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Research Article

FORMULATION AND *IN-VITRO* EVALUATION OF FAST DISSOLVING FILM CONTAINING AMLODIPINE BESYLATE SOLID DISPERSION

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ABSTRACT

Objective: This study concerned with preparation and *in-vitro* evaluation of fast dissolving film of amlodipine besylate solid dispersion, since amlodipine besylate is a sparingly soluble orally administered drug and the rate of absorption is often controlled by the rate of dissolution.

Materials and method: The rate of dissolution can be increased by incorporating the drug in a fast dissolving dosage form as a solid dispersion that prepared using polyethylene glycol (PEG6000) or polyvinyl pyrrolidone (PVP) in different ratios and different methods of preparation. The fast dissolving films were prepared using sodium carboxy methyl cellulose (SCMC) in different concentration orhydroxypropyl methyl cellulose (HPMC) also different concentration of glycerin were used. Different factors affecting the dissolution rate of the solid dispersion and fast dissolving film were studied.

Results: It was seen that as the ratio of drug to PEG6000 or PVP in solid dispersion increased the release rate increased and the solvent evaporation method gave greater release than fusion method. In fast dissolving film it was seen that as the concentration of SCMC increased the release rate decreased significantly and as the concentration of glycerin increased the release rate increased significantly.

Discussion: The release rate increased with increasing the ratio of drug to PEG6000 or PVP in solid dispersionsince both of them are water soluble carriers;so increase their amount in solid dispersion leading to increase the wettability and dispersibility of drug from the dispersion resulting in dissolution of drug in hydrophilic carrier.

Keywords: Amlodipine besylate, Solid dispersion, Fast dissolving film, Solvent evaporation, Fusion method, PEG6000, SCMC.

INTRODUCTION

The idea of fast dissolving drug delivery system developed from the need to provide patient with conventional mean of taking their medication. Fast dissolving dosage forms can be disintegrated, suspended or dissolved, by saliva in the mouth [1]. Despite the drug delivery system advancement, oral route is the most and favored route of administration, tablet capsules are the most preferred dosage form [2], but oral drug delivery systems problems related to particular class of patients which includes pediatric, geriatric and dysphasic patients associated with many medical conditions as they have difficulty in chewing or swallowing solid dosage forms. Many geriatric and pediatric patients are unwilling to take solid preparations due to fear of choking, even with rapid dissolving tablets there is a fear of choking because of its tablet type appearance [3]. Among the plethora of avenues explored oral films gain more attention as it emerging new platform for pediatric and geriatric patients. Efficacy of active pharmaceutical ingredient (API) is enhanced as it dissolves in the oral cavity. Oral films break down rapidly within seconds when it comes in contact with saliva without the need of water. Oral fast dissolving films are useful for the pediatric and geriatric patients and also for the patients suffering from diarrhea, emesis, allergic attacks, cough, mental disorder, bedridden patients etc.[2] Amlodipine besylate(dihydropyri-dine (DHP) class) is a long-acting calcium channel blocker used as an anti-hypertensive and in the management of angina. amlodipine Like other calcium channel blockers, acts by relaxing the arterial wall smooth muscle, decreasing total peripheral resistance and hence reducing blood pressure; in angina it rises blood flow to the heart muscle.[4] Amlodipine is a sparingly soluble drug and the rate of absorption is frequently controlled by the rate of dissolution. The rate of dissolution can be enhanced by incorporating the drug in a fast dissolving dosage form [5] as a solid dispersion.

Solid dispersion is among varies techniques have been used to increase the solubility and dissolution rate of poorly water soluble drugs, it is the most frequently and effectively used one.[6] The methods used to prepare solid dispersion include fusion (melting)method, solvent evaporation method and solvent wetting method [7]. Different water-soluble carriers have been employed for preparation of solid dispersion, the most common ones are various grades of polyethylene glycols (PEG), polyvinyl pyrrolidone (PVP), β-cyclodextrin, lactose, and hydroxypropyl methylcellulose (HPMC) [8].

MATERIALS AND METHODS

Materials

Amlodipine besylate, polyvinyl pyrrolidone and lactose were supplied by Samara Drug Industries (SDI) Iraq, sodium caboxymethyl cellulose and citric acid from Panreac Barcelona Espana, Hydroxypropyl methylcellulose (viscosity 6cp) was purchased from Sigma-Aldrich, USA. Tween 80 from Scharalu Spain. Sodium Saccharin was purchased from Avonchem(UK). PEG 6000 from Sigma (UK), glycerin from GCC (UK), chloroform from BDH chemicals Ltd England, dichloromethane from Fluka Germany, ethanol from TEDIA, USA and hydrochloric acid from H&W, England.

Equipment

United states pharmacopoeia USP dissolution apparatus II (Copley dissolution 8000, copleyscientific, UK.), Oven(Memmert, Germany), UV-visible spectrophotometer (shimadzu, Japan),FTIR spectroscopy (shimadzu FTIR 8000, Japan),PH-meter (OHUS,USA),magnatic hot plate (Stuart, Copley scientific, U.K.), Electrical balance (KERN, Germany),Water bath (LabTech, Korea) and vernier caliper micrometer (Copley, UK.)

Methods

Preparation of solid dispersions

Melting method (fusion method)

Solid dispersion of amlodipine besylate in PEG6000 containing two different ratios (1:2 and 1:3 w/w) as seen in table (1)were prepared by fusion method. Required amount of drug and polymer were mixed in glass vial, the mixture was then heated using water bath at 70°C till it was completely melted, continues stirring during the melting was carried out to prevent the separation of the constituents. The melt was then rapidly solidified. The formulations were kept in a desiccator for further treatment. The solidified mass was then crushed, size reduced in a mortar and pestle and sieved through 0.63 mm sieve [9].

Solvent evaporation method

Solid dispersion of amlodipine besylate in PEG6000 or polyvinyl pyrollidone containing two different ratios (1:2 and 1:3 w/w) as seen in table (1) were prepared by solvent evaporation method. Amlodipine besylate and the polymer were dissolved in 50 ml of chloroform and dichloromethane (2:3). The solvent was stirred on magnetic stirrer at temperature 40°C and then evaporated in oven at 40°C.the resulting residue was dried for 2 h and stored overnight in desiccator. The solidified mass was then crushed, size reduced in a mortar and pestle and sieved through 0.63 mm sieve.[10]

Table 1: different formulas of amlodipine besylate solid dispersion

Formula code	Amlodipine besylate Mg	PEG6000 Mg	PVP mg	Method
F1	500	1000		Fusion
F2	500	1500		Fusion
F3	500	1000		Solvent
F4	500	1500		Solvent
F5	500		1000	Solvent
F6	500		1500	Solvent

Evaluation of solid dispersions

FTIR Spectroscopy

FT-IR spectra of pure amlodipine, and solid dispersionwere obtained by Schimadzu 8000 FT-IR spectrophotometer using potassium bromide pellets. The sample was scanned from 4,000 to 400 cm-1. The compatibility of drug in the formulation was confirmed by IR spectra of pure drug and formulations were determined [11].

Drug content in solid dispersions

The content of amlodipine besylate in optimum formula of solid dispersion (F4) was estimated using shimadzu spectrophotometer. An accurately weighed quantity of solid dispersion (equivalent to 10 mg of amlodipine besylate) was taken and dissolved in 10 ml of methanol, from this solution 1 ml was diluted to 10 ml and assayed for drug content at 239nm.[10]

***In-vitro* dissolution studies**

Dissolution study was performed for all the prepared solid dispersion by using USP-II paddle apparatus. In this 300 ml of phosphate buffer pH 6.8 was used and maintained temperature at 37±0.5°C with 50 rpm. Then 5 ml of sample was withdrawn at a certain intervals for 120 minutes, and then it was analyzed by using shimadzu spectrophotometer at 239 nm.[12]

Preparation of fast dissolving films

Six formulas were prepared (F6-F12), with their composition shown in table (2), using solvent casting method as seen in figure(1)[13], each film with surface area approximately 6 cm^2 as seen in figure (2) is loaded with 11 mg solid dispersion which is equivalent to about 2.5 mg of amlodipine besylate except F11 that containing 2.5 mg drug without solid dispersion. The area and number of films prepared for each batch can be calculated as follows [14]:

Total area of petri dish = 70.9 cm^2

Each film area = 2×3 = 6 cm^2

Number of films in batch =70.9/6 =11.8

approximately 12 films

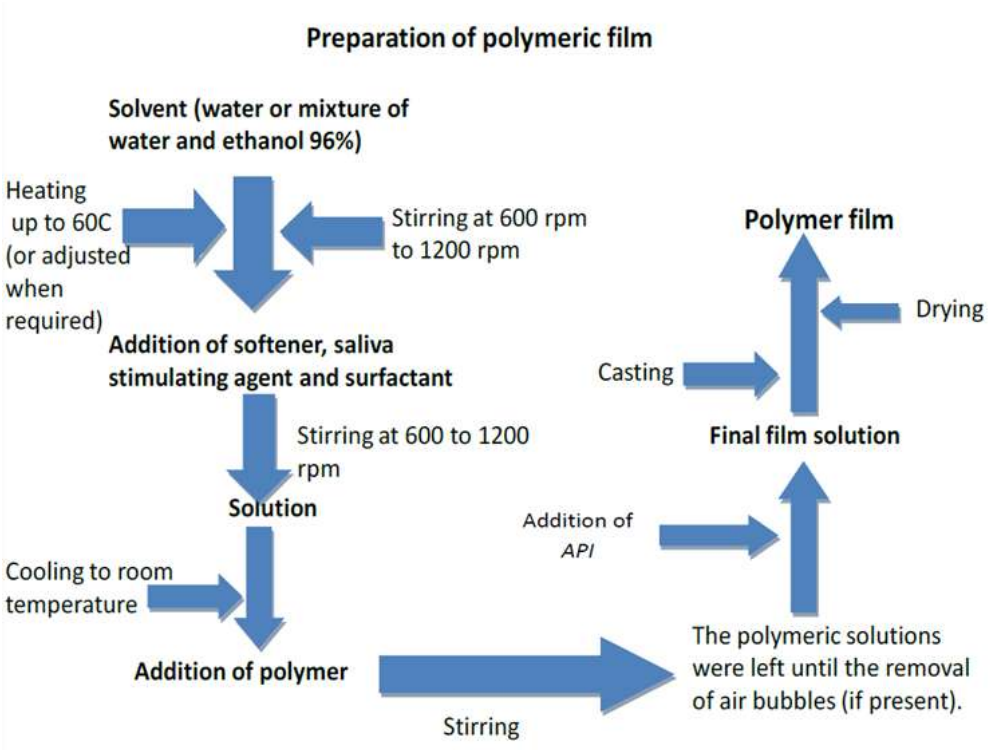

Fig. 1: Preparation scheme of oral films

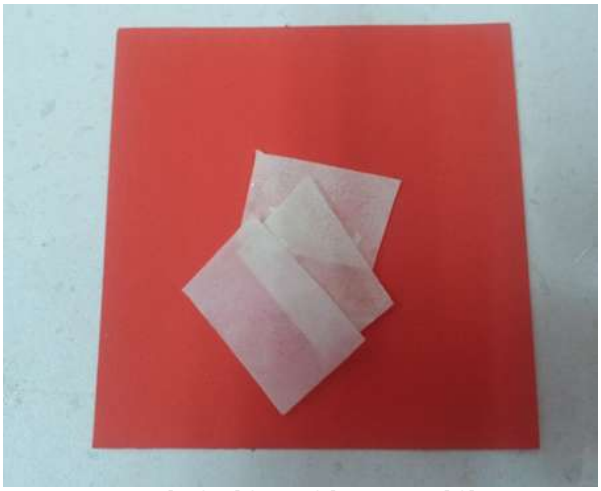

Fig. 2: The final form of the prepared films

Table 2: Different formulas of amlodipine besylate oral film.

Formula code Substance (mg)	F 7	F 8	F 9	F 10	F 11	F 12
Amlodipine besylate solid dispersion	11	11	11	11	_	11
Amlodipine besylate	_	_	_	_	2.5	_
SCMC	28 (40%)	35 (50%)	42 (60%)	_	28 (40%)	28 (40%)
HPMC (6 cp)	_	_	_	28 (40%)	_	_
Glycerin	10 (14%)	10	10	10	10	14 (20%)
Citric acid	1.4	1.4	1.4	1.4	1.4	1.4
Tween 80	2	2	2	2	2	2
Sodium saccharine	0.6	0.6	0.6	0.6	0.6	0.6
Lactose	17	10	3	17	25.5	13
Total weight (mg)	70	70	70	70	70	70

Evaluation of fast dissolving film

Visual inspection

Properties such as homogeneity, color, transparency and surface of the oral films wereevaluated for all the prepared oral films [15].

Weight variation

The weight variation of the amlodipine oral film wasdone by weighting twenty films individuallyand the average weight was calculated. For the film to be accepted, the weight of not more than two films deviate from the average weight by no more than 7.5% and no film deviates by more than 15% .[16]

Thickness measurements

The thickness of each film was measured atfive different locations (centre and fourcorners) using vernier caliper micrometer. The data are represented as a mean± Standard deviation (SD) of three replicate determinations. [17]

Folding endurance test

The folding endurance of randomly selectedfilms was determined by repeatedly foldingone film at the same place till it break or folded maximum 250 times.[18]

Surface pH

The surface pH of fast dissolving film was determined in order to find out the possible any in-vivo side effect. A combined pH electrode was used for this purpose. Oral film was slightly wetted with water. The pH was measured with the glass membrane electrode in contact with the surface of the oral film [19].

Disintegration time

The disintegration time was measured using modified disintegration method. For this purpose a petri dish was filled with 10 ml of water. The film was carefully put in the centre of petri dish. The time for the film to completely disintegrate in to fine particles was noted in Table 3 [20].

Drug content

Drug content of all films was determined by UV-Spectrophotometric method. For this 2x3 cm^2 strip was dissolved in 100ml of buffer (pH 6.8). The solution was filtered and absorbance was recorded at 239 nm. Drug content was calculated by using standard curve of drug.[21]

In-vitro Dissolution Study

The release rate Amlodipine Besylate from fast dissolving film is determined using United State Pharmacopoeia (USP) dissolution testing apparatus II (paddle method). The dissolution test was performed using 300 ml of pH 6.8 buffer, at 37°C and 50 rpm. A sample (5 ml) of the solution is withdrawn from the dissolution apparatus at regular intervals for 60 min. The samples are replaced with fresh dissolution medium of same quantity. The samples are filtered through a 0.45µ membrane filter. Absorbance of these solutions is measured at 239 nm using a Shimadzu UV/Vis double beam spectrophotometer [12].

Statistical Analysis

The results of the experiments are given as a mean of triplicate samples ± standard deviationand were analyzed according to the one way analysis of variance (ANOVA) at the level of ($P < 0.05$).

RESULTS

FTIR Spectroscopy

State of drug molecule (amlodipine besylate) with hydrophilic polymer (PEG6000) was determined using FT-IR.Figures (3,4,5) show FT-IR spectra of amlodipine besylate, PEG6000 and solid dispersion respectively.FT-IR spectra of amlodipine besylate was not

changed in solid dispersion FT-IR spectra where the peak at 1616 cm^{-1} in amlodipine besylate and solid dispersion FT-IR spectra refers to (N—H) bending of amino group of amlodipine besylate while the peak at 3302cm^{-1} in amlodipine besylate FT-IR spectrarefers to (N—H) stretching of amino group of amlodipine besylate that shifted to 3152cm^{-1} in solid dispersion FT-IR spectra. The peak at 1344cm^{-1} in PEG6000 and solid dispersion FT-IR spectrarefers to (O—H) bending of PEG6000.

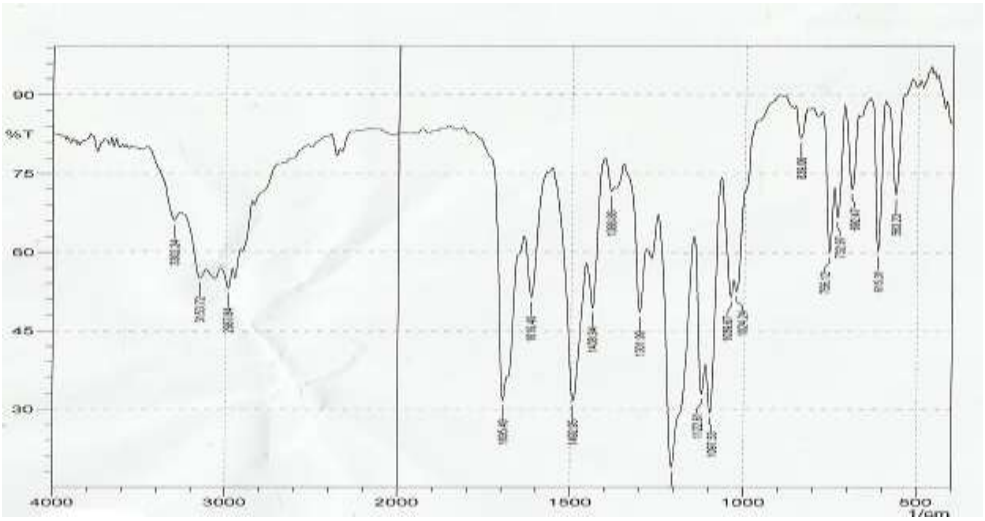

Fig. 3: FT-IR spectra of amlodipine besylate

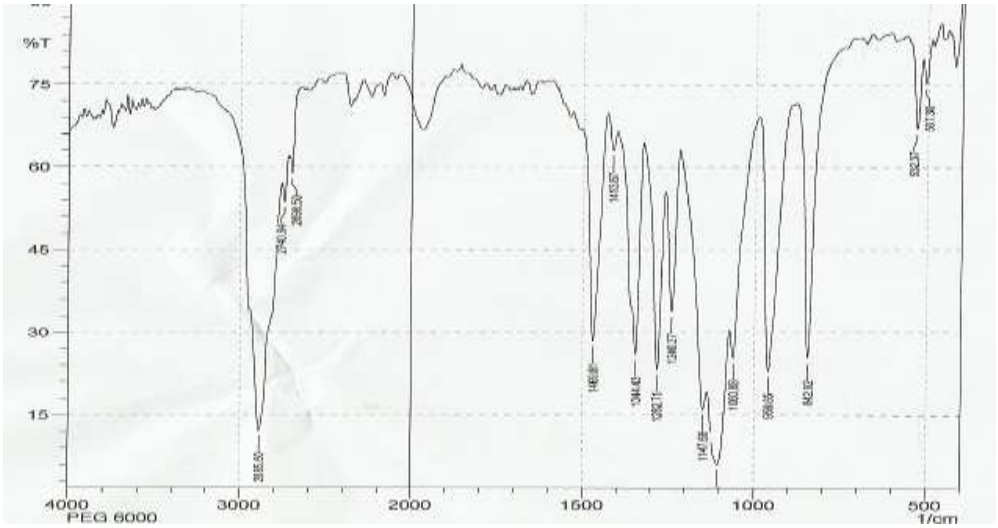

Fig. 4: FT-IR spectra of PEG6000

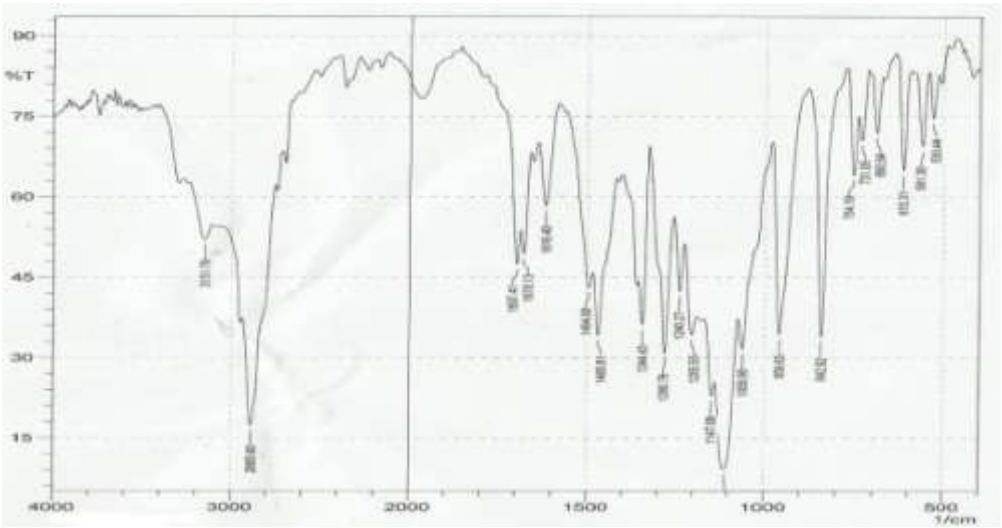

Fig. 5: FT-IR spectra of solid dispersion

Drug Content in Solid Dispersions

It was found that the drug content in optimized formula of solid dispersion (F4) equal to 91%±0.19.

Variables affecting the dissolution profile

Effect of solid dispersion formation

Figure(6) shows the effect of solid dispersion formation on the release of amlodipine besylate. It was seen that the release of amlodipine besylate increased significantly ($p<0.05$) when it formulated as a solid dispersion. 96% of drug released in 5 minutes in comparison with 71% of drug released when it is found in free form.

Effect of drug to polymer ratio

Formulas (F1-F6) were used to study the effect of drug to polymer ratio. It was seen that as the amount of PEG6000 increased the release rate increased significantly ($p<0.05$) while as the amount of PVP increased the release rate increased none significantly ($p>0.05$) as shown in figures (7, 8).

Effect of polymer type

Formulas (F4 and F6) were used to study the effect of polymer type on the release of drug from solid dispersion where PEG6000 and PVP were used in F4and F6 respectively. It was seen that the release of drug from solid dispersion containing PEG6000 was greater than that from solid dispersion containing PVP none significantly ($p>0.05$) as shown in figure (9).

Effect of method of solid dispersion preparation

Figure (10) shows the effect of method of preparation of solid dispersion on the release of amlodipine besylate, formulas (F2andF4) are used for this purpose. It was seen that the release of drug increased when prepared as a solid dispersion by solvent evaporation method than by fusion method none significantly ($p>0.05$).

Evaluation of fast dissolving films

Visual inspection

All the prepared fast dissolving film showed homogenous and smooth surfaces properties but the films prepared by (SCMC) are transparent and colorless while those prepared by using (HPMC) are white in color.

Weight variation

Table (3) gives the physicochemical parameters of oral thin films of amlodipine besylate. The results reveal that the average weights for all the prepared formulas were uniform and comply with referred values.

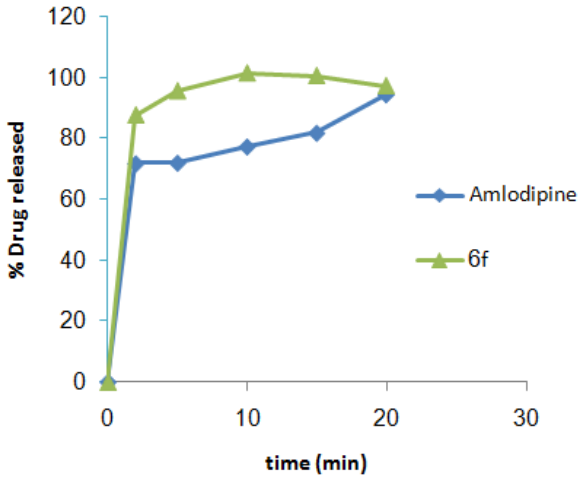

Fig. 6: The effect of solid dispersion formation on the release profile.

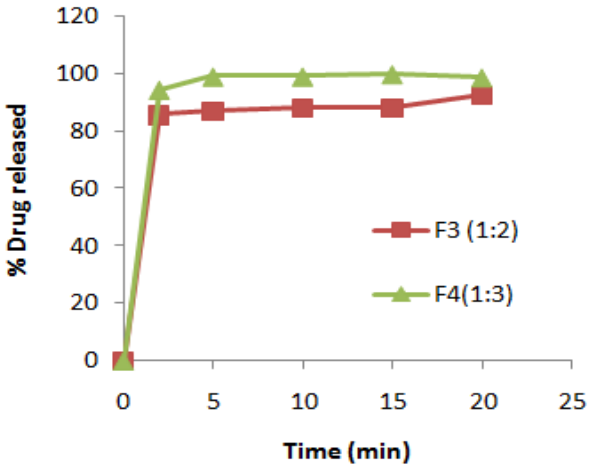

Fig. 7: The effect of (amlodipine besylate:PEG6000) ratio on the release profile.

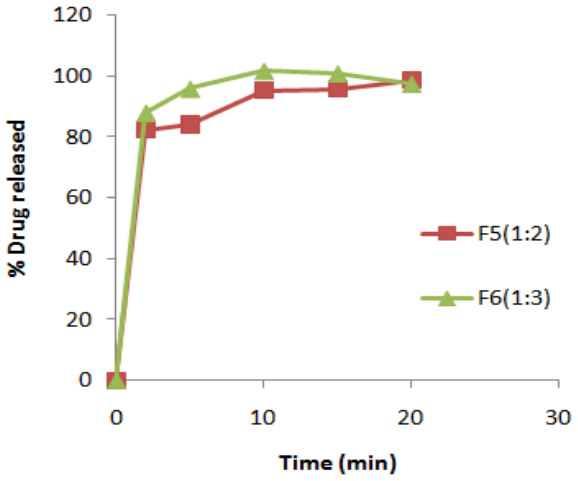

Fig. 8: The effect of (amlodipine besylate:PVP) ratio on the release profile

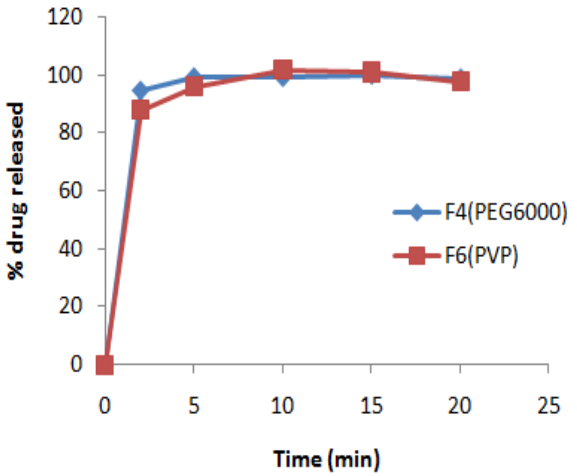

Fig. 9: The effect of polymer type on the release profile

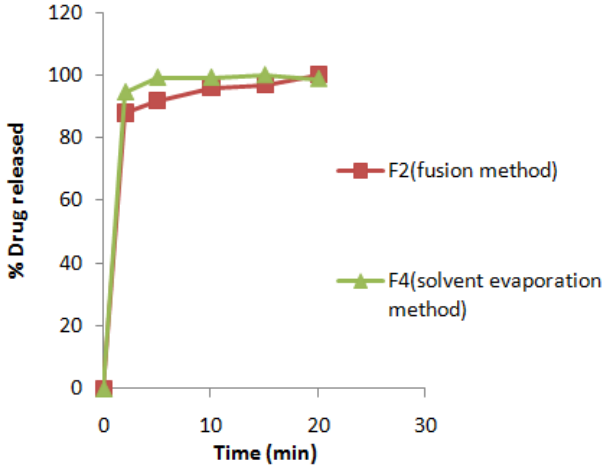

Fig. 10: The effect of method of preparation of solid dispersion on the release.

Table 3: The physicochemical parameters of oral thin films of amlodipine besylate

Formula code	Weight variation	Drug content	Thickness (mm)	Folding endurance	PH	Disintegration time (sec)
F7	69±4	95.6±3	0.086±0.01	270	6	19
F8	75±5	105.3±2.5	0.086±0.01	> 300	6.1	33
F9	77±7	90.8±4.3	0.11±.025	> 300	5.8	36
F10	74±4	110±0.8	0.1±0.017	> 300	6.3	15
F11	72±3	87±0.01	0.083±.006	250	6.1	32
F12	72±5	109.6±5	0.07±0	> 300	6.2	23

Thickness measurements

The thickness was found to vary between (0.07 to 0.11 mm) with very low standard deviation value.

Folding endurance

All the prepared films have folding endurance value more than 250 times.

Surface pH study:

The surface pH of all the films was found between (5.8-6.3), there is no significant difference was found in surface pH of different films.

Disintegration time

It was observed that *in-vitro* disintegration time varies from (19-36) sec for all the formulations.*In-vitro* disintegration time of the films was found to be increased with increasing the concentration of the polymer.

Drug content uniformity

All the prepared films were found to contain an almost uniform quantity of the drug within the range of (85- 115) %.

Variables affecting the dissolution profile of fast dissolving film

Effect of polymer concentration

Formulas (F7,F8,F9) were used to study the effect of concentration of SCMC on the release of amlodipine besylate where (40,50,60)% of SCMC were used in formulas (F7,F8,F9) respectively as seen in figure(11).it was seen as the concentration of SCMC increased the release rate decreased significantly ($p<0.05$).

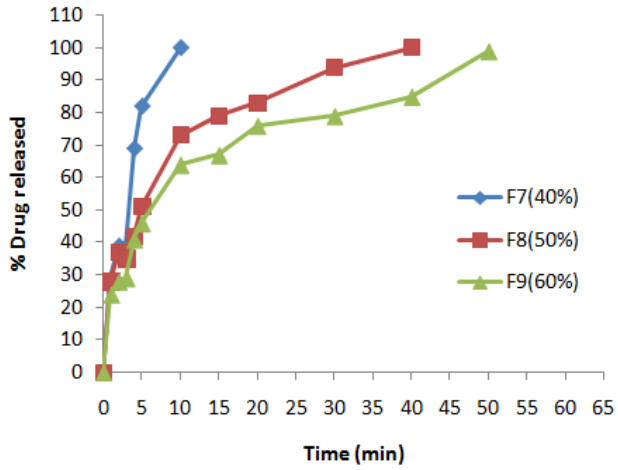

Fig. 11: The effect of SCMC concentration on the release of amlodipine besylate from the fast dissolving film.

Effect of polymer type

Formulas (F7 and F10) containing 40% of SCMC and HPMC respectively, are used to study the effect of polymer type on the release of amlodipine besylate from the fast dissolving film as shown in Figure (12). it was found that release of drug decreased none significantly(P>0.05) on replacing SCMC by HPMC.

Effect of plasticizer concentration

Formulas (F7andF12) were used to study the effect of plasticizer (glycerin) concentration on the release of amlodipine besylate from the fast dissolving film. It was seen that as the concentration of glycerin increased from 14% to 20% the release rate increased significantly ($p<0.05$) as seen in figure (13).

Effect of solid dispersion

Formulas (F7and F11) were used to study the effect of solid dispersion on the release of amlodipine besylate from fast dissolving film as seen in figure (14). It was seen that the release rate increased significantly ($p<0.05$) when the drug used as solid dispersion as in F7 while F11 containing free drug.

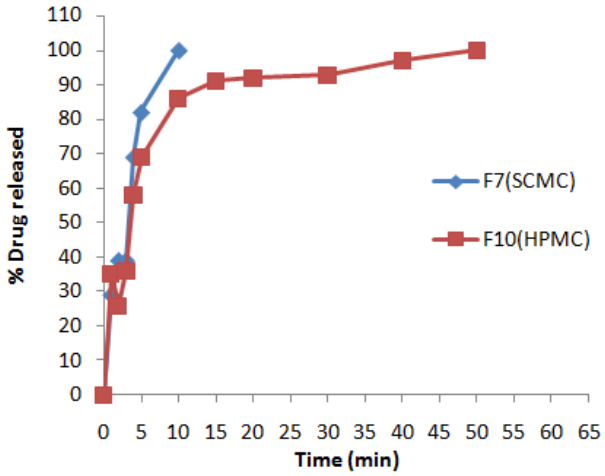

Fig. 12: The effect of polymer type on the release of amlodipine besylate from the fast dissolving film

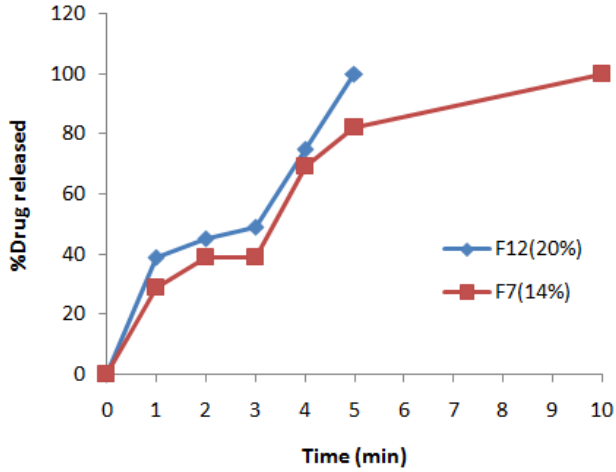

Fig. 13: The effect of plasticizer (glycerin) concentration on the release of amlodipine besylate from the fast dissolving film.

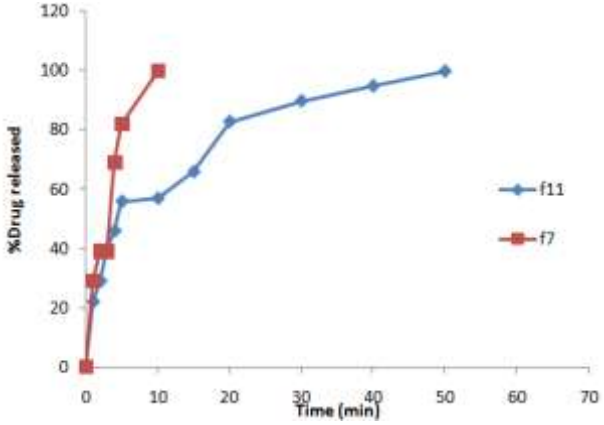

Fig. 14: The effect of solid dispersion on the release of amlodipine besylate from fast dissolving film

DISCUSSION

FTIR Spectroscopy

Figures (3,4,5) show FT-IR spectra of amlodipine besylate, PEG6000 and solid dispersion respectively. FT-IR spectra of amlodipine besylate was not changed in solid dispersion FT-IR spectra where the peak at 1616cm^{-1} in amlodipine besylate and solid dispersion FT-IR spectra refers to (N—H) bending of amino group of amlodipine besylate indicating that there is no change in chemical structure of drug after preparing it into solid dispersion. while the peak at 3302cm^{-1} in amlodipine besylate FT-IR spectra refers to (N—H) stretching of amino group of amlodipine besylate that shifted to 3152cm^{-1} in solid dispersion FT-IR spectra due to the formation of H—bond between amino group of amlodipine besylate and hydroxyl group of PEG6000 . The peak at 1344cm^{-1} in PEG6000 and solid dispersion FT-IR spectra refers to (O—H) bending of PEG6000.

Drug Content in Solid Dispersions

Analysis of the optimized formula of solid dispersion (F4) confirmed that amlodipine besylate could be found to a level of 91% of theoretically added amount in the dispersion. The optimized formula (F4)was found to contain an almost uniform quantity of the drug, the content uniformity studies indicating reproducibility of the technique used. The preparation met the criteria of British Pharmacopeia content uniformity (85- 115) %. On this basis, it was found that the drug was dispersed uniformly throughout the solid dispersion.

Variables affecting the dissolution profile

Effect of solid dispersion formation

Amlodipine besylate powder and formula (F6) are used to study the effect of solid dispersion formation on the release as seen in figure (6). It was seen that the release of amlodipine besylate increased significantly ($p<0.05$) when it formulated as a solid dispersion where 96% of drug released in 5 minutes in comparison with 71% of drug released when it is found in free form, this is due to formation of solid solution of the drug. The particle size is reduced to molecular size when the carrier brings the drug into the dissolution medium. Thus the faster dissolution rate can be explained based merely on the particle size without anything to do with energy changes. The presence of carrier may also prevent aggregation of fine drug particles thereby providing a larger surface area for dissolution. The wetting properties are also greatly increased due to the surfactant property of the polymer resulting in increased interfacial tension between the medium and drug and, hence, the higher dissolution rate. The presence of carrier polymer also inhibit crystal growth of the drug which facilitates faster dissolution[22] this result was similar with that observed in studying the effect of solid dispersion on the release of gliclazide [6]

Effect of drug to polymer ratio

Figures (6,7) shows the effect of drug to polymer ratio on the release of amlodipine besylate from solid dispersion. It was seen that as the ratio of (drug: PEG6000 or PVP) increased from 1:2 to 1:3 the release increased, where at 5 minutes 87% and 99% of drug released from (1:2) and (1:3) of (drug:PEG6000) solid dispersion respectively, while 84% and 96%of drug released from (1:2) and (1:3) of (drug: PVP) solid dispersion respectively, since both of PEG600 and PVP are water soluble carriers.(8) so increase their amount in solid dispersion leading to increase the wettability and dispersibility of drug from the dispersion resulting in dissolution of drug in hydrophilic carrier.[23]This result is consistent with that observed in the enhancement of dissolution of fenofibrate by solid dispersion technique.[22]

Effect of polymer type

As shown in figure (9) formulas (F4 and F6) were used to study the effect of polymer type on the release of drug from solid dispersion where PEG6000 and PVP were used in F4and F6 respectively. It was seen that the release of drug from solid dispersion containing PEG6000 was greater than that from solid dispersion containing PVP none significantly ($p>0.05$), where at 2 minutes 95% and 88% of drug released from solid dispersion containing PEG6000 and PVP respectively, this may be due to the more water solubility and hydrophilicity of PEG6000 than PVP [24] so that more wettability and dispersibility of drug from the dispersion resulting in dissolution of drug in hydrophilic carrier [23]. This result was in agreement with that obtained during the formulation and evaluation of solid dispersions of Rofecoxib for improvement of dissolution profile [24]

Effect of method of solid dispersion preparation

Formulas (F2andF4) are used to study the effect of method of preparation of solid dispersion on the release of amlodipine besylate as shown in figure (10).It was seen that the release of drug increased when prepared as a solid dispersion by solvent evaporation method than by fusion method none significantly ($p>0.05$) since the dissolution was enhanced more by solvent evaporation method.[7]

Evaluation of fast dissolving films

The physicochemical parameters of oral thin films of amlodipine besylate

From the results it was seen that the average weights for all the prepared formulas were uniform and comply with referred values. The thickness was found to vary between (0.07 to 0.11 mm). A very low standard deviation value is indicating that the method used for the formulation of films is reproducible and give films of uniform thickness and hence dosage accuracy in each film can be ensured. All the prepared films have folding endurance value more than 250 which is very accepted. The surface pH of all the films was found between(5.8-6.3), there is no significant difference was found in surface pH of different films, which is within the range of salivary pH. *In-vitro* disintegration time of the films was found to be increased with increasing the concentration of the polymer ,since the disintegration time was (19,33,36) sec when the concentration of SCMC was (40,50,60)% respectively in the fast dissolving film because high concentration of polymer resulted in a thicker gel upon contact with the medium, resulting in longer disintegration time, this result is consistent with that during preparation and evaluation of nicotine hydrogen tartrate fast dissolving films for smoking cessation[25], while the disintegration time was decreased from 32sec to 19 sec in formulas F11 and F7 respectively, this may be due to the presence of drug in F7 as a solid dispersion withPEG600 which is water soluble hydrophilic polymer[9][22] but in F11 the drug present in free form so that the disintegration of F7 was faster than F11. There was no significant difference in the disintegration time between F7 and F10 that containing 40% of SCMC and HPMC respectively, also it was found that the disintegration time increased none significantly on increasing the concentration of glycerin (plasticizer) from 14% to 20% of the weight of film because when the concentration of plasticizer higher than 18% w/w of total dry weight caused blooming phenomena and stickiness[26], this may determine the relevant increase in mouth disintegration time. All the prepared films were found to contain an almost uniform quantity of the drug, the content uniformity studies indicating reproducibility of the technique used. The preparations met the criteria of British Pharmacopeia content uniformity (85- 115) %of the label claim. On this basis, it was found that the drug was dispersed uniformly throughout the 6 cm^2 constant area of the film.

Variables affecting the dissolution profile of fast dissolving film

Effect of polymer concentration

Figure(11) shows the effect of changing concentration of SCMC on the release of amlodipine besylate where (40,50,60)% of SCMC were used in formulas (F7,F8,F9) resulting in a release of (100,73,64)% in 10 minutes respectively. It was seen that increasing the concentration of SCMC in films containing hydrophilic film forming polymer significantly($p<0.05$) reduced the drug release, whereas the opposite is true for films containing hydrophobic filmforming polymers. This finding was also supported by the swelling behavior of the films[27]where the maximum swelling was seen with formulationscontaining high proportion of SCMC[28], although the marked increase in surface area can promote drug release but the increase in diffusion path length of the drug may paradoxicallydelay the release.[27]

Effect of polymer type

Figure (12) shows the effect of polymer type on the release of amlodipine besylate from the fast dissolving film. Formulas (F7 and F10) containing 40% of SCMC and HPMC respectively, it was found that release of drug decreased none significantly(P>0.05) on replacing SCMC by HPMC, where at 10 minutes 100% and 86% of drug released from F7 and F10 respectively, this may be due to H-bonding between HPMC and PEG6000 of solid dispersion that result in retardation of drug release in comparison with formula containing SCMC.

Effect of plasticizer concentration

As seen in figure (13) formulas (F7andF12) were used to study the effect of plasticizer (glycerin) concentration on the release of amlodipine besylate from the fast dissolving film. It was seen that at 5 minutes the release rate increased from 82% to 100% when the concentration of glycerin increased from 14% to 20% , Since glycerin is water soluble[29],it will diffuse out of polymeric films in aqueous media generating void spaces in the film through which diffusion occurs more readily. The result being accelerated release profile of the active ingredient [30]

Effect of solid dispersion

As seen in figure (14) formulas (F7and F11) were used to study the effect of solid dispersion on the release of amlodipine besylate from fast dissolving film. It was seen that the release rate increased significantly (p<0.05) when the drug used as solid dispersion as in F7 while F11 containing free drug so 57% and 100% of drug released from F11 and F7 respectively in 10 minute the reason behind that is the improvement of the solubility and dissolution of amlodipine besylate in solid dispersion compared with drug alone since the drug may exist as an amorphous form in polymeric carriers [7]

Comparison between the release profile of amlodipine besylate fast dissolving film (F7) and amlodipine oral tablet:

As shown in figure (15) a comparison was made between the release profile of amlodipine besylate fast dissolving film (F7)and amlodipine oral tablet(2.5 mg from MICRO Lab, India). It was found that there was significant (p<0.05) increase in the release rate when amlodipine besylate formulated as fast dissolving film indicating the satisfactory of fast dissolving film formulation that can be used as an alternative to the oral tablet.

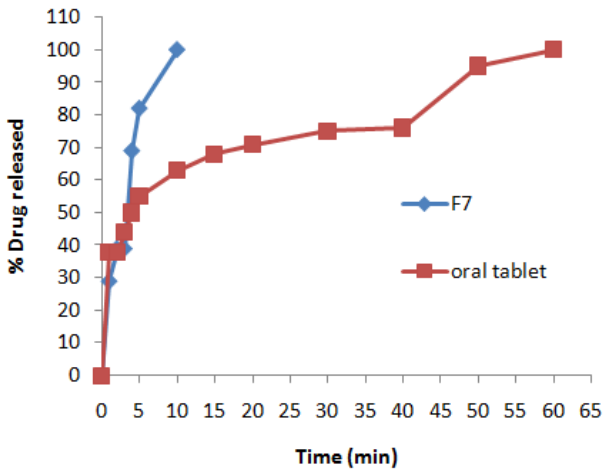

Fig. 15: Comparison between the release profile of amlodipine besylate fast dissolving film (F7) and amlodipine oral tablet.

CONCLUSION

Amlodipine besylate was successfully formulated as solid dispersion and thenorally fast dissolving films for better patient compliance and effective therapy. The release rate from solid dispersion increased with increasing the ratio of drug to polymer (PEG6000 or PVP). As the concentration of SCMC increased in the film the release rate decreased significantly.

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