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Original Article

DESIGN AND EVALUATION OF ATOMOXETINE HCl PELLETS BY MUPS TECHNOLOGY

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ABSTRACT

Objective: Atomoxetine HCl is extremely bitter in taste and is available as capsule dosage forms in various markets. In order to improve the pediatric compliance, the present study was aimed to mask the bitter taste of Atomoxetine HCl.

Methods: Bitter taste of Atomoxetine HCl was masked by multi-unit particulate pellet coating (MUPS) technology using Fluid Bed Processor in two step process. Initially drug layering was done on microcrystalline cellulose pellets followed by Polymer coating on drug layered pellets as Taste masking layer.

Results: Good efficiency of drug layering was observed with the combination of HPMC (Hydroxypropyl methyl cellulose) and HPC (Hydroxypropyl cellulose) as binders. Drug layered pellets were coated with different concentrations of Methacrylate Copolymer as Taste masking polymer. The prepared taste masked pellets were evaluated for taste and drug content. From the *In-vitro* and *In-vivo* taste evaluation, bitter taste of Atomoxetine HCl was masked with 25 mg of Eudragit EPO.

Conclusion: Bitter taste of Atomoxetine HCl was masked using Eudragit EPO with multi-unit particulate pellet (MUPS) technology using Fluid Bed Processor.

Keywords: Atomoxetine HCl, MUPS, Bitter taste, Taste masking, HPMC, HPC, Methacrylate Copolymer, Eudragit EPO.

INTRODUCTION

Even though, oral route is most easy and convenient for administration of various dosage forms; swallowing of solid dosage forms is a major difficult encountered with pediatric population because many children can not or will not swallow which leads to poor patient compliance.

This can be easily overcomed by designing as oral dissolving or disintegrating drug delivery systems. But most of the active pharmaceutical substances are either bitter in taste or can irritate the mouth and throat and thus becomes problematic even designed as pediatric convenient dosage forms [(1)]. In such cases, it is necessary to mask the unpleasant taste or odour of active ingredients.

Various taste masking technologies are available depend upon the bitterness intensity of active ingredients [(2)]. Atomoxetine HCl is the first non-stimulant drug approved by USFDA for the treatment of Attention-Deficit-Hyperactivity Disorder (ADHD) in children[(3)]. Currently Atomoxetine HCl is available as capsules and Tablets which are difficult to administer to pediatrics. Since the objective of the work is to design an orally disintegrating dosage form, the drug substance should not have any characteristic Taste and Odour.

Atomoxetine HCl is extremely bitter in taste and if we design it as orally disintegrating tablets, the drug gets disintegrate in the mouth and the patient can get the sense of bitterness. In the past studies a number of techniques were employed to mask the bitter taste of Atomoxetine HCl. But those techniques were not helpful in the masking the bitter taste of Atomoxetine HCl [(4)]. Hence in the present study an attempt was made to mask the bitter taste of Atomoxetine HCl by pellet coating using a suitable taste masking polymer with Fluid Bed Processor.

Eudragit EPO (exists as powder from) polymers which are basic Butylated Methacrylate Copolymers provides an excellent coating with taste masking properties for fine particles and tablets. These polymers provide taste masking films that are soluble below pH 5 and swellable and permeable above pH 5 and hence dissolve in the stomach, not in the mouth, due to the acid environment [(5)]. Films that are produced by Eudragit E types are sufficiently elastic and require no plasticizers[(6)].

MATERIALS AND METHODS

Materials

Atomoxetine HCl drug substance with two different particle sizes of 75µ and 150µ were procured as gift sample Aurobindo Pharma Limited, Hyderabad. Microcrystalline cellulose spheres (Nonpareil seeds) with the particle size of # 60/70 manufactured by Asahi Kasei were used as neutral pellets. Stearic acid (Vegetable grade) and Polyethylene glycol (Macrogol 6000) manufactured by Merck were used as Salt former and Plasticizer respectively. Hydroxypropyl methylcellulose (Hypromellose E5 Premium LV, Dow Chemical Company) and Hydroxypropyl Cellulose (Klucel LF Pharma, Hercules) were used as binders in drug layering process.

Low-Substituted Hydroxypropyl Cellulose (L-HPC LH 32, Nippon Soda Co., Ltd.) was used as Disintegrant in the formulation. Amino Methacrylate Copolymer (Eudragit EPO, Evonic Industries) and Sodium Lauryl Sulfate (Texapon K 12P PH, Cognis GmbH) were used as polymer and Emulsifier respectively during the taste masked layering. Talc (Luzenac Val Chisone) was used as anti adherent in drug layering and as anti tacking agent in taste masked layering process. FD&C Yellow No. 6 and FD&C Red No. 3 manufactured by Colorcon Asia Pvt. Ltd. were used as pigment. All the above excipients were kindly supplied by Aurobindo Pharma Limited, Hyderabad.

Methods

Evaluation of bitterness threshold of Atomoxetine HCl (7)

Threshold of bitterness concentration of Atomoxetine HCl was determined by a panel of six healthy human volunteers aged about 25 – 30 years. A known concentration of 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10 µg/ ml of Atomoxetine HCl were prepared in purified water. The volunteers were asked to hold 1 ml of each solution in oral cavity for 30 seconds and told them to give the bitterness ratings as 0, 1, 2 which indicate no bitter ness, bitter taste and extremely bitter taste respectively. Gargling the mouth with the purified water and a gap of

15 min was maintained between tasting of two successive concentrations of solutions.

Compatibility studies of Atomoxetine HCl with Eudragit EPO

Compatibility studies of physical mixtures of Atomoxetine HCl drug substance with Amino Methacrylate Copolymer (Eudragit EPO) was evaluated using Fourier transform infrared spectroscopy (Perkin-Elmer FT-IR spectrophotometer) and Differential scanning calorimeter (Universal V4. 7A TA Instruments).

Fourier Transform infrared spectroscopy (FTIR)

Accurately weighed 5 to 10 mg physical mixture of Atomoxetine HCl and Eudragit EPO sample was triturated with 300 to 400 mg of previously dried potassium bromide.

Triturated material was pressed in to pellet using 13 mm die in Hydraulic pellet press. FT-IR spectrum of Atomoxetine HCl was recorded between 650 and 4000cm-1 and background correction was done with plain KBr pellet.

Thermal properties by Differential-scanning calorimetry (DSC) of Atomoxetine HCl

DCS thermograms were obtained by placing the drug-excipient physical mixtures in an aluminium pan with holes, 50 µm, sealed and scanned from 30°C up to 200°C with an increment heating rates of 10°C/ min.

Preparation of taste masked particles

Fluidized Bed Processor (FBP) was used for the manufacturing of taste masked particles. The process of taste masking technique was done in the following steps

1) Drug layering on inert core pellets i.e. microcrystalline cellulose spheres

2) Polymer coating on the drug layered pellets as Taste masking layer

Drug layering on inert core pellets

Table 1 summarizes the various formulations used for the manufacturing of drug layered pellets with different grades of binders at various concentrations.

Table 1: Formulation of Drug layered pellets

Batch No.	ATX - 1	ATX - 2	ATX - 3	ATX - 4	ATX – 5
Ingredients	**Qty per unit (mg)**				
MCC spheres (# 60/80)	60.00	58.00	60.00	58.00	58.00
Atomoxetine HCl	25.00	25.00	25.00	25.00	25.00
Hydroxypropyl methylcellulose	5.00	7.00	--	--	3.50
Hydroxypropyl Cellulose	--	--	5.00	7.00	3.50
Low-Substituted Hydroxypropyl Cellulose	5.00	5.00	5.00	5.00	5.00
Talc	5.00	5.00	5.00	5.00	5.00
Purified Water	Qs	Qs	Qs	Qs	Qs
Total Wt. (mg)	**100.00**	**100.00**	**100.00**	**100.00**	**100.00**

Transferred required quantity of Purified water (18% w/w solids) into a suitable mixing vessel and Hydroxypropyl methylcellulose was added to the vortex under stirring and continued the stirring to dissolve completely. Hydroxypropyl Cellulose was added to the above solution and stirred for 10 minutes until clear solution formed. Low-Substituted Hydroxypropyl Cellulose and Talc were added to the solution under stirring and continued the stirring for 10 minutes. Atomoxetine HCl was added slowly under stirring and continued the stirring for 30 minutes and passed the dispersion through muslin cloth. Required quantity MCC neutral pellets were loaded into wurster column and sprayed the drug dispersion on to neutral pellets with an inlet temperature of 50° – 55°C and bed temperature of 35° – 40°C. After completion of spraying of drug dispersion, Drug coated pellets were dried for 15 minutes with low fluidization at a bed temperature of 40° – 45°C and the percentage yield and also fines generation were checked.

Polymer coating on the drug layered pellets (Taste masking layer)

Drug layered pellets were coated with different concentrations of taste masked polymeric material of Amino Methacrylate Copolymer (Eudragit EPO) as shown in the Table 2.

Sodium Lauryl Sulfate (10% w/w to the dry polymer weight) was added to the vortex of purified water under stirring to get clear solution. Stearic acid (15% w/w to the dry polymer weight) was added under stirring and continued the stirring for 10 minutes. Eudragit EPO was added to the above solution under stirring and continued the stirring for 2 hour till a translucent colloidal suspension was formed (Immediately after adding Eudragit, the polymer gets hydrated and viscosity of the suspension was increased. After the stirring was done for 2 hour, viscosity of the solution was decreased and a translucent colloidal suspension was formed).

Talc (25% w/w to the dry polymer weight), FD&C Yellow No. 6 and FD&C Red No. 3 were added to the solution and kept the suspension for stirring for 30 minutes and passed the suspension through muslin cloth. Drug layered pellets were loaded into wurster column and preheated the pellets at 30°C. Sprayed Eudragit EPO suspension on to the drug layered pellets with an inlet temperature of 40° – 45°C and bed temperature of 25° – 30°C. After completion of spraying the suspension, taste masked pellets were dried for 15 minutes with low fluidization at a bed temperature of 40° – 45°C and the percentage yield and also fines generation were checked.

Table 2: Formulation of Polymer coated pellets

Batch No.	ATX - 6	ATX - 7	ATX - 8	ATX - 9
Ingredients	**Qty per unit (mg)**			
Drug Layered pellets	100.00	100.00	100.00	100.00
Eudragit EPO	6.25	12.5	18.75	25.00
Sodium Lauryl Sulfate	0.625	1.25	1.875	2.500
Stearic acid	0.938	1.875	2.813	3.750
Talc	1.563	3.125	4.688	6.25
FD&C Yellow No. 6	0.50	0.50	0.50	0.50
FD&C Red No. 3	0.05	0.05	0.05	0.05
Purified Water	Qs	Qs	Qs	Qs
Total weight (mg)	**109.926**	**119.300**	**128.676**	**138.050**

Taste Evaluation of Taste masked pellets

In-vitro Taste evaluation

In-vitro taste evaluation of Taste masked pellets of Atomoxetine HCl was done by spectrophotometrically. Taste masked pellets equivalent to 25 mg of Atomoxetine HCl were placed in 25 ml volumetric flask containing 6.8 pH phosphate buffer and kept on vibration for 10, 20, 30, 60, 90 and 120 sec respectively. The mixture of the solution was filtered through 0.45µ filter and the filtrate was analyzed for the content of Atomoxetine HCl at 270 nm using UV-Visible spectrophotometer.

In-vivo Taste evaluation

In-vivo taste evaluation of Taste masked pellets of Atomoxetine HCl was done using time intensity method on 6 healthy human volunteers aged about 25 – 30 years. Taste masked pellets equivalent to 25 mg of Atomoxetine HCl was held in the mouth for 10, 30 and 45 sec and told them to give the bitterness ratings as 0, 1, 2 and 3 which indicate no bitter ness, slightly bitter taste, bitter taste and extremely bitter taste respectively. Gargling the mouth with the purified water and a gap of 15 min was maintained between tasting of two successive formulations.

Characterization of Taste masked pellets

Shape and Surface morphology

Shape and surface characteristics of drug coated pellets and taste masked pellets were sputtered with gold palladium and then observed with a scanning electron microscope (SEM) Philips ESEM XL 30 FEG at a voltage of 5 and 10 KV.

Particle Size distribution

Particle size distribution of taste masked pellets was determined by sieve analysis; using a Retsch sieve analyzer equipped with 850, 600, 425, 250 and 180 µm sieves. Accurately weighed 25g of taste masked pellets were kept on top of the sieve and shaked for 10 minutes. The material left on each sieve was weighed and determined the distribution of quantity versus sieve size.

Drug content

Content of Atomoxetine HCl in taste masked pellets was determined by UV/VIS spectrophotometer. Taste masked pellets equivalent to 100 mg of Atomoxetine HCl were weighed and transferred to 1000 ml volumetric flask. 0.1N HCl was added to the half of the volumetric flask and kept the mixture for sonication for 30 minutes, and then filled up to the volume of 1000 ml with 0.1N HCl. The solution was filtered through 0.45µ filter paper and content of Atomoxetine HCl in the filtrate was determined spectrophotometrically at 270 nm.

RESULTS AND DISCUSSION

Threshold bitterness of aqueous solution of Atomoxetine HCl was given in the Table 3. All the volunteers could not recognize the bitter taste of Atomoxetine HCl upto the concentration of 5 µg/ ml. Two out of six volunteers felt perception of bitter taste at 6 µg/ ml, whereas all the volunteers felt bitter taste from 7 µg/ ml. Thus, the threshold bitterness of Atomoxetine HCl is 6 µg/ ml.

Table 3: Bitter intensity of aqueous solutions of Atomoxetine HCl

Concentration of drug solution (µg/ ml)	Bitter intensity ratings
1	No Bitterness
2	No Bitterness
3	No Bitterness
4	No Bitterness
5	No Bitterness
6	Bitterness
7	Extremely Bitter
8	Extremely Bitter
9	Extremely Bitter
10	Extremely Bitter

Compatibility studies

Chemical compatibility of Atomoxetine HCl with Eudragit EPO at 1:1 ratio were studied using FTIR spectroscopy and DSC thermogram as shown in Figure 1 and figure 2 respectively. The characteristic absorption peaks with FTIR spectroscopy were observed at 2954, 2873, 2821, 2769, 1730, 1600, 1487, 1456, 1388, 1359, 1271, 1242, 1147, 1062, 1043, 1016, 991, 966, 848, 931, 883, 819, 469, 754, 704 and 522 cm–1. These characteristic peaks were also present in the individual FT-IR spectra's of Atomoxetine HCl and Eudragit EPO but with reduced intensity. The DSC thermogram of pure Atomoxetine HCl and Eudragit EPO (figure2) showed a sharp endothermic peak at 168.18°C and 61.60°C respectively. Where as in physical mixtures, Atomoxetine HCl exhibited endothermic peaks ranging from 165.89°C (Figure 2) corresponding to the melting points of the drug. Based on the results of FTIR and DSC studies, it may be concluded that there was no interaction between the drug and the polymer used in this study

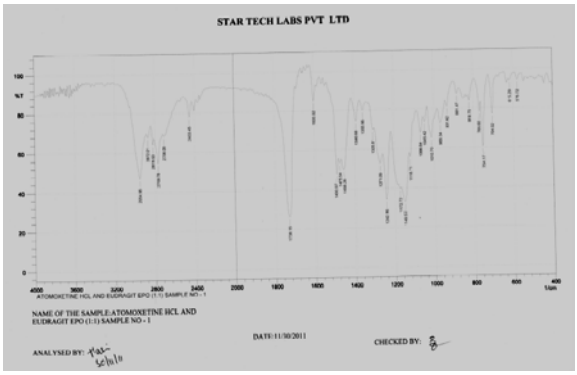

Fig.1: FTIR spectrum of physical mixture of Atomoxetine HCl + Eudragit EPO

Selection of Neutral Pellets

Morphology, porosity and particle size of neutral pellets plays an important role in the process of pellet coating. From the SEM pictures of microcrystalline cellulose (Figure 3) and Sugar pellets (Figure 4), it was observed that MCC pellets are smoother than the sugar pellets and also Sugar pellets are having more porous surface which is critical in aqueous coating processes. On the other hand Sugar pellets are more sensitive to aqueous-based drug layering for which a lower spray rates had to be applied until the first layer was formed since pellets become sticky and also tend to have greater attrition and agglomeration during the production process. MCC beads are insoluble in most organic solvents and in water, offering the advantage of aqueous-based drug layering. The size of neutral pellets influences the segregation of pellets when mixed with extra granular materials and also affects the compaction properties when designed as Multi unit Particulate Systems (MUPS). Hence MCC pellets with a grade of #60/80 mesh with a particle size of 180 to 250 µm were selected for drug layering process.

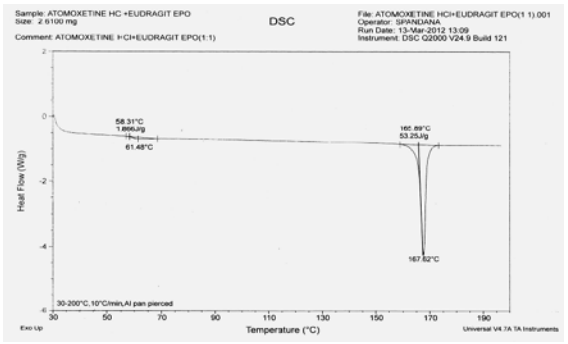

Fig. 2: DSC thermogram of physical mixture of Atomoxetine HCl and Eudragit EPO

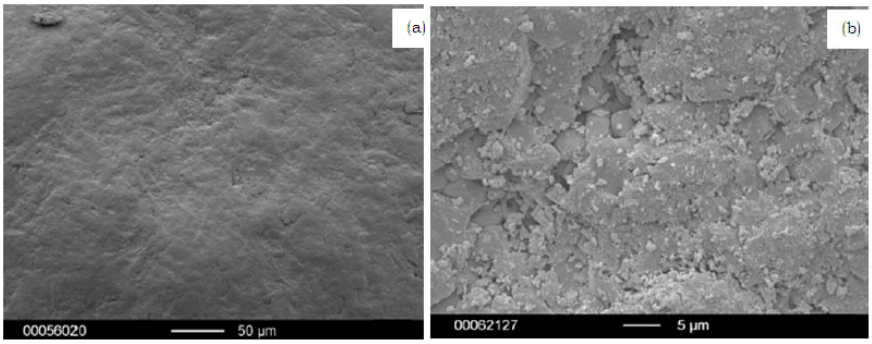

Fig. 3: SEM pictures of a) MCC pellets and b) Sugar pellets

Drug layering on inert core pellets

As shown in Table 4, when Hydroxypropyl methylcellulose and Hydroxypropyl cellulose alone were used at the concentration of 5% w/w, more fines were obtained which results in poor coating efficiency. To improve the coating efficiency, concentration of Hydroxypropyl methylcellulose and Hydroxypropyl cellulose was increased to 7% w/w.

Though yield was good with the increased concentration, more fines were observed. Where as with the combination of Hydroxypropyl methylcellulose (3.5% w/w) and Hydroxypropyl Cellulose (3.5% w/w), no fines were obtained and also a high coating efficiency was observed.

Polymer coating on drug layered pellets (Taste masking layer)

From the results as shown in Table 5, it was observed that even though Eudragit EPO polymer produces sufficiently elastic films, fines generation during the process were observed with 6.25 mg of Eudragit EPO polymer and gradually decreased with increasing concentration of polymer and coating efficiency was good for all the formulations.

Taste Evaluation

***In-Vitro* Taste evaluation**

The following results of Table 6 shows the concentration of Atomoxetine HCl released from Taste masked pellets at different time intervals.

Table 4: Coating efficiency in drug layering process

Batch No.	**ATX - 1**	**ATX - 2**	**ATX - 3**	**ATX - 4**	**ATX - 5**
Binder concentration	**HPMC – 5% w/w**	**HPMC – 7% w/w**	**HPC – 5% w/w**	**HPC- 7% w/w**	**HPMC – 3.5% w/w HPC – 3.5% w/w**
Batch Size (gm)	420.00	420.00	420.0	420.00	420.00
Practical yield (gm)	384.30	394.80	390.70	398.20	414.80
Yield (%)	91.50	94.00	93.02	94.81	98.76
% Pellets	64.48	82.13	88.50	92.30	97.50
% Fines	35.52	17.87	11.50	7.70	2.50

Table 5: Coating efficiency in Polymer coating on drug layered pellets

Batch No.	**ATX – 6**	**ATX – 7**	**ATX – 8**	**ATX – 9**
Drug: Eudragit EPO	**1: 0.25**	**1: 0.5**	**1: 0.75**	**1: 1**
Amount of Eudragit EPO (mg)	**6.25**	**12.50**	**18.75**	**25.00**
Batch Size (gm)	350.00	350.00	350.00	350.00
Practical yield (gm)	339.00	333.45	341.43	337.05
Yield (%)	96.86	95.27	97.55	96.30
% Pellets	92.17	94.45	94.47	95.62
% Fines	5.48	3.15	2.45	1.08
% Twins	2.35	2.40	3.08	3.30

Table 6: Content of Atomoxetine HCl released at different time intervals

Batch No.	**ATX – 6**	**ATX – 7**	**ATX – 8**	**ATX – 9**
Shaking time (sec)		**Content of Atomoxetine HCl released (µg/ ml)**		
10	10.685	7.537	1.611	0.000
20	14.759	10.870	2.537	0.000
30	20.685	16.241	4.574	0.315
60	24.024	18.833	6.796	1.611

Table 7: *In -Vitro* Bitterness Threshold of Taste masked pellets

Batch No.	**ATX – 6**	**ATX – 7**	**ATX – 8**	**ATX – 9**
Shaking time (sec)	**Bitterness Threshold**			
10	Extremely Bitter	Extremely Bitter	No Bitter	No Bitter
20	Extremely Bitter	Extremely Bitter	No Bitter	No Bitter
30	Extremely Bitter	Extremely Bitter	No Bitter	No Bitter
60	Extremely Bitter	Extremely Bitter	Extremely Bitter	No Bitter

The release of Atomoxetine HCl from Taste masked pellets which were coated with 6.25 mg and 12.5 mg of Eudragit EPO was above the threshold bitterness value i. e 7 µg/ ml, where as drug release from Taste masked pellets coated with 18.75 mg was less than threshold bitterness value up to 30 sec of shaking time and there after increased. When drug layered pellets were coated with 25 mg of Eudragit EPO, release of Atomoxetine HCl was below the threshold bitterness value even after 60 sec shaking time.

***In-Vivo* Taste evaluation**

The following results showed taste intensities taste masked pellets of Atomoxetine HCl in healthy human volunteers.

Table 8: *In-Vivo* Taste evaluation in healthy human volunteers

Batch No.	ATX - 6	ATX - 7	ATX – 8	ATX - 9
Drug: Eudragit EPO	**1: 0.25**	**1: 0.5**	**1: 0.75**	**1: 1**
Amount of Eudragit EPO (mg)	**6.25**	**12.50**	**18.75**	**25.00**
Subject 1	Extremely Bitter	Extremely Bitter	No Bitter	No Bitter
Subject 2	Extremely Bitter	Bitter	Slightly Bitter	No Bitter
Subject 3	Extremely Bitter	Extremely Bitter	Slightly Bitter	No Bitter
Subject 4	Extremely Bitter	Bitter	Bitter	No Bitter
Subject 5	Extremely Bitter	Extremely Bitter	No Bitter	No Bitter
Subject 6	Extremely Bitter	Extremely Bitter	No Bitter	No Bitter

All the volunteers felt bitter taste when the drug layered pellets were coated with 6.25 mg of Eudragit EPO.

Whereas in the pellets coated with 12.5 and 18.75 mg of Eudragit EPO, bitter taste was masked upto 15 sec after keeping the tablet in the mouth, and later all the human volunteers felt bitter taste.

When the concentration of Eudragit EPO was increased to 25 mg, Bitter taste of Atomoxetine HCl was completely masked and no volunteer was felt bitter taste.

From SEM pictures of Taste masked pellets (Figure 4 and 5); Drug layered pellets coated with 25 mg of Eudragit EPO appeared smooth and continuous, constituting as a barrier for bitter taste drug layered pellet. In contrast, Drug layered pellet coated with 18.75 mg Eudragit EPO, the film appeared discontinuous and uneven, suggesting that taste mask layering might not be sufficient.

Table 9 summarizes the particle size distribution of Taste masked pellets coated with 25 mg of Eudragit EPO. Most of the Taste masked pellets were ranged between 180 and 250 µm in size.

Characterization of Taste masked Pellets

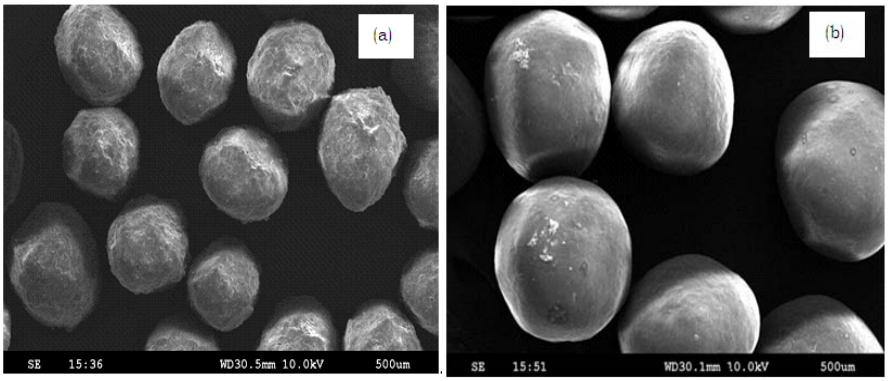

Fig. 4: SEM pictures of Taste masked pellets with a) 18.75 mg and b) 25 mg Eudragit EPO

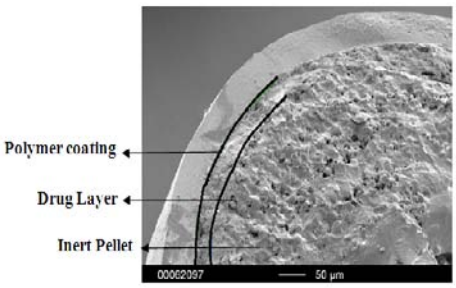

Fig. 5: SEM picture of cross section of a Taste masked pellets coated with 25 mg Eudragit EPO

Drug Content

The percentage content of Atomoxetine HCl in Taste masked pellets was determined by UV-Visible spectrophotometer and the results are presented in Table 10.

Table 9: Particle size distribution of Taste masked pellets

Sieve No.	Mesh size (µm)	Qty of pellets retained (gm)	% Retained	Cumulative % retained
# 30	600	0.00	0.00	0.00
# 40	425	0.00	0.00	0.00
# 60	250	3.42	13.68	13.68
# 80	180	21.58	86.32	86.32
Pan	--	0.00	0.00	0.00

Table 10: Content of Atomoxetine HCl in Taste masked pellets

Batch No.	Concentration (µg/ ml)	Content in mg	% Drug content
ATX – 6	85.836	21.459	85.836 ± 3.45
ATX – 7	88.927	22.232	88.927 ± 1.24
ATX – 8	98.200	24.55	98.200 ± 2.45
ATX – 9	100.564	25.141	100.564 ±1.66

From the above results it can be concluded that content of Atomoxetine HCl in taste masked pellets manufactured with 6.25 mg (Batch No. ATX-6) and 12.5 mg (Batch No. ATX-7) Eudragit EPO is on lower side because of more fines formation.

Where as the taste masked pellets manufactured with 18.75 mg and 25.00 mg of Eudragit EPO, coating efficiency was good which results in 100% drug content.

Effect of Particle size of Atomoxetine HCl in pellet coating

Shape, morphology and particle size of drug substance are an important considerations in the drug layering particularly in pellet coating process. The effect of particle size of Atomoxetine HCl on drug layering process was evaluated using different particle sizes 1) 50% particles are having less than 150 µm and 2) 50% particles are having less than 75µm.

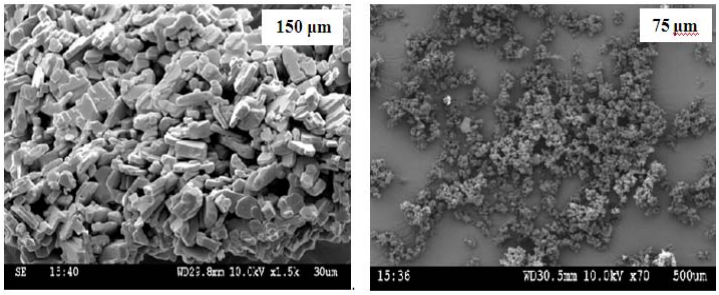

Fig. 6: SEM pictures of Atomoxetine HCl with different particle sizes

From the SEM pictures of Figure 6, Atomoxetine HCl drug substance with particle size of less than 150 µm exists as rod like crystals whereas when the particle size is less than 75 µm no rod shape were seen.

Following SEM pictures (Figure 7) depicts the surface characteristics of drug layered pellets manufactured with non-micronized (150 µm) and micronized (75 µm) Atomoxetine HCl drug substance.

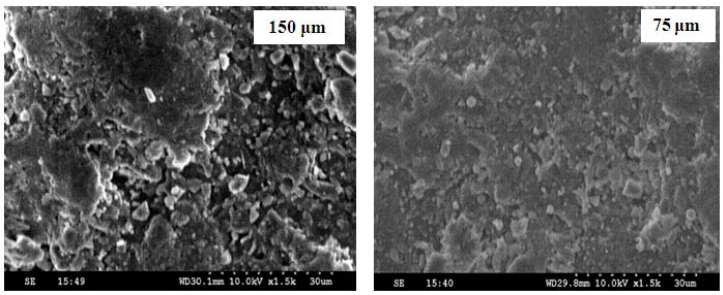

Fig. 7: SEM pictures of drug layered pellets with a) 150 µm and b) 75 µm Atomoxetine HCl

When non-micronized Atomoxetine HCl drug substance was used for drug layering, un uniform distribution of drug solution was observed which results in a rough and porous surface on the drug layered pellets. Since the surfaces of rough and porous drug coated pellets were not completely coated with Eudragit EPO polymer, the taste of Atomoxetine HCl might not be masked sufficiently. Therefore micronization of Atomoxetine HCl was deemed to be necessary for the drug layering process.

CONCLUSION

When Hydroxypropyl methylcellulose and Hydroxypropyl cellulose were used as binders individually, more fines were observed and also coating efficiency was poor in drug layering process. Whereas with the combination of both the binders, good coating efficiency was observed. Eudragit EPO polymer produces sufficiently elastic films on drug layered pellets and the bitterness threshold decreased with increasing the concentration of polymer. Eudragit EPO as a polymer was proven to mask the bitterness of Atomoxetine HCl at a concentration of 25 mg. The size of the taste masked pellets was no more than 250 µm, which means that no gritty feeling of particles in patient's mouth. These results indicated that the fluidized bed process produced the most appropriate taste masked pellets of Atomoxetine HCl for oral disintegrating tablets.

CONFLICT OF INTERESTS

Declared None

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