FORMULATION AND EVALUATION OF TASTE MASKED ORODISPERSIBLE TABLETS OF AMLODIPINE BESYLATE BY DIRECT COMPRESSION

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ABSTRACT

The purpose of this investigation was undertaken to design a simple, rapid, cost effective and highly efficient process to fabricate intensely bitter taste of Amlodipine Besylate by complexing drug with Aminoalkyl methacrylate copolymer (Eudragit EPO) in different ratios by Hot-Melt Extrusion method. Taste masked complex were analyzed with FTIR, DSC and XRD. DCP were tested for Hardness, Thickness, Weight Variation, Drug Content, Water absorption and *In vitro* Dispersion Test in Simulated Salivary Fluid pH 6.8. Taste masked granules were directly compressed into tablets using Kollodion CL and Croscarmellose Sodium (Ac-Di-Sol) as superdisintegrants. Tablets of batch F₆ containing mannitol and 6% wt/wt of Kollodion CL showed faster disintegration with in 24 sec and drug release (t₉₀, 180sec) at Phosphate Buffer pH 6.8. The observed polymer interaction and reduced crystallinity may be reason for increased dissolution rate. Thus results conclusively demonstrate successful masking of taste, disintegration and dissolution of the formulated tablets.

Keywords: Drug Polymer Complex, Hot Extrusion Method, Amlodipine Besylate, Kollodion CL, Croscarmellose Sodium, Oro Dispersible Tablets.

INTRODUCTION

Recent advances in novel drug-delivery system aims to enhance the safety and efficacy of the drug molecule by formulating a dosage form being convenient for the administration. Difficulty in swallowing (i.e. dysphagia) is experienced by patients such as paediatrics, geriatric, bedridden, disabled, mentally ill, including motion sickness and sudden episodes of allergic attacks, hence resulting in higher incidence of noncompliance and ineffective therapy¹. In order to solve this problem and improve patient acceptance and compliance, the development of solid dosage forms that disintegrate rapidly or dissolve even when taken orally without water is being undertaken. oral route of drug administration have wide acceptance, up to 50-60% of solid dosage forms are popular because of natural, uncomplicated, convenient, ease of administration, accurate dosage, self-medication, pain avoidance and most importantly patient compliance. The most popular solid dosage forms being tablets and capsules, one important drawback of these dosage forms for patient is the difficulty to swallow. Swallowing of solid dosage forms like tablets and capsules and improper dosing of suspension and emulsion may produce difficulty for young children because of incomplete development of muscular and nervous system and elderly patients suffering from dysphasia, Parkinson's disorder and tremor. Other groups that may experience problems using conventional oral dosage forms include the mentally ill, the developmentally disabled patients, patients who are uncooperative, or on reduced liquid intake plans or nauseated, patients having a persistent cough or a gag-reflex and travellers who may not have access to water². Oral fast-disintegrating dosage forms (tablet or a capsule) are a relatively novel dosage technology that involves the rapid disintegration or dissolution of the dosage form into a solution or suspension in the mouth without the need for water³⁻⁵. The dosage form begins to disintegrate immediately after coming into contact with saliva, with complete disintegration normally occurring within 30-50 s after administration⁶. The solution containing

the active ingredients is swallowed and the active ingredients are then absorbed through the gastrointestinal epithelium to reach the target and produce the desired effect. Tablet is the most widely used dosage form because of its convenience in terms of self-administration, compactness and ease in manufacturing⁷. Orally disintegrating tablets are also called as Orodispersible tablets, quick-disintegrating tablets, mouth-dissolving tablets, fast-disintegrating tablets, fast dissolving tablets, rapid-dissolving tablets, porous tablets and rapid melts. However, of all the above terms, the United States Pharmacopoeia (USP) approved these dosage forms as Orodispersible tablets (ODTs). Recently, the European Pharmacopoeia has used the term Orodispersible tablets for tablets that disperse readily and within 3 min in the mouth before swallowing. The United States Food and Drug Administration define ODT as “a solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue.” The disintegration time for ODTs generally ranges from several seconds to about a minute⁸. Other advantages of ODTs that have been investigated are their potential to increase the bioavailability of poorly water soluble drug through enhancing the dissolution profile of the drug⁹. Moreover, pharmaceutical companies also have commercial reasons for formulating ODTs. As a drug reaches the end of its patent, the development and formulation of the drug into new dosage forms allow pharmaceutical companies to extend the patent life and “market exclusivity”¹⁰. The ODTs could be prepared using various techniques such as tablet moulding, spray drying, sublimation, lyophilization, solid dispersion, or addition of disintegrants¹¹⁻¹⁵. The basic approach to the development of ODTs is the use of superdisintegrants such as Croscarmellose sodium and sodium starch glycolate. Another approach used in developing ODTs is maximizing the pore structure of the tablet matrix. Freeze drying and vacuum drying techniques have been tried by researchers to maximize the pore structure of the tablet matrix¹⁶⁻¹⁸. However, freeze drying is

cumbersome and yields a fragile and hygroscopic product. Vacuum drying along with the sublimation of volatilizable ingredient has been employed to increase tablet porosity. While in designing dispersible tablets, it is possible to achieve effective taste masking as well as a pleasant feel in the mouth. The main criterion for ODTs is the ability to disintegrate or dissolve rapidly in saliva of the oral cavity in 15 to 60 s and have a pleasant mouth feel. To improve the quality of life and treatment compliance, great efforts have been made to develop fast-disintegrating tablets (FDTs) in the oral cavity, using jelly, water-absorbing and swelling-gelated materials or water-soluble polymers¹⁹. However, of all the above terms, United States pharmacopoeia (USP) approved these dosage forms as ODTs. Recently, European Pharmacopoeia has used the term Orodispersible tablet for tablets that disperses readily and within 3 min in mouth before swallowing. United States Food and Drug Administration (FDA) defined ODT as "A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue." The disintegration time for ODTs generally ranges from several seconds to about a minute²⁰.

MATERIALS

Amlodipine Besylate was chosen as an active ingredient and it was gift sample from Dr. Reddy's Laboratories, Hyderabad, Andhra Pradesh, India. Eudragit EPO, Mannitol, Kollidon CL, Croscarmellose Sodium, Aspartame and Magnesium stearate were purchased from colorcon, Mumbai, India. All other reagents were of analytical grade.

METHOD

Preparation of Drug - Polymer Complex

The drug polymer complex (DPC) was prepared by Hot-melt Extrusion using different ratio of Amlodipine Besylate and Eudragit EPO (1:1 and 1:2). Initially, Amlodipine Besylate is passed through #60 sieves. Later Eudragit EPO is melted at a temperature of 100 °C. After the complete melting of polymer the drug is incorporated slowly with continuous stirring. Then after uniform mixing the mixture is cooled, finely grounded and passed through #30 sieve followed by passing through # 60 sieves.

Formulation of Oral Dispersible Tablets

Oral dispersible tablets were prepared by Direct Compression Method. Initially, Amlodipine Besylate and Drug Polymer complex is weighed individually for each formulation. Kollidon CL, Cross carmellose sodium, Mannitol, Aspartame is passed through sieve No. 60 and individually weighed for each formulation (Table 1). These are mixed with DPC on polyethylene paper. Similarly, Aerosil and Magnesium stearate are individually passed through sieve No. 60 and individual quantities are weighed and mixed thoroughly with the above mixture and finely mixed for 10 Minutes. The mixed blend was punched into individual biconvex tablets weighing 100 mg on a multi punch tablet machine using 6 mm punch for compression. 20 tablets were punched of each formulation. Similarly, blank tablets without containing Eudragit EPO are weighed and punched as per formulation FB6 and SB6.

Evaluation

Characterization of drug-polymer complex

Fourier Transform Infrared (FTIR) Spectroscopy

FTIR spectra were obtained on Shimadzu FTIR Model 8400-S spectrometer. The Spectra was recorded as a dispersion of the sample in Potassium Bromide in IR disk (2 mg sample in 200 mg KBr) with the scanning range of 400 to 4000 cm⁻¹ and the resolution was 1 cm⁻¹.

X-Ray Diffraction (XRD) Studies

X-ray Diffraction analysis was carried out to evaluate the degree of crystallinity. The pure Amlodipine Besylate, pure Eudragit EPO, and drug polymer complex (1:1) were subjected to powder XRD (P.W. 1729, X-Ray Generator, Philips, Netherland) at 2θ angles between 20 and 38° in increments of 0.40²¹.

Drug Content

DPC equivalent to 10 mg of drug was stirred by using magnetic stirrer with 100 ml of Methanol for 60 minutes, till the entire drug leached out from complex, then the solution was filter through whatman filter paper. Further solution was diluted with methanol and the drug content was determined spectrophotometrically at 239 nm²¹.

Characeterization of Powder Blend

Angle of Repose

Angle of repose was determined using funnel method. The blend was poured through a funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and angle of repose (θ) was calculated using the following formula²²⁻²⁴,

$$\tan\theta = h/r$$

Bulk Density

Apparent bulk density (pb) was determined by pouring the blend into a graduated cylinder. The bulk volume (Vb) and weight of the powder (M) was determined. The bulk density (pb) was calculated using following formula,

$$pb = Vb/M$$

Tapped Density

The measuring cylinder containing a known mass of blend (M) was tapped for a fixed time (100 tapings). The minimum volume (Vt) occupied in the cylinder and weight of the blend was measured. The tapped density (pt) was calculated using following formula,

$$pt = Vt/M$$

Compressibility Index

The simplest method of measurement of free flow of powder is compressibility, an indication of the ease with which material can be induced to flow and is given by compressibility index (I) which is calculated as follows,

$$I = \{(pt - pb)/pt\} * 100$$

The value below 15% indicates a powder which usually gives rise to excellent flow characteristics, whereas above 25% indicate poor flow ability.

Hausner's Ratio (H)

This is an indirect index of ease of powder flow. It is calculated by the following formula,

$$H = pt/pb$$

Lower Hausner's ratio (<1.25) indicates better flow properties than higher ones (>1.25).

Post Compression Evaluation

Uniformity of Weight

The test was carried out according to the US pharmacopoeia. 20 tablets, of each formulation were individually weighed and the mean of tablet weights was calculated. Results are presented as mean value²⁵⁻²⁸.

Hardness

The fracture strength, which is defined as the force required breaking a tablet by radial compression was measured with a tablet hardness tester²⁵⁻²⁸ (Monsanto hardness tester).

Friability

The friability of sample of six tablets were measured using a Roche Friabilator (Electrolab EF-2, USP). Six pre-weighed tablets were rotated at 25 rpm for 4 minutes. The tablets were then reweighed after removal of fine's using 60 mesh screens and the percentage of weight loss was calculated²⁵⁻²⁸.

$$\% \text{ Friability} = (\text{Loss in weight} / \text{Initial weight}) \times 100$$

Wetting Time

The wetting time of the tablets has been measured using a simple procedure. Five circular tissue papers of 10 cm diameter are placed in a petridish with a 10 cm diameter. Ten millimetres of water- containing Eosin, a water-soluble dye, is added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time²⁵⁻²⁸.

(%) Water Absorption Ratio

A piece of tissue paper folded twice was placed in a small petridish (Internal Diameter = 6.5 cm) containing 6 ml of water. A tablet was placed on the paper and the time required for complete wetting was then measured. The water absorption ratio (R) was determined using the following equation.²⁵⁻²⁸

$$R = 100 (W_a - W_b) / W_b$$

Where, W_b is the weight of the tablet before water absorption and W_a is the weight of the tablet after water absorption.

Figure 1

Content Uniformity

For the content uniformity test, ten tablets were weighed and pulverized to a fine powder, a quantity of powder equivalent to 10 mg of Amlodipine Besylate was extracted in 10 ml of methanol and liquid was filtered (0.22 μ m membrane filter disc (Millipore Corporation). The drug content was determined by measuring the absorbance at 239 nm (using UV Spectrophotometer, Shimadzu 1800) after appropriate

dilution with methanol. The drug content was determined using standard calibration curve. The mean percent drug content was calculated as an average of three determinations²⁵⁻²⁸.

Taste Evaluation

The objective of this study is to conduct and evaluate the Palatability of different formulations of Amlodipine Besylate oral disintegrating tablets. Amlodipine Besylate ODT was a new development; reference product is not available for ODT in market for this product for comparison of the taste evaluation. Total 16 formulations were selected for taste evaluation study, 14 test formulations (Table 1), one positive control (Placebo for Amlodipine Besylate) and one is negative control (Placebo for Taste enhancers like aspartame and peppermint flavour). All formulations (formulation code) were randomized. Each randomization order was assigned with sequence code. For this study were selected 6 healthy human volunteers 3 male and 3 Female of age around 21-22 years and were assigned volunteer code. All the 6 volunteers were evaluated all eight formulations as per the randomization order. Each of the formulations were transferred to HDPE bottles and labelled only with formulation code. Palatability evaluation feedback format prepared and submitted to each individual volunteer and were provided with instructions before starting study. One tablet of each formulation was given to volunteer for palatability study evaluation. The time interval between evaluations of each test formulation in the same volunteer was 30 min, at after evaluated each formulation, one half of a bread slice was given to each volunteer followed by half glass of water and cocoa powder for neutralizing the taste buds. After completion of the study, data was compiled and evaluated the formulations and allotted the rank for all formulation, based on the average value of the each formulation²⁹.

In vitro dispersion time (with simulated salivary fluid)

This test is performed to ensure disintegration of tablets in the salivary fluid, *In vitro* dispersion time was measured by dropping a tablet in a Petri dish containing 6ml of simulated salivary fluid of pH 6.8.²⁵⁻²⁸

In vitro Drug Release Study

In-vitro dissolution studies of the fast disintegrating tablets of Amlodipine Besylate formulation were performed according to USP XXIII Type-II dissolution apparatus (Electrolab, model TDT-06N) employing a paddle stirrer at 50 rpm using 900 ml of pH 6.8 phosphate buffer at $37 \pm 0.5^\circ\text{C}$ as dissolution medium. One tablet was used in each test. Aliquots of the dissolution medium (10 ml) were withdrawn at specific time intervals and replaced immediately with equal volume of fresh medium. The samples were analyzed for drug content by measuring the absorbance at 239 nm. Drug concentration was calculated from the standard calibration curve and expressed as cumulative percent drug dissolved²⁵⁻²⁸.

Statistical Analysis

The results were analyzed by two tailed Student's t-test using the Graph Pad Instat Software (GPIS; Version: 1.13)³⁰.

Table 1: Formulation of Amlodipine Besylate Orodispersible Tablets

Ingredients	F1	F2	F3	F4	F5	F6	FB6	S1	S2	S3	S4	S5	S6	SB6
Amlodipine Besylate	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Eudragit EPO	10	10	10	10	10	10	-	10	10	10	10	10	10	-
Kollidone CL	1	2	3	4	5	6	6	-	-	-	-	-	-	-
Croscarmellose sodium	-	-	-	-	-	-	-	1	2	3	4	5	6	6
Mannitol	77.8	76.8	75.8	74.8	73.8	72.8	71.8	77.8	76.8	75.8	74.8	73.8	72.8	83.8
Aspartame	-	-	-	-	-	-	4	-	-	-	-	-	-	4
Mg. Sterate	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Aerosil	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Total Weight	100	100	100	100	100	100	100	100	100	100	100	100	100	100

*Each value represents mean $\pm$ S.D (n=3).

Table 2: Characterisation of Powder Blend

Formulation	Angle of repose	Bulk Density	Tapped Density	Percent compressibility Index	Hausner's Ratio
F1	23.29 $\pm$ 0.01	0.51 $\pm$ 0.01	0.676 $\pm$ 0.01	23.71 $\pm$ 0.01	1.31 $\pm$ 0.01
F2	22.47 $\pm$ 0.02	0.45 $\pm$ 0.01	0.526 $\pm$ 0.01	14.41 $\pm$ 0.01	1.16 $\pm$ 0.01
F3	20.18 $\pm$ 0.01	0.45 $\pm$ 0.03	0.543 $\pm$ 0.04	15.6 $\pm$ 0.02	1.18 $\pm$ 0.01
F4	21.8 $\pm$ 0.03	0.49 $\pm$ 0.01	0.555 $\pm$ 0.01	11.76 $\pm$ 0.02	1.13 $\pm$ 0.02
F5	23.89 $\pm$ 0.01	0.43 $\pm$ 0.02	0.515 $\pm$ 0.03	16.38 $\pm$ 0.01	1.19 $\pm$ 0.01
F6	23.8 $\pm$ 0.02	0.41 $\pm$ 0.01	0.495 $\pm$ 0.01	15.83 $\pm$ 0.01	1.18 $\pm$ 0.02
S1	23.12 $\pm$ 0.02	0.43 $\pm$ 0.01	0.515 $\pm$ 0.02	14.91 $\pm$ 0.02	1.17 $\pm$ 0.01
S2	23.19 $\pm$ 0.02	0.46 $\pm$ 0.01	0.549 $\pm$ 0.01	15.74 $\pm$ 0.01	1.18 $\pm$ 0.02
S3	22.86 $\pm$ 0.03	0.43 $\pm$ 0.01	0.51 $\pm$ 0.01	14.03 $\pm$ 0.01	1.16 $\pm$ 0.01
S4	23.61 $\pm$ 0.01	0.44 $\pm$ 0.01	0.537 $\pm$ 0.03	16.96 $\pm$ 0.01	1.2 $\pm$ 0.01
S5	24.21 $\pm$ 0.02	0.42 $\pm$ 0.01	0.532 $\pm$ 0.01	19.66 $\pm$ 0.01	1.24 $\pm$ 0.01
S6	24.16 $\pm$ 0.03	0.42 $\pm$ 0.01	0.49 $\pm$ 0.01	14.29 $\pm$ 0.01	1.16 $\pm$ 0.01

*Each value represents mean $\pm$ S.D (n=3).

Table 3: Post Compression Parameters

Formulation	Hardness Kg/cm ²	Thickness mm	Friability %	Avg. Weight (mg)	Content uniformity (%)	Wetting time (sec)	In vitro Dispersion time (sec)	Water Absorption Ratio (%)
F1	3.25 $\pm$ 0.01	3.1 $\pm$ 0.01	0.64 $\pm$ 0.01	100.12 $\pm$ 0.03	98.19 $\pm$ 0.01	147 $\pm$ 0.02	167 $\pm$ 0.01	41.6 $\pm$ 0.01
F2	3.26 $\pm$ 0.01	3.0 $\pm$ 0.01	0.69 $\pm$ 0.01	99.32 $\pm$ 0.02	97.23 $\pm$ 0.01	113 $\pm$ 0.01	90 $\pm$ 0.02	53.8 $\pm$ 0.02
F3	3.24 $\pm$ 0.02	2.9 $\pm$ 0.02	0.79 $\pm$ 0.01	99.57 $\pm$ 0.01	97.76 $\pm$ 0.01	91 $\pm$ 0.01	79 $\pm$ 0.01	74.6 $\pm$ 0.01
F4	3.11 $\pm$ 0.02	3.0 $\pm$ 0.01	0.94 $\pm$ 0.01	98.97 $\pm$ 0.01	97.89 $\pm$ 0.04	76 $\pm$ 0.01	51 $\pm$ 0.01	74.3 $\pm$ 0.01
F5	3.06 $\pm$ 0.01	2.7 $\pm$ 0.02	0.89 $\pm$ 0.02	98.68 $\pm$ 0.03	97.26 $\pm$ 0.03	59 $\pm$ 0.02	32 $\pm$ 0.02	79.8 $\pm$ 0.04
F6	2.97 $\pm$ 0.01	2.8 $\pm$ 0.01	0.97 $\pm$ 0.03	97.93 $\pm$ 0.01	97.48 $\pm$ 0.02	45 $\pm$ 0.01	24 $\pm$ 0.01	80.9 $\pm$ 0.01
FB6	3.02 $\pm$ 0.03	3.0 $\pm$ 0.01	0.84 $\pm$ 0.02	98.62 $\pm$ 0.02	99.18 $\pm$ 0.02	48 $\pm$ 0.02	26 $\pm$ 0.03	79.6 $\pm$ 0.03
S1	3.12 $\pm$ 0.02	3.2 $\pm$ 0.01	0.91 $\pm$ 0.02	97.21 $\pm$ 0.01	97.42 $\pm$ 0.01	148 $\pm$ 0.01	185 $\pm$ 0.01	39.6 $\pm$ 0.02
S2	3.08 $\pm$ 0.01	3.1 $\pm$ 0.01	0.89 $\pm$ 0.01	98.65 $\pm$ 0.01	98.09 $\pm$ 0.01	104 $\pm$ 0.01	98 $\pm$ 0.04	47.2 $\pm$ 0.01
S3	3.02 $\pm$ 0.01	2.8 $\pm$ 0.02	0.99 $\pm$ 0.01	96.32 $\pm$ 0.01	97.86 $\pm$ 0.01	95 $\pm$ 0.01	80 $\pm$ 0.01	56.3 $\pm$ 0.01
S4	3.16 $\pm$ 0.02	2.9 $\pm$ 0.01	0.85 $\pm$ 0.01	98.59 $\pm$ 0.01	98.01 $\pm$ 0.01	82 $\pm$ 0.03	67 $\pm$ 0.03	69.4 $\pm$ 0.02
S5	3.13 $\pm$ 0.01	3.2 $\pm$ 0.01	0.74 $\pm$ 0.01	98.76 $\pm$ 0.01	97.61 $\pm$ 0.01	73 $\pm$ 0.01	49 $\pm$ 0.02	76.3 $\pm$ 0.01
S6	3.07 $\pm$ 0.01	3.1 $\pm$ 0.01	0.67 $\pm$ 0.01	98.94 $\pm$ 0.01	98.02 $\pm$ 0.01	51 $\pm$ 0.01	36 $\pm$ 0.01	78.5 $\pm$ 0.01
SB6	3.11 $\pm$ 0.01	3.3 $\pm$ 0.01	0.73 $\pm$ 0.01	98.75 $\pm$ 0.01	98.89 $\pm$ 0.01	53 $\pm$ 0.02	39 $\pm$ 0.01	77.4 $\pm$ 0.02

*Each value represents mean $\pm$ S.D (n=3).

Table 4: Evaluation of Taste Masking Effect of Orodispersible Formulations

Formulation Code	Average points by Volunteer	Acceptability	Rank
Negative control	99	Very Good	1
S6	90	Very good	2
F6	86	Very good	3
F5	84	Good	4
S4	83	Good	5
SB6	54	acceptable	6
Positive control	19	worst	7

After 5 Sec

After 25 Sec

After 45 Sec

Figures 2: Wetting Time of Formulation F₆

Figure 3: *In-vitro* Dispersion Time

Figure 4: *In-vitro* Dissolution Studies of Formulations

Figure 5: FTIR Spectroscopy of Pure Amlodipine Besylate Drug, F₆, S₆ Tablet Formulations

Pure Drug

Eudragit EPO

Eudragit EPO and D P C

Figure 6: X-Ray Diffraction Studies

Figure 7: Taste Masking Effect of Orodispersible Formulations

RESULTS

Pre compressional Parameters

Table 2 shows the pre-compressional parameters of power blend. There was change in angle of repose from F_1 to F_6 and from S_1 – S_6 . Angle of repose increased from 23.29 to 23.89 and 23.12 to 24.2 respectively. Bulk Density and Tapped Density of all formulations are shown in the Table 2. The results indicated that both densities range from 0.41 to 0.515 gm/cc and 0.49 to 0.676 gm/cc. % Compressibility ranges from 11.76 to 23.71 and 14.03 to 19.66% in Kollidon CL and Croscarmellose formulation respectively. All the formulations showed good and Fair flow properties.

Post Compressional Parameters

Hardness: Table 3 shows hardness of all tablet formulations. The results indicated that no such appreciable changes were

observed with respect to hardness in all formulations from F_1 to F_6 and from S_1 – S_6 .

% Friability: Table 3 shows the friability values of all tablet formulations. The results indicated that the % friability of formulation was between 0.64% and 0.97%. The low values of friability indicate that tablets were mechanically hard enough.

Thickness: Table 3 shows the thickness of all tablet formulations. The results indicated that the thickness of all formulations was between 3.45 to 3.95 mm.

Weight Variation Test: Table 3 shows the average weight of all table formulations. The results indicated that average

weight of all tablets formulations was between 96.32 to 100.12 mg.

% Water Absorption Ratio: Table 3 shows % water absorption ratio of all tablet formulation. The results indicated that formulation containing 1% Kollidon CL showed least water absorption. This may be due to less swelling property. % water absorption ratio increases from F1 to F6 and from S1 to S6 as the concentration of kollidon CL and croscarmellose increases in tablet formulations.

Wetting Time: Table 3 show wetting studies. The results revealed that wetting studies of formulations F₂ to F₆ were significantly lower ($p < 0.05$) than F₁ (Figure 4a, 4b and 4c). Similarly wetting time of formulation S₂ to S₆ were significantly lower ($p < 0.05$) than S₁ (Figure 2). It may be because capillary action was higher in all formulations F1 to F6 and from S1 to S6 which absorbs water in higher amounts as concentrations Kollidon CL and Croscarmellose increases.

Drug Content of Tablets: Drug Content of tablets ranged between 97.23 to 99.18%. Results are shown in Table 3.

In-vitro Dispersion Time: The *in-vitro* dispersion times of formulations were in the range of 185-23 sec. Here we could clearly observe the effect of the concentration of the Kollidon CL and Croscarmellose Sodium concentration, as the concentration increased the dispersion time decreased. The concentration above 3% showed very good results in Kollidon CL formulation and above 4% concentration in Croscarmellose sodium. And the formulations F4-F6 and S5-S6 showed promising results for the ODT and at the same time the dispersion time of formulations is not effected by polymer complexation when compared with SB6 and FB6 (Figure 3).

In-vitro Release Studies: All the formulations were studied for *In-vitro* release studies. During this study all the formulations showed slight change in the dissolution rate initially. All the formulations could release 85% of the drug with in the 12 Minutes. When the formulations of F1-F5 when compared with FB6 the rate dissolution is not affected, F6 could release 90% of drug within 3 minutes and FB6 showed 90% of drug release in 10 minutes (approx). Similarly, when S6 and SB6 are compared S6 showed 90% of drug release in 8 minutes (approx) and SB6 showed 90% of drug release in 13 minutes (approx) (Figure 4).

FTIR Studies Data: The spectrum of pure Amlodipine Besylate and formulation F6, S6 are shown in (Figure 5). The FTIR spectrum of drug and polymer showed no significant shift or reduction in intensity of peaks of Amlodipine Besylate.

X - Ray Diffraction

The x-ray Diffractogram of pure Amlodipine Besylate, Eudragit EPO and drug polymer complex are shown in (Figure 6). The x ray diffraction confirms its crystalline nature as evidenced from number of sharp and intense peaks. The diffractogram of polymer (Eudragit EPO) showed diffused peak, indicating the amorphous nature while the diffraction pattern of drug polymer complex represents

complete disappearance of crystalline peaks of drug especially those situated between 20° and 600°. These finding suggest the formation of new solid phase with a lower degree of crystallinity due to complexation.

Human Taste Panel: The taste evaluation of Amlodipine Besylate was performed by volunteers in the age group of 18 to 22 yrs. The protocol was explained and written consent as obtained from volunteers. The formulations of Amlodipine Besylate were held in the mouth for 5 seconds by each volunteer. Bitterness levels were recorded instantly and then after 30 to 150 sec. The bitterness level was recorded as positive against Negative controls (Figure 7).

DISCUSSION

The demand for Oro dispersible tablets has enormously increased during the last decade, particularly for geriatrics and paediatrics patients who have difficulty in swallowing conventional tablets and capsules. Oral administration of the drugs is difficult in patients having concomitant vomiting or diarrhoea. Oro dispersible dosage forms are advantageous for such patients. Oro dispersible dosage forms are meant to dispersible immediately upon contact with the saliva leading to faster release of the drugs in the oral cavity. In the present work, mouth dissolving tablets of taste masked Amlodipine Besylate were prepared by direct compression. All the tablet formulations compressed individually using biconcave 6mm punches in Rimek mini press 1, a 10 station rotary compression machine. Tablets were evaluated for changes in parameters by changing the concentration of superdisintegrants from 1 to 6% and Eudragit EPO used as taste masking agent. Precompressional parameters, angle of repose, % compressibility and Hausner's ratio studies indicated that most of the formulations showed fair and good flow properties. Postcompressional parameters, hardness, friability, *In-vitro* Dispersion time, Wetting time, drug content and dissolution studies were studied. All the formulations showed no appreciable change in hardness, while friability of tablets ranged between 0.64% and 0.91%. Drug Content of tablets ranged between 97.23 to 99.57%. *In-vitro* dispersion time, formulations containing >5% Kollidon CL and 5% of Croscarmellose Sodium were found to be promising. The *In-vitro* dispersion time of Amlodipine Besylate tablets prepared by Kollidon CL was found to be in the range of 167-24 Seconds and for those of Croscarmellose Sodium was found to be in the range of 185-39 Seconds. Wetting time of promising formulations was found to be within 1 minute, which facilitates their faster dispersion in the mouth. Amongst the two super disintegrants used, namely, Kollidon CL and Croscarmellose Sodium, the Kollidon CL (6%) superdisintegrant was found to be good. The 1:1 ratio of Eudragit EPO to drug was promising in masking the bitter taste of Drug. The *In-vitro* Dissolution studies states that formulations containing Eudragit EPO polymer didn't affected on rate of dissolution when compared with blank formulations. All the formulations showed 85 % of drug release in < 12 minutes. FTIR-spectroscopic studies indicated that there are no drug-excipient interactions. Similarly X-ray Diffraction studies suggested the formation of new solid phase with a lower degree of crystallinity due to complexation. From the results of present study indicates the complexation of Amlodipine Besylate and Eudragit EPO can not only mask its bitter taste significantly but also improve

the dissolution profile. By employing direct compression method, Orodispersible tablets of 100 mg weight with a taste acceptable to patients and sufficient structural integrity could be prepared. From all the superdisintegrants studied, tablets containing 6% Kollidon CL gave the highest improvement in disintegration and dissolution profile of Amlodipine Besylate.

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