EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 8
Issue: 2
215-224
Year: 2021

ENHANCEMENT OF DISSOLUTION RATE OF EBASTINE FOR THE PREPARATION OF ORODISPERSIBLE TABLETS

***Marwa A. Shama, Ebtessam A. Essa and Mona F. Arafa**

Department of Pharmaceutical Technology, College of Pharmacy, University of Tanta, Egypt.

***Corresponding Author: Marwa A. Shama**
Department of Pharmaceutical Technology, College of Pharmacy, University of Tanta, Egypt.
DOI: https://doi.org/10.17605/OSF.IO/GP28U

Article Received on 17/12/2020 **Article Revised on 07/01/2021** **Article Accepted on 27/01/2021**

ABSTRACT
The aim of this work was to explore solid dispersion strategy as a tool to enhance the dissolution rate of the hydrophobic drug, Ebastine. The drug was allowed to co-precipitate from its organic solvent with a hydrophilic polymer. polyvinyl pyrrolidone (PVP 40T), hydroxypropylmethylcellulose (HPMC E5) and polyethylene glycol (PEG 6000) were selected as the hydrophilic polymers. The effect of presence of carrierof large surface area during the precipitation step was also investigated. Aerosil 200 was used as carrier upon which the drug would deposit. Coprecipitation was achieved by solvent evaporation method. The prepared formulations were evaluated regarding their in vitro drug release. Solid state characterization was also evaluated for selected formulations. Unprocessed ebastine showed no release during the experiment time course. Precipitated ebastine in presence of hydrophilic polymers significantly improved the dissolution compared to control, with ebastine-PVP40T co-precipitate being superior to the other two polymers. Addition of Aerosil during the recrystallization step improved further the dissolution parameters. The Thermal behavior and X-ray powder diffraction results indicated reduced drug crystalinity. Infra-red spectroscopy alleviate any possible drug-excipient interaction. This strategy thus provided a simple technique for dissolution enhancement of low soluble drugs. Optimum formulations were successfully formulated as orally disintegrating tablets with subsequent fast dissolution.

KEYWORDS: Ebastine, Aerosil 200, solid dispersion, enhance dissolution rate, fast dissolving tablets.

INTRODUCTION
Solid dosage forms, such as tablets and capsules, remain the most convenient way of drug administration. In the last decade, development of fast disintegrating tablets (FDT), also called orodispersible tablets, has gained wide interest among researchers. This specialized type of compacts undergo fast disintegration in the mouth with the aid of salivary secretion with subsequent rapid drug release. This dosage form is more convenient for both geriatric patients who always develop difficulty in swallowing as they get aged[1] However, the poor aqueous solubility of many drugs hinder the formulation of these tablets. This necessitate improving drug solubility prior to formulating these specialized tablets. There are several strategies to enhance the solubility of poorly water-soluble active pharmaceutical ingredients such as liquisolid tablet,[2] self -emulsifying system,[3] controlled pricipitation[4] cocyrstal formation,[5] salt formation[6] and inclusion complexation with cyclodextrin,[7] These techniques were adopted taken into consideration the physical properties of the active pharmaceutical ingredients and the nature of the selected excipients.

It should be noted that solid dispersion, though has been used for long time, remains the most convenient and cost effective way for enhancing drug solubility.[8]

Ebastine (Fig. 1) is a potent second generation selective histamine antagonist (histamine-H1-receptor antagonist) agent. Ebastine is usually indicated for the treatment of allergic rhinitis and chronic idiopathic urticaria. It lack the capability to through the blood brain barrier in a significant amount and so it combines the effective block of the H_1 receptor in peripheral tissues with little central side effects such as sedation or drowsiness.[9] Ebastine is classified as Class II drug as per the biopharmaceutical classification system, i.e. poorly soluble and highly permeable through the gastro-intestinal tract.[10]

The aim of this work was to improve the solubility of ebastine using solid dispersion technique. The technique employed solvent evaporation method using hydrophilic polymers where the drug-polymer copricipitate over carrier in a trial to increase the surface area of the obtained crystals. Formulations showing highest dissolution parameters was formulated into fast disintegrating tablets.

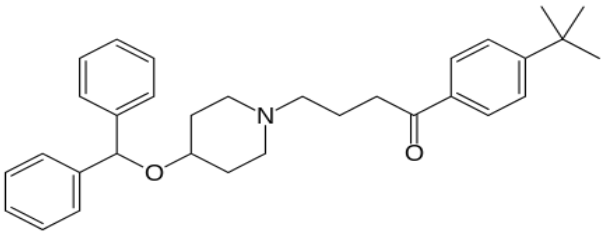

Fig. 1: Chemical structure of ebastine.

The aim of this work was to improve the solubility of ebastine using solid dispersion technique. The technique employed solvent evaporation method using hydrophilic polymers where the drug-polymer copricipitate over carrier in a trial to increase the surface area of the obtained crystals. Formulations showing highest dissolution parameters was formulated into fast disintegrating tablets.

MATERIALS AND METHODS

Materials

Ebastine was a gift sample from (Marcyrl) Pharmaceutical Industries Company, Cairo, Egypt. Aerosil 200, Crosscarmelose, crospovidone, magnesium stearate, granular mannitol, polyvinyl pyrrolidone (PVP 40T), hydroxypropylmethylcellulose (HPMC E5), polyethylene glycol (PEG 6000) and Microcrystalline cellulose (Avicel PH 101), were kindly supplied by Sigma Co., Qwesna, Egypt. Methanol and Methylene chloride purchased from El-Gomhoria Chemicals Co., Egypt.

Methods

Construction of the Calibration Curve

Calibration curve of Ebastine was prepared by preparing serial concentrations, in the range of 2-8 µg/ml, of pure drug in methanol from methanolic stock solution (1000 µg/ml). The prepared solutions were analyzed spectrophotometrically at λ max of 253 nm. using UV-spectrophotometer (Thermo, Evo300pc, USA) and the absorbancies obtained were recorded. The standard curve was linear (R^2=0.996) over the range of the used concentrations.

Preparation of drug co-precipitate

Table 1 represents the composition of the prepared formulations. The aim of this study was to prepare drug crystals by precipitation over solid carrier with large surface area in presence of hydrophilic polymers. Aerosil 200 was used for this purpose. The drug/polymer co-precipitate were prepared according to Essa and co-workers with some modification.[4]

The selected polymers were PEG 6000, HPMC E5 and PVP 40T. At constant carrier weight ratio (if present), different drug: polymer ratios were used (Table 1). The drug and polymer were dissolved in the least amount of methylene chloride (about 30ml). Aerosil 200 was then dispersed and the organic solvent was allowed to evaporate by gentle heating at 50ºC over water bath, while mixing with glass rode. The drug and polymer were precipitated on the surface of the dispersed Aerosil. Precipitated drug alone was used as positive control. The precipitate was recovered, air dried and kept in a desicator overnight to ensure removal of any residual methylene chloride. Each powder sample was gently grinded and sieved through a 300µm sieve and stored in a tightly closed container till use.

Characterization of the prepared formulations

Drug content

The drug content was determined by dissolving a weight equivalent to 20mg of the drug from each formulation in methanol followed by centrifugation at 3000 rpm for 10 minutes, to remove the un-dissolved Aerosil. The clear supernatant was suitably diluted with methanol before spectrophotometric assay.

Physical state characterization

These studies were conducted to evaluate the physical properties of the drug after processing and to detect any possible interaction with the used additives. Differential Thermal Anaylsis (DTA), Fourier transform infrared spectroscopy (FTIR) and powder X-ray diffraction were used to achieve this purpose.

Differential thermal analysis (DTA)

The thermal behavior of unprocessed and processed ebastine, Aerosil 200, PEG 6000, HPMC E5, PVP 40T and selected formulations was investigated using differential thermal analyzer (PerkinElmer STA 6000 module, Waltham, MA). Each sample was loaded into an aluminum pan which were crimped. The pan was heated at a rate of 10ºC per minute in the temperature range.

Table 1: The compositions of the prepared controlled precipitation systems together with the dissolution parameters represented as %amount releases after 5 minutes (Q5) and Dissolution efficiency (DE).

Formula	Drug (mg)	Aerosil (mg)	PEG6000 (mg)	HPMC (mg)	PVP (mg)	Q5	DE(%)
Control	20	-	-	-	-	0%	0%
Positive control	20	10	-	-	-	9.7±0.29	16.4±.26
F1	20	-	20	-	-	10.8±0.46	18±0.16
F2	20	-	60	-	-	15.11±1.7	24.27±1.0
F3	20	-	100	-	-	32.3%±1.3	50.96±0.9
F4	20	10	20	-	-	62.6±1.76	74.6±0.88
F5	20	10	60	-	-	69.6%±1.14	77.9±1.5
F6	20	10	100	-	-	66%±2.4	88±2.3
F7	20	-	-	20	-	41.3%±0.76	49±0.77
F8	20	-	-	60	-	56.3%±1	69±3.5
F9	20	-	-	100	-	61±2.1	73±2.2
F10	20	10	-	20	-	59.8±1.8	72±3.4
F11	20	10	-	60	-	78±1	84.5±1
F12	20	10	-	100	-	61±1.1	75.9±0.65
F13	20	-	-	-	20	26.3±1.2	33±1.1
F14	20	-	-	-	60	39.6±1.9	50.9±1.5
F15	20	-	-	-	100	74.3±1.2	79±1.4
F16	20	10	-	-	20	36.5±2.8	51.3±0.8
F17	20	10	-	-	60	46.4±2.6	58±2.5
F18	20	10	-	-	100	83.5±0.8	85.2±0.84

From 25 to 400 ºC, using empty pan as reference. Data analysis was conducted using Pyris software.

Fourier–transform infrared spectroscopy (FTIR)

FTIR spectra was conducted for pure Ebastine, Aerosil 200, PEG 6000, HPMC E5, PVP 40T and selected formulations using FTIR instrument (Bruker Tensor 27, Ettlingen, Germany). Samples scanning from 5000 to 400 cm^{-1} after compression with potassium bromide into disks using hydraulic press. Data analysis was performed using Opus IR, FT IR spectroscopy Software.

X-ray powder diffraction (XRPD)

X-ray diffractograms were obtained for pure drug, processed drug, pure polymers and some selected formulations using XRPD system (Crystal Impact, Bonn, Germany). The scanning rate employed was 8°/min over a 2θ range from 3 to 65º.

Preparation of orally dispersible tablets (ODT)

Formulations showed the best dissolution parameters were selected to prepare ODT. This process employed single punch tablet machine (Royal Artist, Kapadia Industrial Estate, BLDG, Mumbai, India) using direct compression technique**.** Each tablet was prepared to contain 20mg of pure drug (control tablets) or its equivalent of co-precipitate. The tablet ingredients, according to Table 2, were mixed for 10 minutes using the bottle method. The compaction force of the tablet machine was adjusted to produce tablets having a hardness in the range of 4–5 KP using 10mm punch.

Pre-compression parameters

Bulk density (D_B) and tapped density (D_T) were determined for each tablet powder blend prior to compression. Fixed weight of each blend was introduced into a 10 ml measuring cylinder and the initial volume was noted and taken as bulk volume. The cylinder was tapped for 15 minutes or until fixed powder volume, this was taken as tapped volume. From these values both bulk and true densities were calculated, by dividing mass over the corresponding volume, and used in measuring compressibility index (Carr's Consolidation Index) and Hausner ratio.[11]

Table 2: Master formula for preparation of ebastine fast disintegrated tablets.

Ingredients (mg/tablet)	Control tab.	F18
Ebastine or its an equivalent from F18	20	130
Mannitol (granular)	120	120
Avicel PH101	170	60
Croscarmellose sodium	15	15
Crospovidone	10	10
Magnesium stearate	5	5
Aerosil	5	5

Evaluation of fast disintegrating tablets

Uniformity of weight*:* Conducted by recording the average weight of 15 tablets of the selected batch and the percentage weight deviation of the individual tablets from that average was calculated. Limits for acceptance was done considering tablet weight.[12]

Tablet friability*:* Determined by calculating the percentage loss in weight after exposing 10 tablets to 100rpm in a friabilator (Erweka Friabilator, Western, Germany). The allowed percentage should not exceed 1%.[12]

Drug content: The test employed 10 tablets, randomly selected from tablet batch. Each tablet was crushed and dissolved in methanol. The insoluble tablet additives were separated by centrifugation. The drug content in each tablet was determination by UV spectrophotometric assay. The accepted limit is that each tablet should contain 85 to 115% of the labelled dose, with only one tablet is allowed to deviate this limit.[12]

Disintegration test: The time taken for complete disintegration of 6 tablets placed in tablet disintegration tester (Copley Scientific NE4-cop Nottingham, UK) was determined using distilled water at 37ºC was as a disintegration media.[12]

Wetting time: A small amount of Allura red powder was carefully sprinkled over the surface of each tablet before placing the tablet over filter paper placed in a petri-dish containing 6ml of distilled water. The wetting time was taken as the time required for developing a red color on the surface of each tablet.[13]

***In vitro* Dissolution studies**

The dissolution rate of Ebastine from different formulations (co-precipitated formulations, orally dispersible tablets) was determined using the USP II dissolution apparatus (Copley, NG 42 JY, Nottingham, UK). Unprocessed pure drug was used as control for the co-precipitated samples. The dissolution medium consisted of 1.2 N HCL, containing 1.0% sodium laurel sulphate. The paddle rotation was adjusted at 100 rpm and the dissolution medium (900 ml) was maintained at 37 ºC ±0.5 ºC. these conditions were used to study the dissolution of the prepared powder formulations as well as OD tablets. An amount of 20 mg of Ebastine or its equivalent of the prepared co-precipitate particles or the prepared OD tablets were loaded in the dissolution vessels. An aliquots of 5 ml each were collected at predetermined time intervals and replaced with fresh dissolution medium. The samples were filtered and analyzed spectrophotometrically at 253 nm after suitable dilution, when necessary. The cumulative amount of dissolved ebastine, expressed as percentage of the loaded amount, was plotted as a function of time (in minutes) to obtain the dissolution profiles.

Statistical Analysis

All experiments were conducted at least in triplicates and statistical analysis employed Student *t*-test. Results were quoted as significant when *P*-value is less than 0.05 and non-significant when more than 0.05.

RESULTS AND DISSCUSION

Solid state characterization of drug/polymer co-pricipitate

The drug content of the prepared formulations was in the acceptable range. The drug content values were in the range of 86.8 – 96.4 % w/w.

Differential thermal analysis (DTA)

The thermograms of unprocessed ebastine, pure polymers, aerosil and and selected formulations F5, F11 and F18 (prepared using PEG, HPMC and PVP, respectively) are presented in **Fig. 2**. These formulations were selected as they showed the best drug dissolution parameters.

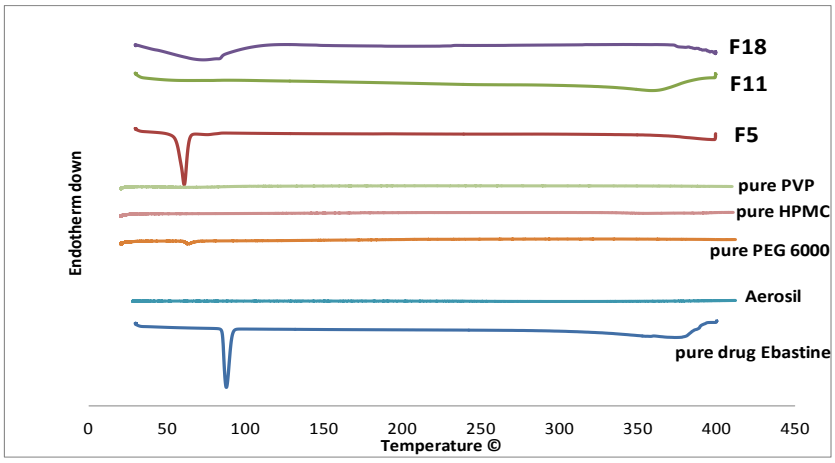

Fig. 2: The thermograms of unprocessed ebastine, pure polymers, aerosil and and selected formulations F5, F11 and F18 (prepared using PEG, HPMC and PVP, respectively).

The thermogram of unprocessed drug showed sharp endothermic peak at 86.5°C with onset of 73.2 and endset of 91.2 °C. the first endotherm is attributed to the melting transition of the drug and reflects its crystalline nature, in agreement with the published information.[14,15] The thermogram also showed a broad endotherm above 350°C that could be attributed to drug degradation at such high temperature.

For aerosil, the thermo-gram reflects its amorphous nature with no detected endothermic or exothermic peaks agreeing, thus with reported data.[16] The thermogram of pure PEG 6000 showed an endothermic peak at about 55.8 °C corresponding to its melting transition. This thermogram is in close agreement to published data for the same polymer.[4] For pure PVP, the thermo-grams showed a broad endothermic peak beginning at 28.27 ºC and ending at 88.4 ºC with Tm at around 51.28 ºC (Fig. 2). This can be explained by the evaporation of the adsorbed moisture[17,18] Similarly, the thermal behavior of pure HPMC E5 revealed similar broad endothermic peak with Tm of 39.7 ºC onset of 28.9 ºC and endset of 62.1 ºC and can be explained in the same way as that for PVP.[4]

The thermogram of F5 using PEG 6000 showed sharp endothermic peak at 55.8 °C. The thermal analysis of F11 and F18 using HPMC and PVP respectively showed disappear of the sharp peak of ebastine which indicates reduction of the crystallinity and formation of amorphous form.

Powder X-ray diffraction

The X-ray diffraction pattern of unprocessed ebastine, pure polymers**,** pure aerosil and the selected formulations (F5, F11 and F18) are presented in Fig. 3. These formulations were selected as they showed the best drug dissolution parameters.

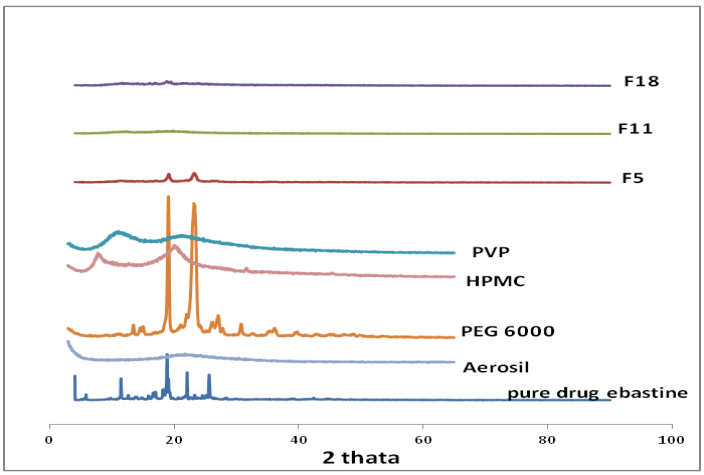

Fig. 3: The X-ray diffraction pattern of unprocessed ebastine, pure polymers, pure aerosil and the selected formulations F5, F11 and F18 prepared using PEG, HPMC and PVP, respectively.

The x-ray pattern of pure ebastine reflected the crystalline nature of the drug with sharp peaks detected at diffraction angles (2θ) of 11.4, 16.5, 17.3, 22.3 and 25.1°. this diffractogram is in good agreement with previously published data of the same compound.[19,20] The diffraction pattern of pure PEG6000 reflected its crystalline structure with characteristic peaks appearing as intense peaks with the highest ones recorded at 2 theta of 19.1 and 23.7°.[21] For aerosil, PVP 40T and HPMC E5 the diffractograms showed diffuse pattern characterized by the complete absence of any specific diffraction peaks. These patterns coincide with the reported data for the same polymers and indicate their amorphous nature.[4] The x-ray spectra for formulations prepared using HPMC (F11) and PVP (F18) showed complete disappearance of the diffraction peaks of the drug. This indicates the reduced crystallinity of the drug and its transformation into amorphous form. For formula F5 prepared using PEG6000, the characteristic peaks of the drug was disappeared indicating amorphization. The spectrum also showed two small peaks at 18.7 and 22.6° with reduced intensity compared to the pure polymer. These peaks may resulted from the extra amount of PEG 6000.

FT-IR spectrum

Fig. 4 shows FTIR spectra for unprocessed drug, aerosil, polymers and the selected formulations. Ebastine spectrum shows its characteristic bands where peak corresponding to C-H stretching of the ring appears at 3051cm^{-1} while that for CH3 appears at 2947cm^{-1}. The C=C stretching aromatic ring at 1450cm^{-1}, C-N stretching at 1267cm^{-1} and C=O stretching band at 1677cm^{-1}. This spectrum is in a reasonable agreement with the published data for the same drug.[22]

The FTIR spectrum of pure HPMC showed the characteristic absorption bands at 3341 cm^{-1} corresponds to the OH stretching. The aliphatic C-H stretching appears at 2902 cm^{-1} and that of the aliphatic C-O stretching at 1121 cm^{-1}. Similar spectrum was reported by other investigators.[23] For pure PVP 40T the spectrum showed a characteristic band at 1658 cm^{-1} for the carbonyl group. The very broad band at 3450 cm^{-1}

indicate the adsorbed moisture, (Goddeeris and Van den Mooter, 2008). The spectrum of Aerosil showed broad peak at about 3392 and 3126 cm^{-1} that can be attributed to O-H stretching vibration modes of hydrogen bonded to OH of polymeric association. The Si-O symmetric stretching vibration of silica appeared at 1119 cm^{-1}. The band at around 1610 cm^{-1} corresponds to H-O-H bending of crystallized water,[4] For PEG 6000, the characteristic bands can be detected at 2903, 1160 and 3250 cm^{-1} corresponding to C–H stretching at, C–O stretching and –OH stretching, respectively.[21]

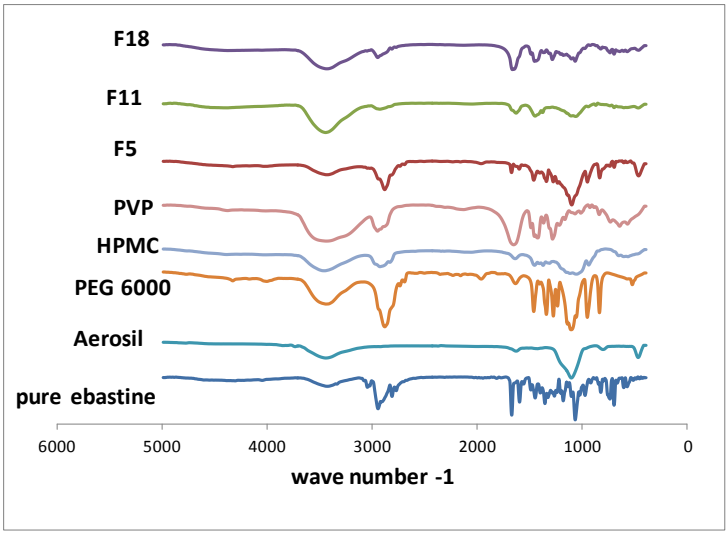

Fig. 4: FTIR spectra of unprocessed ebastine, pure polymers, pure aerosil and the selected formulations F5, F11 and F18 prepared using PEG, HPMC and PVP, respectively.

Regarding the tested formulations (F5, F11 and F18), the characteristic peaks of the drug can be detected, though reduced in intensity. This would indicate the compatibility between the drug and the used excipients.

In vitro drug release from the prepared formulations

The dissolution profiles, represented as cumulative amount of drug released versus time plots, are shown in Fig. 5. Table 1 contains the dissolution parameters represented as percentage drug released after 5 minutes (Q5) and dissolution efficiency (DE). The later is computed as the area under the dissolution curve between time points t_1 and t_2, expressed as a percentage of the area of the rectangle described by 100% dissolution in the same time.[24]

For positive control, precipitation drug from its methylene chloride solution over Aerosil in absence of hydrophilic polymer, improved drug dissolution was noticed over the unprocessed drug ($P < 0.05$). This enhanced Q5 can be explained by the presence of aerosil provided a large surface area during the precipitation step acting as a carrier upon which drug crystal would deposit. This increased surface area exposed to the dissolution media would increase dissolution process as stated by Noyes–Whitney equation.[4] Moreover, the precipitation process may have a potential to produce partial change into amorphous structure with subsequent enhancement in the dissolution rate as suggested by the physical characterizations.

Precipitation of ebastine in presence of hydrophilic polymer, in absence of aerosil, largely improved drug dissolution, the extent of which depended on polymer type and concentration. All formulations, except F1, F2, produced significant improvement in drug dissolution as reflected by increased Q_5 ($P<0.05$) over that for unprocessed drug and positive control (Fig. 5 and Table 1).

Formulations prepared using HPMC (formulation F7-F9) and PVP (F13-F15) polymers were superior to those prepared using PEG6000 (F2-F4). Increasing polymer concentration in ebastine co-precipitate, increased the dissolution parameters (Table 1). The superiority of formulations containing hydrophilic polymers could be explained by the possible adsorption of the polymer chains on the microstructure of the drug microparticles during the precipitation and solvent evaporation steps. Upon exposure to the dissolution medium, the hydrophilic polymer undergoes rapid wettability and/ or solubility upon producing high concentration in the diffusion layer of the drug around each drug particle. The dissolved polymer is expected to prevent aggregation of drug particles and increases drug wettability and consequently the dissolution rate.[8,26] Similar results were obtained when flurbiprofen when precipitated from its organic solution in presence of hydrophilic polymers.[4]

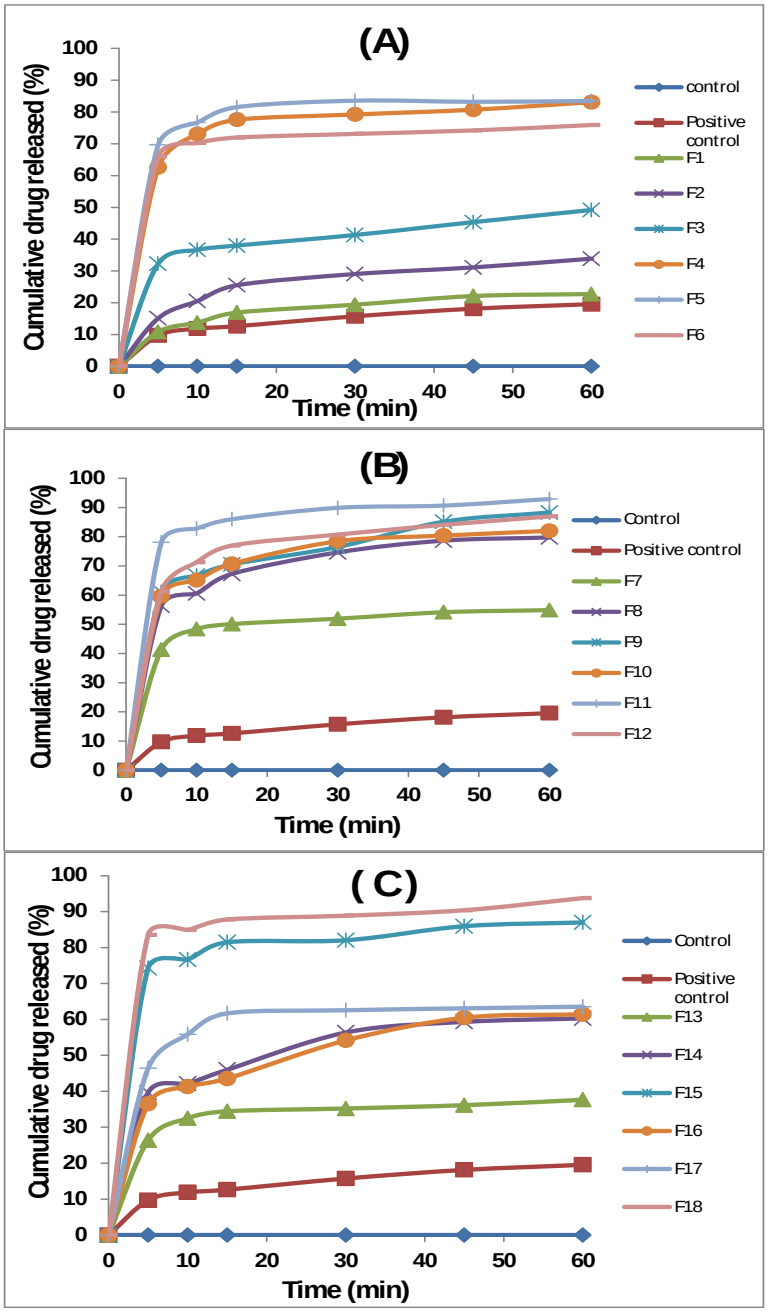

Fig. 5: Dissolution profiles of Ebastine from different formulations prepared in presence of PEG6000 (A), HPMC (B) and PVP (C). For detailed formulations refer to Table 1.

The dissolution profile of the unprocessed drug showed very low solubility. There was no drug throughout the experimental time which reflects a very high hydrophobicity of the pure drug. A similar dissolution pattern was recorded by other investigators.[25]

Precipitation of the drug in presence of both hydrophilic polymers and Aerosil showed a considerable improvement in the dissolution parameters. The results of dissolution studies indicated the superiority of PEG 6000 in one concentration and HPMC in one concentration while PVP 40T in two concentration with best dissolution over other polymers in improving dissolution parameters (Table 1). It was noticed that PEG 6000 1:1 there was unremarkable improve in the dissolution of the dug, while in other polymers with the same concentration there was noticeable change of dissolution improvement.

While increasing the concentration of HPMC from 1:1 to 1:3 ratio enhanced the dissolution, increasing the concentration of the same polymer from 1:3 to 1:5 ratio reduced drug release. This could be due to increased interaction between HPMC polymer and drug microparticles surface with possible increased thickness of the adsorbed polymer layer. This may lead to increased viscosity of the diffusion layer around the drug particles with subsequent slow drug partitioning out through it.[27]

Characterization of fast dissolving tablets

Based on the in vitro dissolution studies formulation F18, prepared using PVP 40T, were selected to prepare oral dispersible tablets as it showed the highest Q5. Tablets were prepared using 20mg of unprocessed drug (control tablet) or an equivalent amount of each formulation (Table 2). Tablets were prepared by direct compression method, after using suitable formulation aids, according to compositions shown in Table 2.

To ensure dose uniformity among tablets, the flow properties of each powder mixture was evaluated prior to compaction. The results of powder flowability are shown in Table 3. The two powder blends showed a good flow properties and were suitable for manufacture of tablets.[35] There was a good correlation between Carr's compressibility and Hausner ratio values. Such good flow properties resulted in uniform tablet weight that complied with the US pharmacopeal requirements with a deviation from average weight being less than 2%.

The drug content uniformity was 97.8% and 98.1% for PVP tab and control tabs, respectively of the labeled dose. Tablet hardness and friability were in the acceptance criteria of the US pharmacopeia.[36] Regarding disintegration time, both tablets showed a rapid disintegration, with PVP tab being superior with only 14 second. The reason for such rapid disintegration could be due to the incorporation of the croscarmellose sodium and crospovidone with their super-disintegrating effect. For the wetting time, short time of 31.2 and 25.0 seconds was recorded for control and PVP tablets, respectively. This indicates the hydrophilicity of the tablet surface with good tablet porosity.

For the in vitro dissolution studies for both tablets, the dissolution profiles are shown in Fig. 6 and the dissolution parameters are in Table 3. Though pure ebastine did not release any detectable amount of the drug (Table 1), control tablets showed a considerable drug release of about 15.6% of the loaded dose after 5 minutes with a total release of 26.7% after 60 minutes. This unexpected release could be due to the adsorption of the drug over the surface of the tablet additives that increased the surface area available for drug dissolution. For PVP tab there was a prompt release of the drug with a Q5 of 80.4% and a dissolution efficiency of 82.6%.

Table 3: Results of powder flowability, tablet quality control tests, together with in vitro dissolution parameters of oral dispersible tablets represented as percentage drug released after 5 min (Q5) and dissolution efficiency (DE).

	Powder Flowability		Content uniformity (%)	Disintegration time (sec)	Friability (%)	Hardness	Wetting time (Sec)	Q5	DE(%)
	Carr's Index	Hausner ratio							
Control tab.	19.3	1.24	98.4± 1.7	33±1.8	0.21	4.75	31±1.6	15.5±0.3	23.8±0.28
PVP tab.	14.0	1.16	97.7±1.8	14±1.9	0.11	4.75	25±0.6	80.4±2	82.56±1.2

All formulations showed rapid disintegration time that ranged from 10 to 33 seconds, for PVP Tab and control Tab respectively. Such rapid disintegration could be due to the presence of super-disintegrant that swells and break tablets apart. The recorded disintegration time values are acceptable taking into consideration the FDA specification of orodispersible tablets which recommends a disintegration time of approximately less than or equal to 30 seconds.[28]

For wetting time test, PVP Tab showed a time of 25 seconds. The control Tab showed a longer time of about 31 seconds. This could be attributed to the presence of hydrophilic polymers in the former tablet types that would increase tablet wettability.

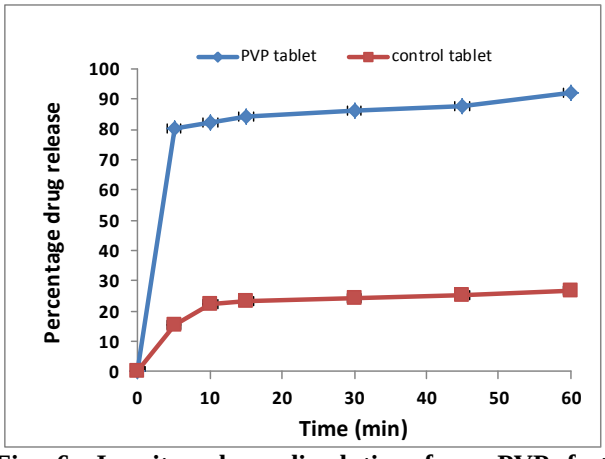

Fig. 6: In vitro drug dissolution from PVP fast disintegrating tablets. For detailed composition refer to Table 2.

The dissolution profiles of two tablet batches are shown in Fig. 6. The control tablet exhibited a trend of better dissolution parameters compared with the unprocessed drug powder (Table 3). This could be due to the

adsorption of the drug on the surface of tablet excipients with subsequent rapid dispersion in the dissolution medium. Regarding tablets containing processed drug, both tablets showed improved dissolution profiles fast dissolution. PVP tablets liberated 80% of the labeled amount in the first 5 minutes. This results is similar to that obtained from the dissolution study of the prepared microparticles ($P > 0.05$).

CONCLUSION

Precipitation over Aerosil in presence of hydrophilic polymers improved the dissolution rate of Ebastine. Such improvement depended on the type of polymer used and its concentration. Presence of aerosil as carrier further enhanced the dissolution. Deposition of amorphous drug microparticles on the large surface area of aerosil explains such enhancement. The optimized drug formulation was formulated as oral dispersible tablets with rapid dissolution of ebastine. The rapid dissolution with subsequent rapid absorption is expected to improve bioavailability of the drug and decrease the time needed to reach liver for the conversion into the active form, carebastine, in the liver.

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