The obtained microparticles were evaluated using differential scanning calorimetry (DSC), Foriur Transform Infrared (FTIR), X-ray powder diffraction and in vitro drug release studies. Binary solid dispersion slightly improved drug dissolution over unprocessed drug. The optimum SD combination was formulated into oral disintegrating tablets using different ODT bases namely Pearlitol® Flash, Pharmaburst ® 500 and Ludiflash®. Incorporation of meglumine markedly increased telmisartan dissolution with about 80% of the loaded dose librated after 5 minutes. Physical characterization indicated compatibility between ingredients and reduced drug crystallinity. The optimum formulation was sucessfully used to prepare orodispersible tablets, with those prepared using Pharmaburst ® 500 as filler showed optimum tablets quality and drug release pattern, compared to other fillers.

KEYWORDS: Telmisartan, meglumine, solid dispersion, pH modifier, fast disintegrating tablets.

INTRODUCTION

Orally Disintegrating tablets (ODTs) are specially designed solid dosage forms that rapidly disintegrate in the mouth without chewing or even the need for water. The ODTs system, also known as Fast disintegrating tablets (FDTs) or mouth melting tablets(MMTs) or mouth dissolving tablets[1]. They have the unique property of disintegrating in the mouth in matter of seconds making them very useful in acute disease conditions. For chronic conditions, it is assumed to improve patient compliance to the medication due to the easy to use properties[2]. These tablets fulfilled the medical needs for pediatric and geriatric patients who usually experience great difficulty in swallowing tablets. In addition to increased patients acceptability, these tablet offer many advantages compared to traditional tablets. An appreciable amount of the drug will be absorbed from oral mucosa bypassing the gastrointestinal tract and hepatic portal systems. This is expected to increase the bioavailability of orally administered drugs which can otherwise undergo hepatic first-pass metabolism[3].

In the year of 2016, the European Pharmacopoeia adopted the term orodispersible tablet as a tablet to be placed in the oral cavity where it disintegrates in less than 3 minutes before being swallowed[4,5]. There was no specification concerning neither the hardness nor the friability of this kind of tablets. Commercially available ODTs are prepared by various techniques, such as lyophilization, moulding and direct compression. The lyophilisation and molding techniques produce ODT with a disintegration time within about 30 seconds, but suffer from low physical resistance and require specific packaging and handling conditions. On the other hand, tablets obtained by direct compression are less friable but disintegrate in a slightly longer time[6]. Orodispersable tablets show many advantages over traditional one such as; it bypasses the gastrointestinal tract and hepatic portal systems, increases the bioavailability of orally administered drugs which can otherwise undergo hepatic first-pass metabolism[3]. However, this sequence requires rapid drug dissolution which is difficult to achieve with many valuable drugs. Optimizing drug dissolution rate is thus the limiting factor in formulation of these systems. Enhancing drug dissolution prior to formation of ODTs

have been previously conducted for many Class II drugs[7-9].

Telmisartan is an angiotensin-II receptor antagonist. It is useful in the treatment of hypertension, heart diseases, heart strokes and bladder diseases. Telmisaratn is manufactured and supplied in the free acid form and is characterized by its very poor intestinal solubility, which depended on the pH of the medium as a BCS Class II drug with an aqueous solubility of about 0.09mg/mL. Poor solubility results in its low bioavailability. Many approaches have been conducted to improve the solubility of telmisartan such as co-grinding with different alkalizer[10], preparation of solid dispersions[11] and incorporation in nanoparticles[12,13].

The aim of this study was to prepare oral disintegration tablets of telmisartan for intra-oral administration. To achieve this goal, drug dissolution was improved by solid dispersion of the drug with hydrophilic polymer, in presence and absence of meglumine as pH modifier. The optimum formulation was incorporated in different co-processed fillers specially designed for oral dispersible tablets. Comparisons were made in order to obtain the best combination that produced optimum drug dissolution parameters.

MATERIALS AND METHODS

Materials

Telmisartan, polyethylene glycol PEG 4000, meglumine, magnesium stearate, colloidal silicon dioxide were kindly supplied by European Egyptian Pharmaceutical Company (Alex, Egypt). Pharmaburst®500 was purchased from SPI Supplier, Pearlitol® Flash was purchased from Roquette Supplier, Ludiflash® was purchased from O-BASF supplier. All other chemicals were of analytical grade.

Methods

Construction of the Calibration Curve

Calibration curve of Telmisartan was constructed by dissolving 100mg of the drug in 100 ml methanol. A serial dilutions were made to obtain solutions in the range of 2-20 µg/ml. The prepared solutions were analyzed spectrophotometrically at λ max of 295nm using UV-spectrophotometer (Shimazuuv2450, Japan). The obtained standard curve was linear (R^2=0.999) over the range of concentrations used.

Preparation of Telmisartan solid dispersion

Binary solid dispersions of telmisartan:PEG4000 at different weight ratios (1:1, 1:2 and 1:3) were prepared.Additionally, ternary solid dispersions were prepared by adding meglumine at different molar ratios to the drug using the 1:1 telmisartan: PEG4000 binary combination (Table 1). Solid dispersion was prepared by solvent evaporation technique. Telmisartan and PEG4000 were dissolved in the least amount of methanol, in presence or absence of meglumine, by the aid of gentle heating at 40ºC. The solution was subjected to continuous stirring at ambient temperature to evaporate the organic solvent, until liberation of the solid materials and obtaining a dry powder. The precipitated microparticles were collected, grinded, sieved through 300 mesh and stored in a descicator till use.

Table 1: The composition of different solid dispersion formulations with dissolution parameters represented as percentage amount released after 5 minutes (Q5) and percentage dissolution efficiency (%DE).

Code	telmisartan	PEG 4000	Meglumine	Q5%	%DE
Pure drug	40mg	--	--	5.1± 0.1	5.88
F1	1	1	--	15.1 ±0.7	17.1
F2	1	2	--	10.6 ±0.2	11.8
F3	1	3	--	6.6 ±0.4	10.3
F4	1	1	1	80.2±3.6	80.9
F5	1	1	3	79.4 ±1.9	81.4
F6	1	1	5	76.5±4.9	74.2
PM	1	1	1	18.4± 1.5	13.8

Preparation of physical mixtures

Physical mixtures (PM) for selected formula (F4) were prepared according to the compositions presented in Table1. This was achieved by geometric dry blending of the telmisartan, meglumine and PEG4000 with the aid of a mortar and a pestle.

Characterization of Solid dispersion

Drug content

The drug content was determined by dissolving an amount equivalent to 40 mg of the drug from each formulation in 100 ml methanol. The solution was suitably diluted with methanol before spectrophotometric determination of the drug concentration.

Physical characterization of the prepared formulations

Differential Scanning Calorimetry (DSC)

The thermal behavior of the unprocessed Telmisartan, PEG 4000 and meglumine as well as their selected solid dispersion formulations was monitored. This employed differential thermal analyzer (PerkinElmer STA 6000 module, Waltham, MA). The dry sample (about 5mg) was loaded into aluminum pan which was crimped using Shimadzu crimper, a crimped empty pan was used as reference. The two pans was gradually heated using temperature range from 25 to 400 ºC at an increasing rate of 10°C/min This was conducted under steady flow of

nitrogen gas. The recorded data were analyzed using Pyris software.

Fourier–transform infrared spectroscopy (FTIR)

FTIR Spectra of Telmisartan, meglumine, PEG4000 and selected formulations were recorded using FTIR system (W. N 200-5000 Tensor 27). The test powder was mixed with potassium bromide (spectroscopic grade) prior to compression into thin disks. Each disk was carefully loaded into the sample holder and subjected to scanning from 5000 to 400 cm^{-1}. The position of each absorption band was determined employing Opus IR, FT IR spectroscopy Software.

X-ray powder diffraction

The X-ray diffraction patterns of the target samples were monitored using X-ray powder diffractometer(Crystal Impact, Bonn, Germany). The diffraction pattern was detected with a position sensitive detector (VAo NTEC-1). The diffraction pattern was collected at ambient conditions with a 2□ axis with continuous scan mode. The scanning was established in the range of 5-70º at step size of 0.03º.

Preparation of oral dispersible tablets (ODTs)

The microparticle formulation showing the best dissolution parameters (F4) was used to prepare the ODTs that supposed to liberate most of the drug immediately after disintegration. Each tablet was prepared to contain an amount equivalent to 40mg of the drug. The composition of the prepared tablets are presented in Table 2. Tablets were prepared using three different brands of fast disintegrating tablet bases as filler with the aim of optimized tablet formulation concerning tablet disintegration time and drug release rate. The used fillers were Pearlitol® Flash, Pharmaburst ® 500 and Ludiflash®. For each ODT base, two tablet batches were prepared. These comprised tablet batch containing microparticles formula F4 (test batch) and control batch containing unprocessed drug. And This to elucidate the role of the adopted processing technique on the drug release pattern.

Pure drug (control tablets) or its equivalent of formula F4 was mixed with the excipients for 10 min using the bottle method. The mixtures were compressed into 300 mg tablets using flat round nonscored10mm punch. This process employed single punch tablet machine (ErwekaAR 400, Rieckermann, hamburg, Germany). The compression force of which being adjusted to produce tablets having a hardness of about 4–5 kP.

Quality attributes of ODTs

Tablet batches were tested for tablet quality in reference to US Pharmacopeal specifications (2000).The prepared tablets were characterized with respect to the uniformity of weight, hardness, drug content uniformity, disintegration time and drug release. Additionally, the wetting time test was also performed[14]

The uniformity of weight was performed using randomly selected tablets (20 tablets), the weight of which was recorded and the average weight was calculated. The deviation of each tablet from the calculated mean weight was calculated and expressed as percentage. If no more than 2 tablets deviates by ±7.5%, the tablets pass this test but none of them should deviate by more than double the limit.

The tablet hardness was conducted using 6 tablets and the test was performed using hardness tester (DR. Schleuniger Pharmatron tablet tester 8M). The content uniformity was assessed using 10 tablets, each tablet was individually analyzed for telmisartan content. This was achieved by crushing the tablet before dispersion in 50ml methanol. Complete dissolution of drug was assisted by bath sonication for 10 minutes. The dispersion was filtered and suitably diluted with methanol before analysis for drug content. The tablets are considered acceptable if the individual content of at least 9 tablets was within the allowed limit (85–115%) of the claimed drug.

The disintegration time was determined using 6 tablets employing disintegration equipment (LIJ-3, vanguard pharmaceutical machinery, USA). Each tablet was loaded into one of the disintegration 6-unit basket which was immersed in 1 liter of distilled water maintained at 37± 0.5°C. The time necessary for complete breakup of tablets and passage through the screen of the disintegration unit was taken as a measure for disintegration time.

Tablet porosity was evaluated using wetting time test, employing allura red as an indicator. Allura red powder was sprinkled on the tablet surface before placing over a filter paper (previously wetted with 6ml water) placed in a Petri dish. The wetting time was noted as the time required for the indicator to convert from the dark brown color to red color on the tablet top surface. The test was conducted in triplicate and the results were expressed as the average wetting time[14].

DISSOLUTION STUDIES

The dissolution rate of unprocessed Telmisartan (control) and that from different solid dispersions, physical mixture and the prepared tablets was determined using the USP II dissolution apparatus (Hanson SR8 Plus, virtual instrument, USA). The paddle rotation was adjusted to 75 rpm and the dissolution medium (900 ml phosphate buffer PH 7.5±0.5) was maintained at 37 ºC ±0.5 ºC. An amount of 40 mg of telmisartan or its equivalent weight of different formulations or ODT tablet was added in the dissolution medium. Aliquots of 5 ml each were taken at predetermined time intervals for 60 minutes and replaced with fresh dissolution medium. The samples were immediately filtered through 0.45 mm Whatman membrane filter. The filtrate was suitably diluted with the fresh dissolution medium before spectrophotometric analysis for drug content at 295 nm.

Dissolution profiles were obtained by plotting cumulative amount of telmisartan dissolved (expressed as % of the loaded amount) as function of time. These plots were used to calculate the dissolution parameters namely percentage drug dissolved in the first 5 minutes (Q5) and the dissolution efficiency (DE). The latter was calculated according to Khan, from the area under the dissolution profile at time t expressed as a percentage of the area of the rectangle described by 100% dissolution in the same time[15].

Statistical Analysis

All experiments were conducted in triplicates and Statistical analysis employed Student *t*-test. Results were quoted as significant where $P < 0.05$.

RESULTS AND DISCUSSION

The drug content of the prepared formulations was in the range of 95 to 97% w/w. This finding indicates good recovery of the drug and suggests the coexistence of the drug, polymer and meglumine (if present).

FTIR spectroscopy

Figure 1 shows the recorded FTIR spectra of pure telmisartan, PEG 4000, meglumine and ternary solid dispersion (F4 and F6) microparticles. The FTIR spectrum of unprocessed telmisartan showed the characteristic spectral pattern which correlates to its chemical structure. The characteristic peak at 1695 $cm^{-1}$for CO stretching vibrations, characteristic peak of 1, 2-disubstituted benzene can be detected at 757 cm^{-1}. Absorption band for OH group was noted at 3406cm^{-1}, CN stretching vibrations at1350–1000 cm^{-1}, CH3 bending vibrations at 1455 and 1381 cm^{-1}, C-C aromatic band and stretching at1599 cm^{-1}, CH bending at1460 cm^{-1}. This spectrum is similar to the published spectrum for the same drug[7].

The spectrum of PEG 4000 revealed broadband at 3466 $cm^{-1}$for the OH group. The aliphatic C–H stretching was shown at 2914 $cm^{-1}$with a band appearing at 1133 $cm^{-1}$for C–O stretching. This spectrum correlates with the published spectrum of the same polymer[8]. Regarding meglumine, the spectrum shows the characteristic absorption bands according to its structure. Free and bounded OH group can be detected at about 3290 and 3450 and cm^{-1}.

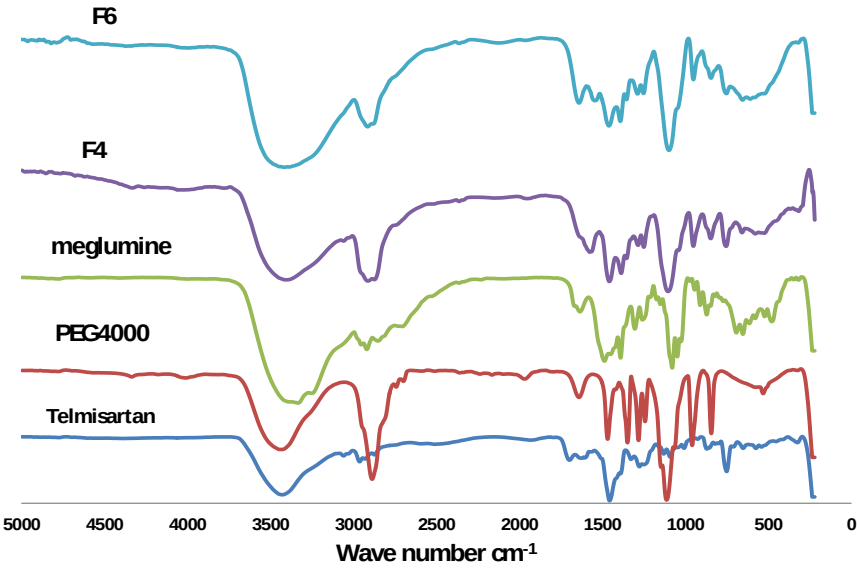

Figure 1: Samples FTIR spectra of pure telmisartan, polyethylene glycol (PEG) 4000, meglumin, formulations F4 and F6. For detailed formulation refer to Table 1.

The FTIR for solid dispersion F4 and F6 produced compromised spectral pattern. The characteristic absorption band of temisartan can be detected. The broad band due to OH groups can be detected in both spectrum, with that for F6 more broaden due to increased meglumine concentration in the formula. This finding is in a good agreement with previous work implying salt formation of telmisaratn and meglumine after co-grinding using vibrational mill[10].

Differential Scanning Calorimetry

Thermal analysis was employed to investigate further the interaction between telmisartan and other ingredients. Representative thermograms of unprocessed telmisartan, PEG4000, meglumine and their solid dispersion formula F4 and F6 are shown in Figure 2. These DSC traces have been used to compute the thermodynamic parameters of each transition peak including the onset, endset and transition midpoint (Tm).

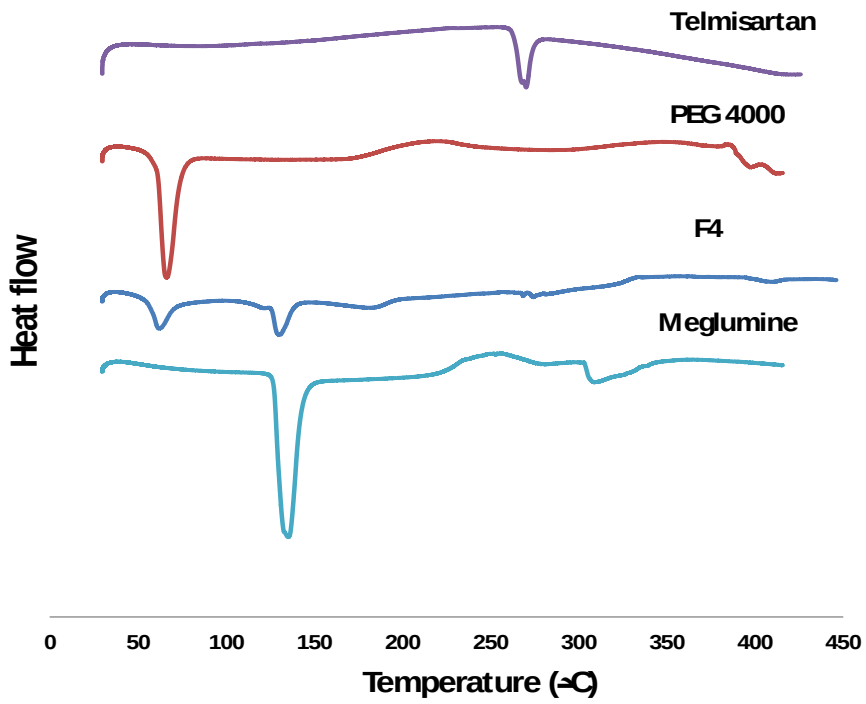

Figure 2: Sample DSC traces of pure telmisartan, polyethylene glycol (PEG) 4000, meglumin, formulations F4. For detailed formulation refer to Table 1.

The DSC tracing of unprocessed drug showed a distinct endothermic peak with an onset of 243°C, endset of 277°C, Tm of 267°C. This endotherm corresponds to the melting transition of telmisartan and implying its crystalline nature[10]. The thermal behavior of PEG4000 showed a sharp endothermic peak with an onset of 47.1°C, endset of 76.5°C of and Tm of 64.5°C. The thermogram also showed broad exothermic peaks at about 211.3°C, that could be taken as polymer decomposition. This thermal behavior coincide with the reported melting transition of the polymer[16]. Regarding meglumine, a sharp endothermic peak with onset of 120.5°C, endset of 145.6°C and melting transition at131.9°C was noted. It worth noting that there is another endothermic peak appeared at around 304.8°C that can be taken as decomposition of meglumine.

For formula F6, the endothermic peak of PEG showed reduced intensity with peak broadening. The onset was shifted to 43.6°C and Tm reduced to 59°C. The same behavior was noted for the characteristic transition endotherm of meglumine in the same formula (Figure 2). The endothermic peak of telmisartan was disappeared, indicating formation of amorphous form. Possible formation of solid solution and/or microcrystal formation can be considered based on the change of PEG endothermic parameters.

X-ray powder diffraction

The diffractograms of pure drug, excepients and selected formulations are shown in Figure 3. Diffraction pattern of the pure telmisartan showed its highly crystalline nature, indicated by many distinctive peaks at a diffraction angle of 2 theta of 6.8º, 14.3º and 22.3º throughout the scanning range. This diffraction pattern is similar to published data for telmisartan by other investigators. Meglumine exhibited its characteristic most intense peak at 9.0º in addition to other diffraction at 2 theta values of 12.3º, 17.9º and 21.8º in agreement with published data[10]. The diffractogram for PEG showed the characteristic peaks of its crystalline nature with the most intense peaks being recorded at 19.06º and 23.22º[8].

The characteristic drug peaks disappeared in both F4 and F6 microparticles indicating reduced drug crystalline nature and formation of amourphous form. Only the two characteristic peaks of PEG, but of low intensity, can be noticed in both diffractograms. For F6, some of meglumine peaks can be detected due to its high concentration (1:1:3 drug: PEG: meglumine, respectively) compared to F4 (see table 1).

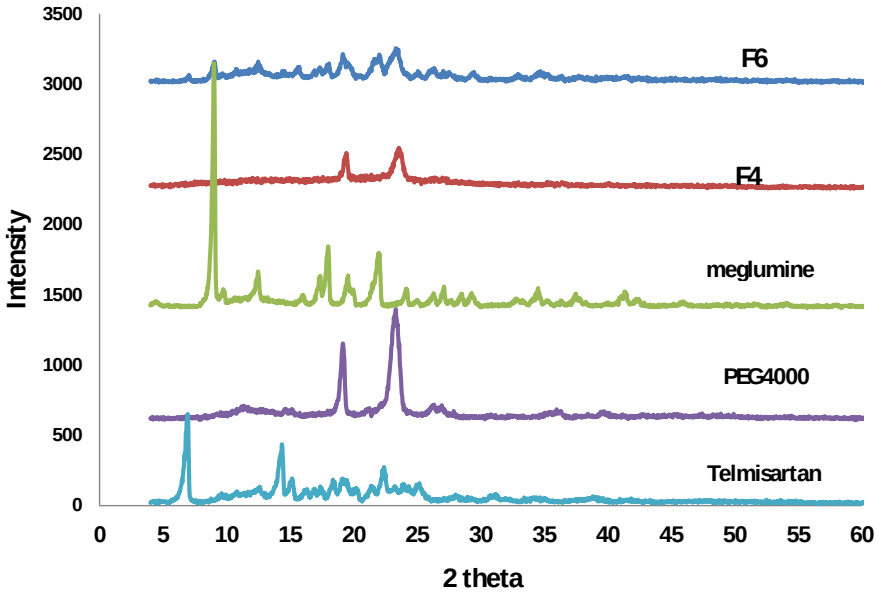

Figure 3: Sample X-ray diffractograms of pure telmisartan, polyethylene glycol (PEG) 4000, meglumin, formulations F4 and F6. For detailed formulation refer to Table 1.

In vitro drug release from the prepared formulations

The dissolution profiles of telmisartan from unprocessed powder and binary and ternary solid dispersions formulations are shown Figure 4. The dissolution parameters were extracted from these profiles as the percentage drug released after 5 min (Q5) and the dissolution efficiency (DE). These data are shown in Table 1.

Pure unprocessed drug showed slow and incomplete dissolution with only 5% of the loaded dose liberated during the first 5 minutes. The total amount released during the time course of the experiment was only 7.3%. The dissolution efficiency was found to be about 6%. This poor dissolution data could be due to the hydrophobic property of the drug that resisted wettability by the dissolution medium and consequently hindering dissolution. This was visually confirmed by observing powder floating on the surface of the dissolution medium.

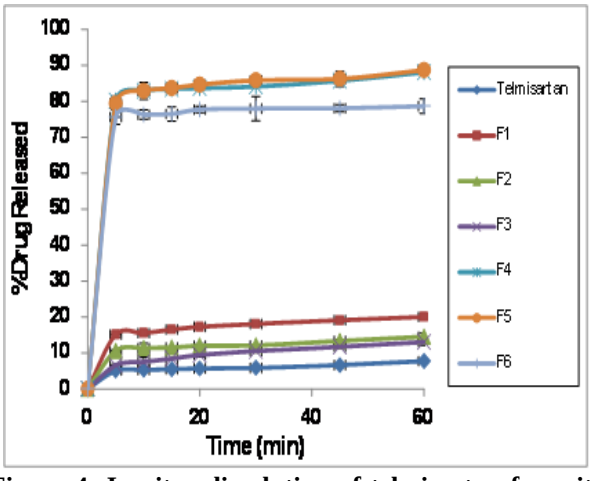

Figure 4: In vitro dissolution of telmisartan from its unprocessed form and different solid dispersion formulations. For detailed tablets composition refer to Table 1.

Polyethylene glycols are a widely used group of hydrophilic polymers used to enhance dissolution of many poorly water soluble drugs[8,17]. Therefore it was selected as matrix former for telmisartan in a trial to improve its wetability and consequently its dissolution rate. Three different drug to polymer weight ratios (1:1, 1:2 and 1:3 drug: PEG4000) were prepared. Formula F1 (1:1 ratio) improved drug dissolution over control (Figure 4A). There was about 3-fold enhancement in Q5 and dissolution efficiency (Table 1). This enhancement could be due to the molecular and colloidal dispersion of the drug in the hydrophilic carrier matrix.As the soluble carrier dissolves, drug gets exposed to dissolution medium in the form of fine particles. In the solid dispersion and/or solution, particle size reduction and consequently surface area increment results in the improved dissolution parameters in reference to unprocessed drug.

Interestingly, increasing PEG4000 concentration resulted in decreased drug dissolution. This may be explained by the strong interaction between PEG4000 and drug surface leading to formation of viscous diffusion layer in the microenvironment around the drug microparticles during dissolution process, thus reducing the diffusion coefficient of the drug.

As the aim of this study was to enhance telmisartan dissolution with the goal of preparing orodispersible tablets, the obtained dissolution data was not satisfactory to achieve this goal. Telmisartan is supplied as a free acid form that shows a pH dependent solubility. Therefore, alkalizers were usually incorporated as an pH

modifier to enhance its dissolution. Meglumine was previously reported to improve dissolution rate of telmisartan when cogrounded together using milling technique[10]. Therefore, meglumine was added as a third component to the solid dispersion formula F1, that showed the best dissolution parameters. Meglumine was incorporated at different molar ratios to telmisartan to obtain formulations F4(1:1), F5(1:2) and F6(1:3) drug:meglumine, respectively, at fixed weight ratio of drug:PEG4000 of 1:1. The dissolution profiles are shown in Figure 3B. Incorporation of meglumine resulted in a marked increase in dissolution rate with the liberation of about 80% of the loaded dose in the first 5 minutes. The dissolution efficiencies were similarly increased (Table 1). This marked increase in initial drug release could be attributed to the increased pH value in the microenvironment around drug particles during the dissolution step augmented by amorphisization of drug due to the processing technique. It worth noting that increasing meglumine concentration in the solid dispersion showed similar dissolution parameters ($P > 0.05$) indicating that meglumine at 1:1 molar ratio with the drug is the optimum concentration required to impart alkaline environment.

To confirm our assumption that the obtained enhancement in drug dissolution is due to reduced crystallinity, physical mixture of the same compositions of F4 was prepared (Table 1). Physical mixture significantly ($P < 0.05$) increased drug dissolution compared to pure drug. The obtained 4-fold enhancement in Q5 could be due to increased drug wettability imparted as a result of PEG4000 and increased pH value due to meglumine. Despite such enhancement, the dissolution parameters of drug from physical mixture was way below that of solid dispersion F4 formulation. Preparation of solid dispersion resulted in presence of both hydrophilic polymer and meglumine microparticles in close proximity to that of telmisartan resulting in obtaining the desired enhancement in drug dissolution.

Characterization of the prepared ODTs

According to the results of in vitro drug release of solid dispersion microparticles, F4 was selected to prepare oral disintegrating tablets as it showed similar dissolution pattern to F5 and F6 but in presence of lower amount of alkalizer. Tablets were prepared according to the master formula presented in Table 2. To study the effect of tablet excipients on drug release, tablets were prepared using three different ODT bases namely Pearlitol® Flash, Pharmaburst ® 500 and Ludiflash®. These co-processed excipients were selected as they are mannitol-based fillers. Mannitol is a commonly used filler in chewable tablets or tablets dissolved in the mouth where good taste is important. Tablets were prepared to contain 40 mg of pure drug (control tablets) or an equivalent amount of F4 formulation. This design was

Table 2: Composition of the prepared oral disintegration tablets, together with the results of tablets evaluation studies.

	Pharmaburst® 500		Pearlitol® Flash		Ludifalsh®	
Ingredients (mg/tablet)	**Control tab**	**SD tab**	**Control tab**	**SD tab**	**Control tab**	**SD tab**
Pure drug	40mg	---	40mg	---	40mg	---
SD (F4)	---	100	---	106	---	100
ODT base	255.2	195.2	255.2	189	255.2	195.2
Aerosil	1.8	1.8	1.8	1.8	1.8	1.8
Magnesium Stearate	3	3	3	3	3	3
Q5	7.5 ±0.8	83.1 ±2	7.8±0.5	70.6 ±4.8	5.3 ±0.5	47.4±1.7
%DE	7.2±0.7	81.3±1.6	9.4±0.8	81±2.1	9.1±0.7	57±1.8
Disintegration time (sec)	38±6.0	60±4.0	35± 6.2	142±9.6	150±9.4	302±13.6
Wetting time (sec)	33	32	39	50	37	45

- SD is solid dispersion microparticles F4
- Q5 percentage drug released after 5 minutes, %DE is the percentage dissolution efficiency

Adopted based on the fact that some reports depends mainly on the tablet excipients, which are specially designed for fast dissolving tablets, for Class II drugs without pretreatment to solve the poor solubility problem.

During tablet preparation, it was noticed that Pharmaburst®500 base was more compactable and its tablets were less friable and more rapidly disintegrating compared to other fillers. The weight of all prepared tablets was in the range of 291 to 306 mg with deviation from the mean weight being within the limits stated by the US pharmacopeia[18]. Tablets drug content was in the range of 97 to 105% of the stated potency indicating homogeneity of mixing. For disintegration time, the European pharmacopeia assigned 3 minutes as the acceptable limit for fast disintegration tablets[4]. Tablets prepared using Pharmaburst® 500 showed the shortest disintegration time followed by Pearlitol® Flash tablets. ODTs containing Ludifalsh® as filler showed

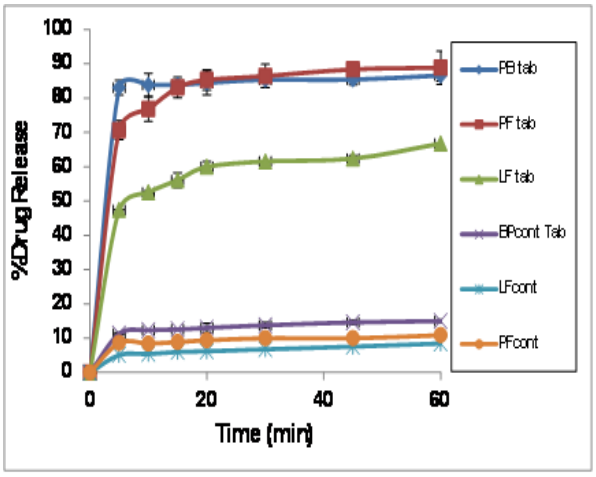

Figure 5: In vitro drug dissolution from different fast disintegrating tablets prepared using different bases; Pharmaburst ® 500 (PB tab)Pearlitol® Flash (PF tab), and Ludiflash® (Lf tab). For detailed tablets composition refer to Table 2.

Considerably slower disintegration that may be attributed to its composition that contains considerable amount of maize starch.

For tablets containing unprocessed drug, there was a slight improvement in drug dissolution (Table2). This may be due to adsorption of the drug on the surface of the filler during the mixing step[8]. Meantime, all oral disintegrating tablets prepared using solid dispersion showed significant increase (P>0.05) in drug dissolution parameters compared to those containing pure drug. Tablets prepared using Pharmaburst ® 500 as filler was superior to other fillers. ODTs containing Ludifalsh® base showed considerably slower dissolution of telmisartan compared to ODTs containing Pharmaburst®500 and Pearlitol Flash®. This may be attributed to the composition of each filler. According to the manufacturer specifications, both Pharmaburst®500 and Pearlitol Flash® contain crosspovidone, in addition to mannitol, while Ludifalsh® contains maize starch. This may have resulted in the slower disintegration due to the binding properties of starch that affected the overall tablet properties. These findings are in good agreement with other report investigations where Ludifalsh® decreased carvedilol release from ODTs relative to Pharmaburst ® 500 and Pearlitol Flash®[19].

CONCLUSION

Preparation of solid dispersion of temisartan with PEG4000 in presence of meglumine, as alkalizer, markedly improved in vitro dissolution characteristics. The enhancement could be attributed to reduced drug crystalline nature and modification of the pH value in the micro-distance from drug particle surface. The optimum formulation was successfully used in preparing oral disintegrating tablets. The type of the oral disintegrating tablet base has significant impact on the quality of the prepared tablets with those prepared using Pharmaburst ® 500 produced the best tablet batch.

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