Formulation and Evaluation of Fast Dissolving Tablets of Taste-Masked Ondansetron Hydrochloride by Solid Dispersion

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Abstract

Ondansetron hydrochloride (ONH) is a very bitter, potent antiemetic drug used for the treatment and/or prophylaxis of chemotherapy or radiotherapy or postoperative induced emesis. The objective of this study is to formulate and evaluate of taste masked fast dissolving tablet (FDTs) of ONH to increase patient compliance.

ONH taste masked granules were prepared by solid dispersion technique using Eudragit E100 polymer as an inert carrier. Solvent evaporation and fusion melting methods were used for such preparation.

Completely taste masking with zero release of drug in phosphate buffer pH 6.8was obtained from granules prepared by solvent evaporation method using drug: polymer ratio of 1:2, from which four formulas pass pre-compression evaluation and compressed to FDTs and evaluated for their drug content, in-vitro disintegration time, *in-vivo* disintegration time, wetting time and in vitro drug release profile.

F7 which is prepared from solid dispersion product equivalent to the required dose of ONH , Crosspovidone as superdisintegrant, Aspartame as sweetener ,Ross berry as flavor ,Polyvinylpyrolidone K30.3.as binder ,Avicil PH102 and , mannitol as diluents give best *in- vitro, in-vivo* disintegration time and best drug release profile.

Key words: Ondansetron hydrochloride, taste masking, solid dispersion, Eudragit E100.

تصييغ وتقييم حبوب سريعة الذوبان مكسوة الطعم للاوندانسيترون هايدروكلورايد بواسطة المنتشر الصلب

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الخلاصة

هيدروكلورايد الاونداسيترون دواء مر جداً يستخدم ، للعلاج و/أو الوقاية من الغثيان والتقيؤ الناتج من العلاج الكيميائي أو العلاج الإشعاعي أو بعد العملية الجراحية. الهدف من هذه الدراسة هو صياغة وتقييم حبوب سريعة الذوبان مكسوة الطعم لزيادة امتثال المريض للدواء . تم تحضير حبيبات مكسوة الطعم لدواء هيدروكلورايد الاونداسيترون باستخدام تقنية المنتشر الصلب واستعمال بوليمر يودراجيت E100 لاخفاء الطعم المر للدواء حيث حضرت هذه الحبيبات اما بطريقة تبخر المذيب او بطريقة الصهر لليودراجيت E100 وقد تم الحصول على إخفاء كامل للطعم بعدم تحرر الدواء في وسط مشابه للعاب من حبيبات تم الحصول عليها بطريقة تبخر المذيب لبوليمر اليودراجيت E100 وبنسبة دواء: البوليمر ١:٢ وقد تم استخدام هذه الجبيباب لاعداد سبعة صيغ للحبوب السريعة الذوبان والتي تم تقييمها من حيث كمية الدواء ، الوقت اللازم لترطيبها و الوقت لتتفككها داخل وخارج الجسم وقد استنتجت الدراسة ان الصيغة السابعة والتيي تتكون من حبيبات المنتشر الصلب مكافئة للجرعة المطلوبة ، كروسبوفيدون كعامل مفكك ، اسبارتام كمادة محلية ، نكهة الروزبري ، بولي فاينيل بوفيدون كمادة رابطة، افيسيل PH102 والمانتول كمواد مخففة هي الافضل من حيث سرعة تفككها وتحرر الدواء منها .

الكلمات المفتاحية:- هيدروكلورايد الاونداسيترون ، اخفاء الطعم ، المنتشر الصلب ، اليودراجيت E100 .

Introduction

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been discovered for the systemic delivery of drugs through various pharmaceutical products of different dosage forms, because it is convenient, self-administration, compactness and easy manufacturing, accurate dosage and most importantly the patient compliance [(1)].

Administration of an oral drug delivery system having bitter taste with acceptable level of palatability has always been challenge in manufacturing of a formulation for pediatric and old age patients. The bitterness of drug or drug product is minimized or completely masked by various physical, chemical and physiological means such as lipophilic vehicles ,coatings , inclusion complexation, ion exchange, effervescent agents, rheological modification, solid dispersion system, group alteration and prodrug approach, freeze drying process, wet spherical agglomeration technique and continuous multipurpose melt technology[(2)].

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Solid dispersion involves the dispersion of one or more active ingredient in an inert carrier or matrix in solid state. It is prepared by melting, dissolution in solvent or melting solvent methods.[3]

Carriers used in solid dispersion system include povidone, polyethylene glycols of various molecular weights, hydroxy propyl methyl cellulose, urea, mannitol and ethyl cellulose, Eudragit E100 and Eudragit EPO.[4]

ONH is a competitive serotonin type 3 receptor antagonist. It is effective in the treatment of nausea and vomiting caused by cytotoxic chemotherapy drugs, including cisplatin and it has reported to act as anxiolytic and neuroleptic agent .It is also used in early onset of alcoholism[5]. Generally emesis is preceded by nausea and in such condition it is difficult to administer drug with a glass of water; hence it is beneficial to administer such drugs as FDTs. ONH is an intensely bitter drug; hence, if it is incorporated directly into a FDTs the main challenge behind formulation of such a dosage form will definitely get an acceptable dosage form to the patient [6]

Thus, in the present study an attempt has been made to mask the taste of ONH and to formulate FDTs with complete taste masking and good mouth feel so as to prepare a "patients friendly dosage form."

Materials and Methods

Materials

Ondansetron hydrochloride (ONH) was purchased from Hangzhou Hyperchemical Limited china, Avicel PH102 Hyperchem China, Cross povidone (CP), Cross carmellose sodium (CCS), Sodium starch glycolate (SSG) and Magnesium stearate from Middle east laboratories , Eudragit E100 from Evonic company Germany, Talc from Samara drug industries,.Polyvinylpyrolione (PVP) K30 Hyperchem China.

Preparation of solid dispersion

Fusion method

Solid dispersion of ONH was prepared by fusion method. In this method the drug and carrier (Eudragit E100) were mixed with a drug: polymer ratio of 1:1, 1:2, 1:3, and 1:4 in a china dish and heated on a paraffin bath until the solid mixture is melted. The mixture was poured on a tile and cooled. The resulted solidified mass was dried pulverised and passed through sieve no 20[7].

Solvent evaporation

ONH was mixed with powdered Eudragit E100 using a mortar and pestle in different drug: polymer ratios (1:1, 1:2). The mixture was transferred into a stainless steel vessel. Then 10% ethanol (15ml) was added to the mixture of each ratio. The mixture was stirred constantly on a magnetic stirrer till a thick gel was formed the temperature was kept at 40 °C with a stirring speed of 350 rpm. The ethanol was removed by evaporation overnight and subsequently the solidified gel was crushed into particles using mortar and pestle and then sieves through sieve no. 20 [8]

Characterization of ONH solid dispersion

Percentage yield of solid dispersion

The prepared solid dispersion granules were collected and weighed. The measured weight was divided by the total amount of drug and polymer which were used for the preparation of solid dispersion

Percentage yield = [Wp/Wt] × 100

Where, Wp is actual weight solid dispersion obtained and Wt is the total weight of drug and polymer. [8]

Drug content

10 mg of solid dispersion was stirred by using magnetic stirrer with 100 ml of 0.1 N HCl for 60 minutes, till the entire drug leached out from polymer, then the solution was filtered through filter paper and diluted with 0.1 N HCl. The drug content was determined spectrophotometrically at 310 nm [9].

In vitro taste evaluation

In- vitro taste was evaluated by determining drug release in phosphate buffer (pH 6.8) to predict release of drug in the human saliva. Solid dispersion equivalent to 8 mg ondansetron (OND), ie, its dose, was placed in 10 ml of phosphate buffer 6.8 and shaken for 60 seconds. The amount of drug released was analyzed at 310nm [10]. The solid dispersion product that gives zero release is considered the optimum to be used for further study [11]

Fourier transforms infrared spectroscopy (FTIR)

The FTIR spectra of pure ONH , Eudragit E100, physical mixture of drug and eudragit E100 and the selected solid dispersion product were obtained using FTIR spectrophotometer (FTIR -8300 Shimadzu, Japan) by potassium bromide (KBr) pellet method. This study was achieved to identify any sign of interaction between the drug and polymer used. The scanning range was (4000-400 cm-1) [12]

Powder X-Ray Diffraction (PXRD)

Powder X-ray diffraction can be used to confirm the crystalline nature of materials. So, this information is used to verify whether the substances are crystalline or amorphous. The diffractograms of ONH, a physical mixture of

drug and eudragit E100 and the selected solid dispersion product powders were obtained. The study was confirmed by using Shimadzu XRD-6000 powder X-Ray diffractometer at continuous scan range of 5°-80° of 2ΘThe operating voltage was 40 (kV) and current 30mA. [10]

Preparation of ONH FDTs

Tablets containing 10mg taste masked ONH equivalent to 8mg OND were formulated by the direct compression method using various superdisintegrants like (CP) (3 and 4%) for F4 and F7 respectively , (CCS) (3%) for F5, (SSG) (3%) for F6 as shown in table (1) .

All the ingredients were passed through a sieve number 20 prior to mixing. ONH - Eudragit E100 solid dispersion, mannitol, Avicel PH102, the superdisintegrants, rossberry flavor, aspartame and PVP K30 were properly mixed for 20 minutes in a mortar to obtain a uniform blend. The blend was further lubricated with magnesium stearate, talc for 2 minutes. Then powder was compressed into tablets using a 6mm flat punch tablet press.

Table (1): Formulation of ondansetron hydrochloride FDT.

Formula code / Ingredient(mg)	F1	F2	F3	F4	F5	F6	F7
Solid dispersion(1:2)	30	30	30	30	30	30	30
Cross Povidone(CP)	4.5	4.5	4.5	4.5			6
Cross Carmillose Sodium(SCC)					4.5		
Sodium Starch Glycolate(SSG)						4.5	
Ross berry flavor	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Aspartame	1.5	1.5	1.5	1.5	1.5	1.5	1.5
Avicel PH102		15	30	45	45	45	45
Talc	3	3	3	3	3	3	3
Mg. stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5
PVP K30	3.75	3.75	3.75	3.75	3.75	3.75	3.75
Mannitol Q.S	150	150	150	150	150	150	150

Pre compression evaluation of powder blend

Flow Properties

These properties were determined in terms of angle of repose, Carr's index and Hausner's ratio for tablet blend powder in comparison with pure drug powder and the selected solid dispersion product.

Determination angle of repose

One of the methods for assessing flow properties of powder is the angle of repose. It was determined using fixed funnel method, by permitting a powder to flow throughout a funnel and pass freely onto a surface. The height and diameter of the resultant cone were measured and the angle of repose was calculated from this equation:

Tan (θ) = h/r

Where: **h** is the height of the powder cone and **r** is the radius of the powder cone. [13]

Bulk density

It is a ratio of the powder mass to bulk volume. The bulk density depends on particle size distribution, shape, and cohesiveness of particles. The weighted amount of the powder carefully poured into the graduated measuring cylinder through the large funnel and volume was measured, which is the initial bulk volume. Then it was expressed in g/ml. Bulk density was calculated by the following equation. [13].

Bulk Density =

Weight of powder / Bulk volume

Tapped density

The graduated cylinder containing a known mass of mixture was tapped for a permanent time. The volume was measured, and the tapped density was calculated by the following equation [13].

Tapped Density =

Weight of powder / Tapped volume

Carr's index (compressibility index) and Hausner's ratio

Carr's index indicates the flow properties of the powder. It was expressed in percentage and was calculated by the following equation:

Carr's index =

[(Tapped density – Bulk)/(Tapped density)]×100

Hausner Ratio is an indirect index of powder flow [13]. It was calculated by the following equation:

Hausner's ratio =

(Tapped density)/(Bulk density)

Evaluation of FDTs

Hardness test

Monsanto hardness tester was used to determine the tablet hardness. Three tablets were randomly chosen from each formulation of. The mean of three determinations ± SD was recorded.

The hardness was expressed as a force in kg/cm^2 required to crush the tablets [14].

Friability test

Friability test is performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap or break. Roche Friabilator was used for the purpose. It is expressed in percentage (%). Twenty tablets were initially weighed (W initial) and transferred into friabilator. The friabilator was run 25rpm for 4 minutes. The tablets were weighed again (W final). The percentage friability was then calculated using the following equation:

%Friability =

{(W initial - W final) / W initial} x 100 %

Friability of tablets less than 1% are considered acceptable [14]

Weight variation

Twenty tablets were weighed individually and the average weight was calculated .Then each weighed tablet compared with average weight, whether it's within the acceptable limit or not according to USP [14].

Wetting time

The wetting time of tablets was measured using a simple procedure. A filter paper folded twice was placed in a small petri-dish (Internal diameter = 6 cm) containing 6 ml of phosphate buffer pH6.8 .The method was slightly modified by maintaining phosphate buffer at 37 ºC. A tablet was placed on the filter paper and the time required for the complete wetting of the tablet was recorded as a wetting time. The mean of three tablets wetting time were recorded and standard deviation calculated [15].

In vitro disintegration test

The in-vitro disintegration study, of the oral dispersible tablet, was determined using disintegration test apparatus as per USP specifications. One tablet was placed in each of the six tubes of the basket, the disc was added to each tube and running the apparatus using 900 ml of phosphate buffer pH 6.8 as the disintegration liquid[16]. The assembly should be raised and lowered between 30 cycles per min in disintegration liquid which was kept at 37ºC.The time in seconds for complete disintegration of the tablets with no mass remaining in the apparatus was measured and recorded [14,16].

In vivo disintegration test

The time required for complete disintegration in the oral cavity was estimated from five healthy volunteers. All volunteers were told about the purpose of the test. The tablet was placed on the tongue, and subsequently the tongue was gently moved. The time required for the elimination of any residue or fragment of the tablet was measured with a stopwatch and recorded as a disintegration time [17].

Drug content

Five tablets were powdered and the blend equivalent to 10mg ONH was weighed and dissolved in 100ml of 0.1 N HCl, filtered and 1ml withdrawn and diluted to 10ml and drug content analyzed spectrophotometrically at 310 nm[18].

In vitro dissolution studies

The dissolution profile of ONH from FDTs was determined using United State Pharmacopoeia (USP) dissolution testing apparatus II (paddle method). The dissolution test was performed using 500 ml of 0.1N HCl pH 1.2 as dissolution medium, at 37 ± 0.5°C and 50 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus at 1, 2, 3, 4, 5, 10, minutes. The samples were filtered through a 0.45µm membrane filter syringe.

Absorbance of these solutions was measured spectrophotometrically at 310 nm. Cumulative percentage of drug release was calculated using an equation obtained from a standard curve [14].

The time required for 80% of drug to be released ($t_{80\%}$) and percent drug dissolved in 2 minutes ($D_{2min\%}$) were considered for comparing the dissolution results [19].

The $t_{80\%}$ and $D_{2min\%}$ were determined by fitting the dissolution data to a four parametric logistic model using the Marquardt-Levenberg algorithm (Sigmaplot 11 SPSS) [20].

Results and Discussion

Characterization of ONH solid dispersion

Percentage yield and drug content of solid dispersion (fusion method and solvent evaporation) are shown in table (2).

Table (2): Percentage yield and percentage of drug content of solid dispersion products

Fusion method	%yield	%drug content	Solvent evaporation	%yield	%drug content
1:1	87%±2.3	90%±1.5			
1:2	86.8%±1.3	93%±0.85			
1:3	94%±1.75	103%±0.96			
1:4	96%±1.5	96.2±0.55			
			1:1	95.5%±1.5	97%±2
			1:2	96%±1.35	100%±0.25

In vitro taste evaluation

The in vitro taste evaluation show that solid dispersion produced by fusion method in the ratio of 1:4 drug: polymer gave less release of drug. On the other hand, no drug release was obtained in phosphate buffer pH 6.8 from solid dispersion produced by of solvent evaporation method with ratio of 1:2 drug: polymer as shown in table (3).Therefore, this ratio was considered the optimal solid dispersion with complete masking of bitter taste of drug for further studies and for the preparation of fast dissolving tablet [(5)] .

Table (3): In vitro taste evaluation of solid dispersion in buffer pH6.8

Fusion method	Drug release	Solvent evaporation	Drug release
1:1	35µg/ml	1:1	3.3 µg/ml
1:2	27 µg/ml	1:2	zero
1:3	20 µg/ml		
1:4	3.6 µg/ml		

Fourier Transform Infrared Spectroscopy

The FTIR spectrum of ONH show broad band O-H stretching of H_2O at 3410 cm^{-1} -3492 cm^{-1} , C-N stretching at 1281 cm^{-1}, CH_3 at 1458 and 1479 cm^{-1},C=C aromatic stretching at 1531 cm^{-1}C=N ,C=O stretching in six member ring at 1639 cm^{-1}[(12)].

The FTIR spectrum of the physical mixture of drug and polymer showed no significant shift or reduction in intensity of peaks of (ONH). However, the FTIR spectrum of solid dispersion product 1:2 show no interaction between drug and polymer and no change in peak of drug.

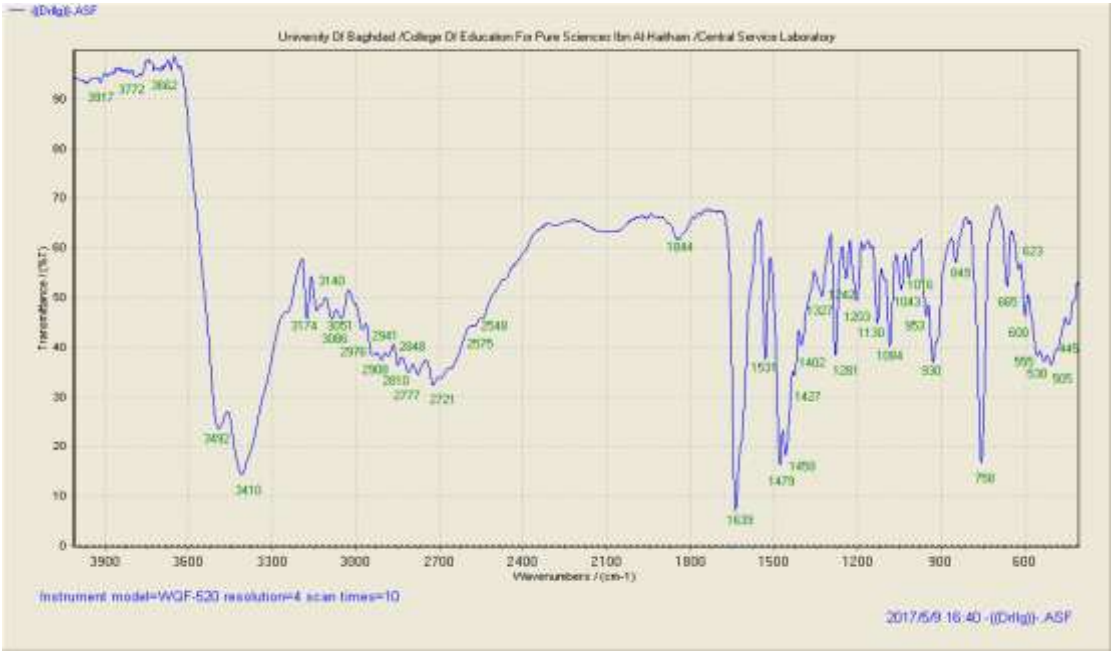

Figure (1): FTIR spectroscopy of ondansetron hydrochloride

Figure (2): FTIR spectroscopy of Eudragit E100

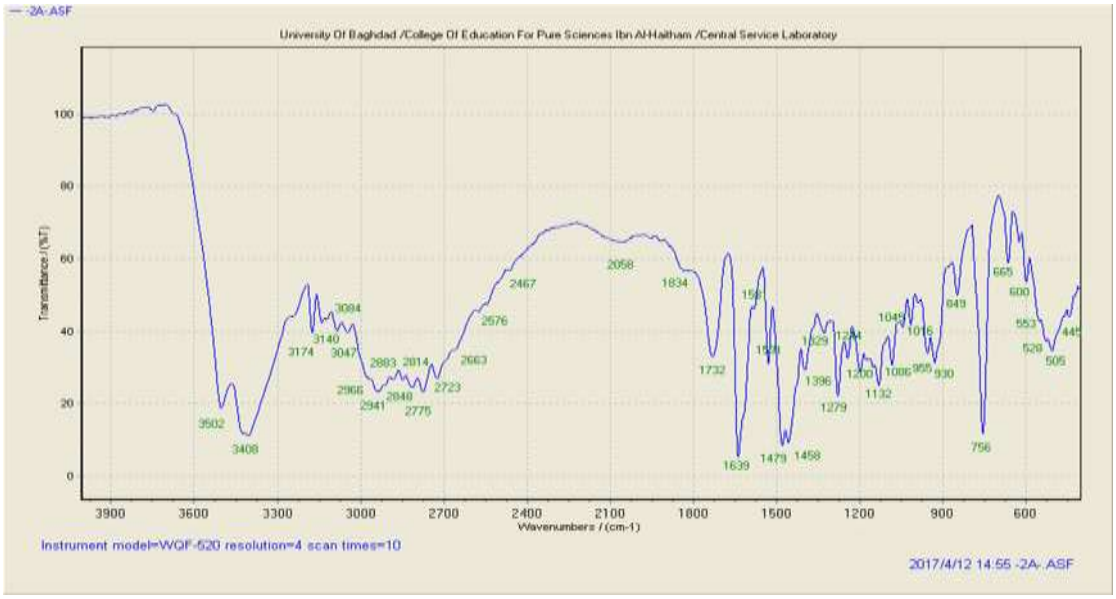

Figure (3): FTIR spectroscopy of physical mixture 1:2 drug:Eudragit E100

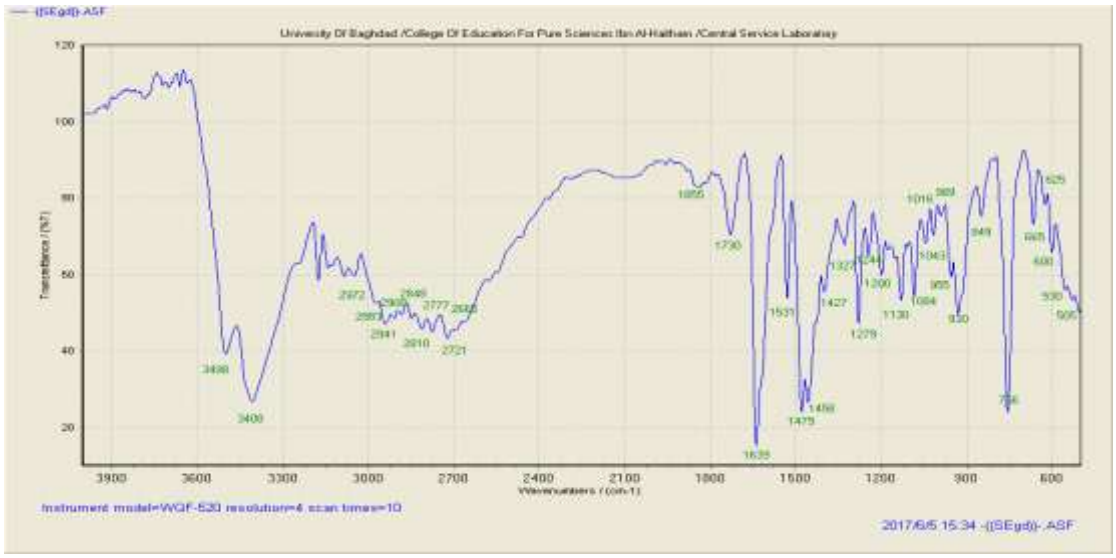

Figure (4): FTIR spectroscopy of solid dispersion product prepared by solvent evaporation (1:2) drug:Eudragit E100

Powder X-Ray Diffraction

The x-ray diffractogram of (ONH) confirms its crystalline nature, as evidenced from the number of sharp and intense peaks as shown in figure (5).However, the diffraction pattern of solid dispersion represents complete disappearance of crystalline peaks of drug especially those situated at 6° ,12°, 24°,28° and 30° - (2θ).These findings suggest the formation of a new solid phase with a lower degree of crystallinity due to solid dispersion

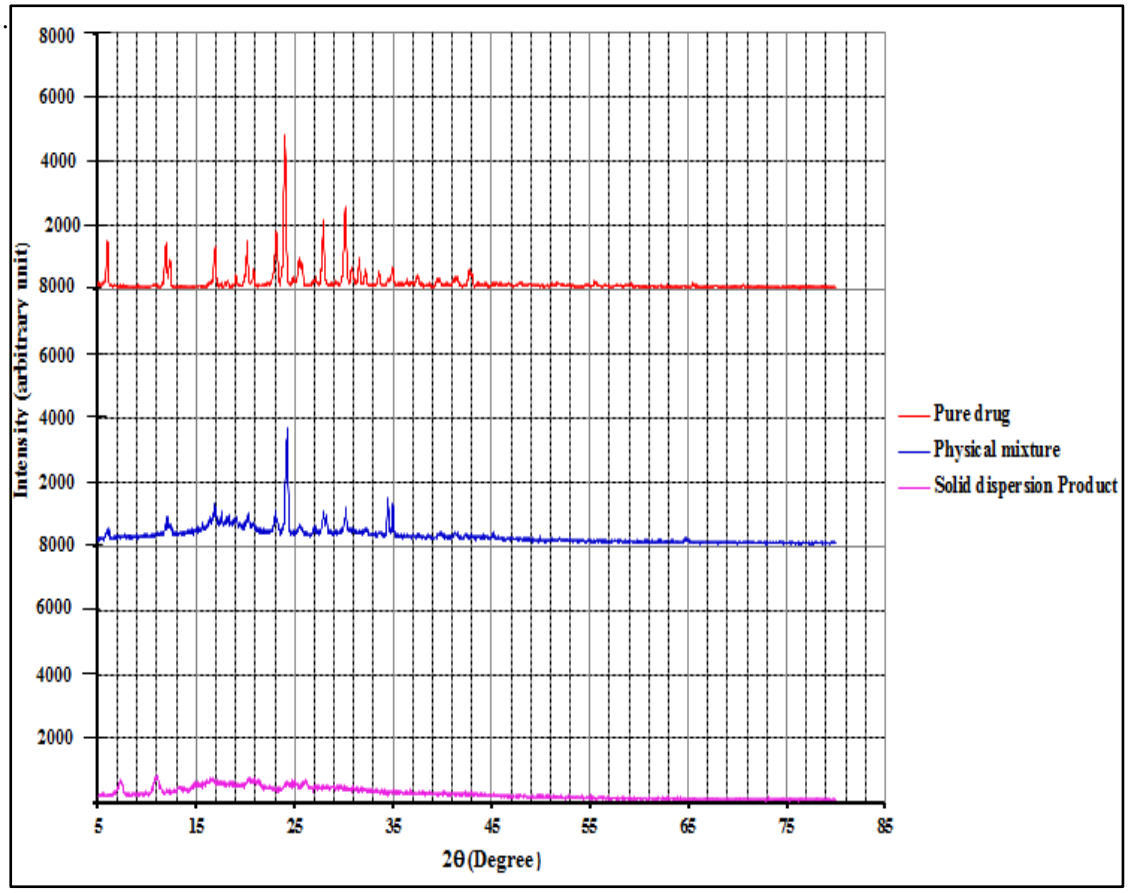

Figure: (5):X-Ray Diffraction Of Pure ONH , Physical Mixture , Solid Dispersion

Preparation of ONH FDTs

ONH solid dispersion prepared by solvent evaporation method with 1:2 drug: polymer ratio was incorporated in all formulas because it has the best drug content and complete taste masking (zero release in phosphate buffer pH (6.8) and all these formulas evaluated for their properties at pre- and post-compression stages.

Pre-compression evaluation of powder blend

It was found that the pre-compression parameters for the powder blend affected by the type and concentration of the diluent. F1 show fair flowability and fair compressibility which may be due to the effect of mannitol (diluent) which has poor flowability and compressibility therefore, Avicel PH 102 which has good flow properties and good compressibility due to its granular in nature was added to the other formulas as a trial to improve the flow property[21] .

Better flow properties were obtained as the concentration of Avicel PH102 was increased with in the formulas. Excellent flow properties resulted by the use of 30% Avicel PH102 (F4 to F7). All results are listed in table (4).

In addition to the effect of diluent; the presence of magnesium stearate and talc within the powder blend produce further improvement in its flowability.[22] .

Table (4): Pre-compression parameters for pure drug, solid dispersion and FDTs powder blend (mean ± SD) n=3.

Formulation code	Angle of repose	Carr's index	Hausner's Ratio	Flow character
Pure drug	32±0.5	23.2±1.8	1.29±0.04	Good and Passable
Solid dispersion	27.4±0.51	5.3±0.2	1.05±0.01	Excellent and Excellent
F1	41±1.82	21.2±0.72	1.26±0.015	Fair and Passable
F2	38±1	18.16±1.25	1.17±0.025	Fair and fair
F3	35.3±1.52	15.76±1.89	1.2±0.015	Good and fair
F4	29.3±0.77	9.5±0.5	1.07±0.011	Excellent and Excellent
F5	30.5±1.32	10±1.52	1.09±0.01	Excellent and Excellent
F6	31.3±2.08	9.46±1.85	1.09±0.01	Good and excellent
F7	29±1	8.13±1.05	1.06±0.015	Excellent and Excellent

Evaluation of FDTs

The formulas that pass pre-compression tests were compressed into tablets and evaluated for their hardness, friability, weight variation, *in –vitro* disintegration time, *in-vivo* disintegration time and dissolution.

Hardness and friability

All the prepared FDTs were within acceptable range of hardness (3.5±0.5-4.2±0.3) Kg/cm^2 and this is very important to resist breaking during handling, packaging and hard enough for fast disintegration in the mouth. [14, 23]

In addition the friability of all these prepared FDTs were within acceptable range less than (1%) as shown in table (5)

Weight variation

All prepared FDTs were within acceptable limit according to USP standards as shown in table (5).

Table (5): Hardness, Friability and weight variation for prepared ONH FDTs.

Properties / Formula No	Hardness (Kg/cm^2)	Friability (%)	Weight variation
F4	4±0.25	0.45	149.7±0.25
F5	3.5±0.5	0.659	150.2±0.35
F6	3.75±0.35	0.609	149.5±0.5
F7	4.2±0.3	0.3	150±0.45

In-vitro disintegration time for the prepared FDTs

The disintegration time of the prepared FDTs was directly related to the wetting time and significantly affected by the type and concentration of super dis integrant ($p<0.05$) as shown in table (6). F4 (3% CP) disintegrate with the shortest time (11±1seconds) in comparison with F5(3% CCS), F6(3% SSG); This short disintegration times of CP containing FDTs can be explained to be due to the properties of CP which has rapid capillary activity and pronounced hydration with little tendency to gel formation[24]. In addition CP is highly porous and this unique, porous nature facilitates wicking of liquid into the dosage systems and causes rapid disintegration [25].Further decrease in disintegration time to a more favorable value which is less than stated in USP for preparation of ONH fast dissolving tablet [14]. (7±1.5 seconds) was obtained by increasing the concentration of cross povidone to 4% (F7).

In-vivo disintegration time for the prepared FDTs

The results showed that there is high correlation between the *in-vitro* and *in-vivo* disintegration time, but in all cases the *in-vitro* disintegration time has lower values compare with that of *in-vivo* one, this is due to large volume of phosphate buffer pH 6.8 and the strong agitation used during the *in vitro* test. The correlation between wetting time, *in-vitro* and *in-vivo* disintegration time is illustrated in table (6).

Table (6): Disintegration time and wetting time of prepared ONH FDTs (mean± SD) n=3.

Formula code	*In-vitro* DT (sec.)	*In-vivo* DT (sec.)	Wetting time (sec.)
F4	11±1	15.3±0.577	24.3±2.51
F5	15.6±1.15	23.3±1.52	32.6±3.05
F6	20±2	32±2	40±3.6
F7	7±1.5	10.6±2.08	18.3±1.52

Drug content

All the prepared ONH fast dissolving tablets were within acceptable range of drug content according to USP standards (90 -110 %) [(14)] as shown in table (7).

Table (7): Drug content of prepared ONH FDTs.(mean ±SD)n=3.

Formula code	%Drug content
F4	97±0.5
F5	96±1.5
F6	95±1
F7	100±2

In vitro dissolution study

The prepared ONH FDTs disintegrate rapidly in the mouth. By swallowing the disintegrated fast dissolving tablets, the dissolution process completes in the stomach. Therefore, 0.1N HCl was used to study the dissolution and release profile of the ONH FDTs.

The time required for 80% of the drug to be released ($t_{80\%}$) from the tablets and percent drug dissolved in 2 minutes ($D_{2\ min\%)}$ is shown in table (8).

Once a tablet disintegrates, the solubility properties of the drug, either alone or assisted by other variables, determine the drug's subsequent dissolution rate and extent of release [(26)]

Table (8): *In-vitro* dissolution parameters of prepared ONH FDTs.

Formula no.	$t_{80\%}$ (min)	$D_{2\ min\ (\%)}$
F4	1.82	83
F5	3.12	70.3
F6	4.14	66.9
F7	1.29	93.4

Factors affecting the dissolution

Effect of type of superdisintegrant on release profile of drug

The effect of type of superdisintgrant was studied by comparing the release profile of F4,F5 and F6 containing the same concentration (3%) of CP, CCS and SSG respectively. and the results are shown in figure(6). Significant difference was obtained ($p<0.05$) by comparing $t_{80\%}$ min. and $D_{2min\%}$ of the above formulas. Fastest release was obtained with F4 (shortest t80% and highest $D_{2min\%)}$. This result is attributed to the characteristics of CP which absorbs a huge amount of water when exposed to dissolution medium and promote the disintegration of tablets, enhance the dispersibility of the drug particles which increase the dissolution rate of the drug [(27)] .

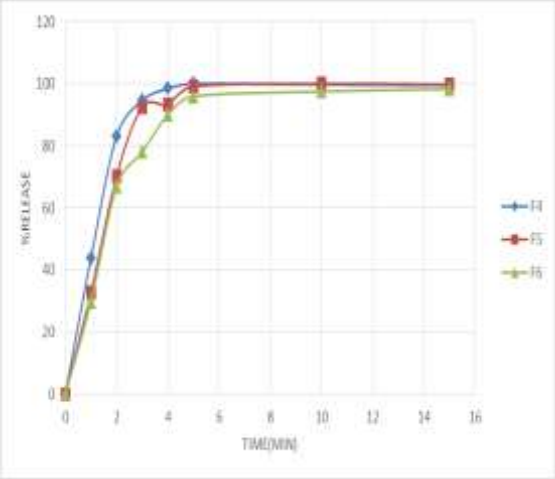

Figure (6): Effect of superdisintegrants type on release profile of ONH FDTs in 0.1NHCl at 37°C±0.5°.

Effect of superdisintegrant concentration on release profile

F4 and F7 were used to study the effect of the concentration of crospovidone on release of ONH from FDTs as shown in figure (7). Which contain 3%w/w and 4% w/w respectively, F7 show higher dissolution result than F4 [(28)].

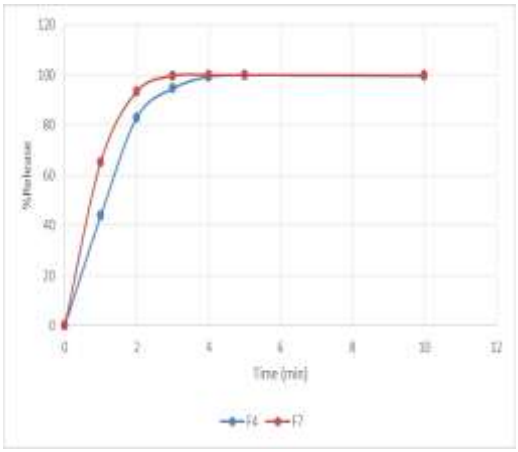

Figure (8): Effect of concentration of superdisintegrants on release of ONH from FDTs in 0.1N HCl at 37±0.5C°.

Selection of the best formula

According to the USP requirements; all the prepared tablets of F4-F7 were within the accepted limit regarding their dissolution results (not less than 80% of the drug is released within 10 minutes), but only F7 with shortest disintegration time (7 sec.)

Comply with the USP (disintegration time should be not more than 10 seconds). Therefore F7 was selected as the best formula for the preparation of ONH FDTs.

Conclusion

Taste masked ONH can be successfully prepared with the use of the solid dispersion techniques by solvent evaporation method using Eudragit E100 as a carrier in a ratio of 1:2 drug: polymer. FDTs of ONH with an acceptable taste and rapid disintegration in the mouth can be prepared by direct compression technique with 4% CP as a superdisintegrant to give the maximum drug release in minimum time.

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