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Formulation and Evaluation of Mouth Dissolving Tablets of Atenolol

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ABSTRACT
The objective of this study was to synthesize and characterize mouth dissolving tablets of Atenolol. Seven formulations were prepared based on different concentrations of superdisintegrants and other polymers. Direct compression method was used to study the effect of manufacturing processes, nature and concentration of superdisintegrants on various features of these tablets. The pre-compression parameters like bulk density, tapped density, Carr's index and angle of repose were determined. The post-compression parameters like the thickness, hardness, friability and in vitro disintegration time, wetting time and in vitro drug release were carried out and the values were found to be within IP, BP limits. The drug-polymer compatibility was confirmed by FTIR and DSC studies. The results obtained by FTIR and DSC studies revealed that there was no chemical interaction between the pure drug and excipients. Direct compression method was employed to formulate the tablets, because of its cost effectiveness and due to reduced number of manufacturing steps. The final formulation showed acceptable flow properties.

Key words: Atenolol, croscarmellose sodium, Microcrystalline cellulose (MCC) ,sodium starch glycolate (SSG), crosscarmellose sodium and crospovidone (CP) mouth‑disintegrating tablet (MDT)

I. INTRODUCTION

1.1 INTRODUCTION TO MOUTH DISSOLVINGTABLETS

Oral administration is the most popular route due to ease of ingestion, accurate dosage, self medication, pain avoidance, and most importantly patient compliance. Also, solid oral delivery systems do not require sterile conditions and therefore, less expensive to manufacture. Several novel technologies for oral delivery have recently become available to address the physicochemical and pharmacokinetic characteristics of drugs, while improving patient compliance[1]. Taking these requirements into consideration, attempts have been made to develop a mouth dissolving tablet. Since such a tablet can disintegrate in only a small amount of water in the oral cavity, it is easy to take for any age patient, regardless of time or place. For example, it can be taken anywhere at any time by anyone who do not have easy access to water [2,3].

Theyrelease the drug as soon as they come in contact with the saliva, thus obviating the need for water during administration[4].It is also easy to dose the aged, bed-ridden patients, or infants who have problems in swallowing tablets and capsules. Also Swallowing a tablet is a major difficulty encountered in case of geriatric and pediatric patient this leadsto poor patient compliance due to unpalatable taste of drug. To troubleshoot these problems a new dosage formknown as fast-dissolving tablet, has been developed which rapidly disintegrate and dissolve in saliva[5].

Recently, many companies have researched and developed various types of fast-disintegrating dosage form technologies with the potential to accommodate various physicochemical, pharmacokinetic and pharmacodynamic characteristics of drugs[6].

US FDA defined MDT tablets as "A solid dosage form containing medicinal substances which disintegrates rapidly usually within a matter of seconds, when placed upon the tongue".

Recently European Pharmacopoeia used the term „Orodispersible tablet" as a tablet that is to be placed in the mouth where it disperses rapidly before swallowing[7].Most of the MDTs includecertain super disintigrants and taste maskingagents. Fast or mouth dissolving tablets havebeen formulated for pediatric, geriatric, andbedridden patients. Such formulations provide anopportunity for product line extension in themany elderly persons will have difficulties

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intaking conventional dosage forms (viz.,solutions, suspensions, tablets, and capsules)because of hand tremors and dysphagia[8].

These 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 rapimelts. However, of all the above terms, United States of pharmacopoeia (USP) approved these dosage forms as ODTs (orally disintegrating tablets). Recently, European Pharmacopoeia has used the term orodispersible tablet for tablets that disperses readily within 3 minutes in mouth before swallowing. United States of 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 minute[9, 10].

IDEAL PROPERTIES OF MOUTH DISSOLVING TABLETS [11, 12, 13]

Not require water to swallow, but it should dissolve or disintegrate in the mouth in a matter ofseconds.
Be compatible with other excipientsused.
Be portable without fragilityconcern.
Have a pleasant mouthfeel.
Leave minimum or no residue in the mouth after oraladministration.
Exhibit low sensitive to environmental conditions as temperature andhumidity.
Ease of administration to the patient who cannot swallow, such as theelderly, stroke victims, bedridden patients, patient affected by renal failure and patient who refuse to swallow such as pediatric, geriatric and psychiatricpatients.
No need of water to swallow the dosage form, which is highly convenientfeature for patients who are traveling and do not have immediate access towater.
Rapid dissolution and absorption of the drug, which will produce quick onset of action.
Pregastric absorption can result in improved bioavailability and as a result of reduced dosage; improve clinical performance through a reduction of unwantedeffects.
Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatricpatient.

MERITS OF MOUTH DISSOLVING TABLETS [6, 14, 15]

Bitter taste can be masked by use of flavour and sweetener to produce good mouth feel particularly for paediatricpatients.
The risk of chocking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided, thus providing improvedsafety.
This is beneficial for travelling patients and busy people, who do not have easy access towater.
Accurate dosing as compared toliquids.
Convenience of administration and accurate dosing as compared toliquids.

LIMITATIONS OF MOUTH DISSOLVING TABLETS[16, 17]

Drugs with relatively larger doses are difficult to formulate into FDT e.g. antibiotics like ciprofloxacin with adult dose tablet containing about 500 mg of thedrug.

Patients who concurrently take anticholinergic medications may not be the best candidates for MDT. Similarly patients with Jorgen's syndrome or dryness of the mouth due to decreased saliva production may not be good candidates for these tabletformulations.

The tablets usually have insufficient mechanical strength; hence, careful handling is required.

The tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly. Different techniques and patent technologies are available for conversion of a raw material into mouth disintegrating tablets. These include direct compression, sublimation and effervescent method. Each method has its own advantages and disadvantages but most commonly direct compression is used in preparing mouth disintegrating tablets.

Atenolol a β_1 selective antagonist acting selectively and competitively on β- adrenoreceptor and by blocking the actions of catecholamines used in the treatment of diverse cardiovascular diseases like hypertension, angina pectoris, cardiac arrhythmias and myocardial infarction. The drug is also indicated in the prophylactic treatment of migraine[18].

Administration of conventional tablets of Atenolol has been reported to exhibit fluctuations in the plasma drug levels resulting in either manifestation of side effects or reduction in drug concentration at the receptor site.

Oral bioavailability of Atenolol is around 50% and having half life 6 to 7 hrs[19]. In recent years drug formulation scientists have recognized

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that single component excipients do not always provide the requisite performance to allow certain active pharmaceutical ingredients to be formulated or manufactured adequately[20].Hence, there is a need to have excipients with multiple characteristics built into them such as better flow, low/no moisture sensitivity, superior compressibility and rapid disintegration ability[21].

In the present study MDTs of atenolol and atorvastatin were formulated by using direct compression method andsuperdisintegrants in order to reduce dose frequency and to enhance patient compliance towards therapy.

There are various challenges in formulation of MDTs like palatability, mechanical strength, hygroscopicity, aqueous solubility etc[22]. Different methods of preparation of MDTs are TabletMolding, spray drying, mass extrusion, Freeze-Drying orLyophillization, sublimation, direct compression[23, 24]

OraSolv technology is a patented technology unlike Zydis, disperses in the saliva with the aid of almost imperceptible effervescence. The OraSolv technology is best described as a fast-disintegrating tablet; the tablet matrix dissolves in less than one minute, leaving coated drug powder[25].

WOW tab technology is patented by Yamanouchi Pharmaceutical WOW means "without water". This process uses a combination of low mouldability saccharide (rapid dissolution) and high mouldability saccharide (good binding property) to obtain a rapidly melting strong tablet[26].

Advantol™ 200 is a directly compressible excipients system offering "Soft-Melt" functionality and specially formulated for nutraceutical applications. SPI Pharma's Advantol platform uses proprietary co-processing technology[27].

II. MATERIALS AND METHODS

Atenolol was kindly gifted by Litaka Pharmaceuticals, Pune. Microcrystalline cellulose(MC) was purchased from Rajesh chemicals, Mumbai. Sodium starch glycolate, Crosscarmellose sodium, Crospovidone, Mannitol, Magnesium stearate, Aspartame, Talc were purchased from Loba chemicals, Mumbai.

2.1 Preparation of Mouth Dissolving Tablets Of Atenolol

2.1.1 Formulationdevelopment[28, 29]

In the present study mouth dissolving tablets of Atenolol were formulated by direct compression method using three superdisintegrants sodium starch glycolate(SSG), crosscarmellose sodium(CCS) and crospovidone(CP), microcrystalline cellulose (MCC) as diluent with other excipients like sweetener and flavours. Atenolol tablets are available in 50mg-100mg doses in the market. Dose of 75 mg is selected for the present study.

Development of the formulation in the present study was mainly based on the type and concentration of polymers and the properties of the drug. Various polymers in different concentrations were used so as to get tablets with good physical properties. The formulation design of mouth dissolving tablets of Atenolol is shown in Table 1

Sr. no.	Ingredients (mg/tablet)	A1	A2	A3	A4	A5	A6	A7
1.	Atenolol	75	75	75	75	75	75	75
2.	Sodium starch Glycolate	20	10	-	-	-	-	5
3.	Crosscarmellose Sodium	-	-	20	10	-	-	5
4.	Crospovidone	-	-	-	-	20	10	5
5.	Microcrystalline Cellulose	45	45	45	45	45	45	45
6.	Mannitol	93	99	93	99	93	99	94
7.	Aspartame	6	6	6	6	6	6	6

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 1 Jan-Feb 2022, pp: 135-148 www.ijprajournal.com ISSN: 2249-7781

8.	Magnesium Stearate	6	7	6	7	6	7	7
9.	Talc	5	8	5	8	5	8	8

Table 1-Formulation design of Atenolol mouth dissolving tablets

2.1.2 Formulation of mouth dissolving tablets ofAtenolol

All the materials were passed through 60# screens prior to mixing. Atenolol, Croscarmellose sodium, Sodium Starch Glycolate, and Mannitol were mixed using a glass mortar and pestle. All the materials were directly compressible so this uniformly mixed blend was compressed into tablets using concave face round tooling on a8-station rotary tablet machine. The compositions of the batches are shown in Table 1.

III. EVALUATION OF ATENOLOL TABLETS.

3.1 Drug–polymer compatibilitystudies

In the preparation of tablets formulation, drug and polymer may interact as they are in close contact with each other, which could lead to the instability of drug. Preformulation studies regarding the drug-polymer interaction are therefore very critical in selecting appropriate polymers. FT-IR spectroscopy was employed to ascertain the compatibility between Atenolol and the selected polymers.FT-IR spectrum of Atenolol was compared with FT-IR spectra of polymers. The spectras were shown in Figures 1 and 2.

3.2 Pre-compression parameters[30,31]

3.2.1 Angle of Repose(θ)

The angle of repose was determined using funnel method. Funnel that can be fit vertically withstand at 1.5 cm. height. The opening end of funnel are closed with thumb until drug are poured. The 5 gm. of powder was poured into funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap (r) was measured and the angle of repose θwas calculated using the formula.

$\theta = \tan^{-1}(h/r)$

Where, □ is the angle of repose h is height of pile
r is radius of the base of pile.

3.2.2 Bulk Density(ρ_b)

Apparent bulk density was determine by pouring the powder into a 100 ml measuring cylinder. The bulk volume (V) poured drug was determined. The bulk density was calculated using the formula.

$\rho_b = M / V$ Where, $\rho_b$is bulk density M is weight of powder V is volume ofpowder.

3.2.3 Tapped Density (ρ_t)

Weight the powder and placed in a measuring cylinder. Measuring cylinder containing known mass of powder was tapped for 100 times or fixed time. The minimum volume (Vt) occupied was measured. The tapped density was calculated using following formula.

$\rho_t = M / Vt$

Where, $\rho_t$is tapped density
M is weight of powder Vt is tapped volume.

3.2.4 Compressibility Index (Carr'sIndex)

The simplest way for measurement of free flow of powder is compressibility, a indication of the ease with which a material can be induced to flow is given by CompressibilityIndex. Thevaluebelow15%indicatesapowderwithgiveriseto good flow properties, whereas above 25% indicate poor flowability. Which is calculated follows.

Compressibility index = Tap density – Bulk density / Tap density ∗100

3.2.5 Hausner ratio

Hausner ratio is an indirect index of ease of powder flow. Hausner ratio is the ratio of tapped density to bulk density. Lower the value of Hausner ratio better is the flow property.

Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).

Hausner ratio = Tapped density / Bulk density

3.3 Post-compressionparameters

The tablets after punching of every batch were evaluated for in-process and finished product quality control tests i.e. thickness, weight uniformity test, hardness,friability, drug content, in vitro disintegration time, wetting time and in vitro drug release studies.

3.3.1 Thickness

Tablet thickness can be measured using a simple procedure. 5 tablets were taken and their thickness was measured using Verniercalipers.

3.3.2 Hardness

It is the force required to break a tablet by compression in the radial direction, it is an important parameter in formulation of mouth dissolve tablets because excessive crushing strength significantly reduces the disintegration time.In the presentstudy the crushing strength of the tablet was measured using Pfizer hardness

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 1 Jan-Feb 2022, pp: 135-148 www.ijprajournal.com ISSN: 2249-7781

testers. An average of three observations is reported.

3.3.3 Uniformity ofweight

I.P. procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug contentuniformity.

3.3.4 Disintegrationtime

The test was carried out on 6 tablets using the apparatus specified in I.P.1996 distilled water at 37ºC ± 2ºC was used as a disintegration media and the time in second taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds.

3.3.5 Friability test

Friability of the tablets was determined using Roche friability. This device subjects the tablets to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inches in each revolution. Pre-weighed sample of tablets was placed in the friabilator and were subjected to 100 revolutions. Tablets were de dusted using a soft muslin cloth and reweighed. The friability (f) is given by the formula.

% Friability = Initial weight – Final weight / Initial weight * 100

3.3.6 Wetting time

Five circular tissue papers of 10 cm diameter are placed in a petridish with a 10 cm diameter. Ten millimeters 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 wettingtime.

Procedure of determining drugcontent

Randomly selected ten tablets were weighed and powdered, 50 mg. equivalent of Atenolol was weighed and dissolved in 500 ml. of phoshphate buffer pH 6.8. The drug was allowed to dissolve in the solvent, the solution was filtered, and 1ml of filtrate was suitably diluted with respective buffer and analyzed spectrophotometrically at 225 nm. The amount of Atenolol was estimated by using standard calibration curve of the drug. Drug content studies were carried out in triplicate for each batch of formulation.

In vitro drugrelease[28]

The release rate of Atenolol from mouth dissolving tablets was determined using United State Pharmacopoeia (USP) dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml. of phosphate buffer pH 6.8 as dissolution medium, at 37 ± 0.5^0 rpm. A sample (10 ml.) of the solution was withdrawn from the dissolution apparatus at 2, 4, 6, 8 and 10 min. The samples were filtered through a 0.45µ membrane filter. Absorbance of these solutions was measured at 225 nm using Shimadzu UV-1700 UV/VIS spectrophotometer. Cumulative percentage of drug release was calculated using an equation obtained from a standardcurve.

IV. RESULTS

4.1 PREFORMULATIONSTUDIES

4.1.1 Determination ofsolubility

Atenolol was found to be freely soluble in methanol and sparingly soluble in ethanol, slightly soluble in water andisopropanol.

4.1.2 Determination of meltingpoint

The melting point of Atenolol was found to be in the range of 152^0C to 156^0C.

4.1.3 Determination ofλ_{max}

$\lambda_{max}$of Atenolol in phosphate buffer pH 6.8 was found to be 225 nm

4.2 EVALUATION PARAMETERS OF ATENOLOLTABLETS

4.2.1 Drug–polymer compatibility by FTIRstudies

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 1 Jan-Feb 2022, pp: 135-148 www.ijprajournal.com ISSN: 2249-7781

Fig. 1- IR spectra of Atenolol

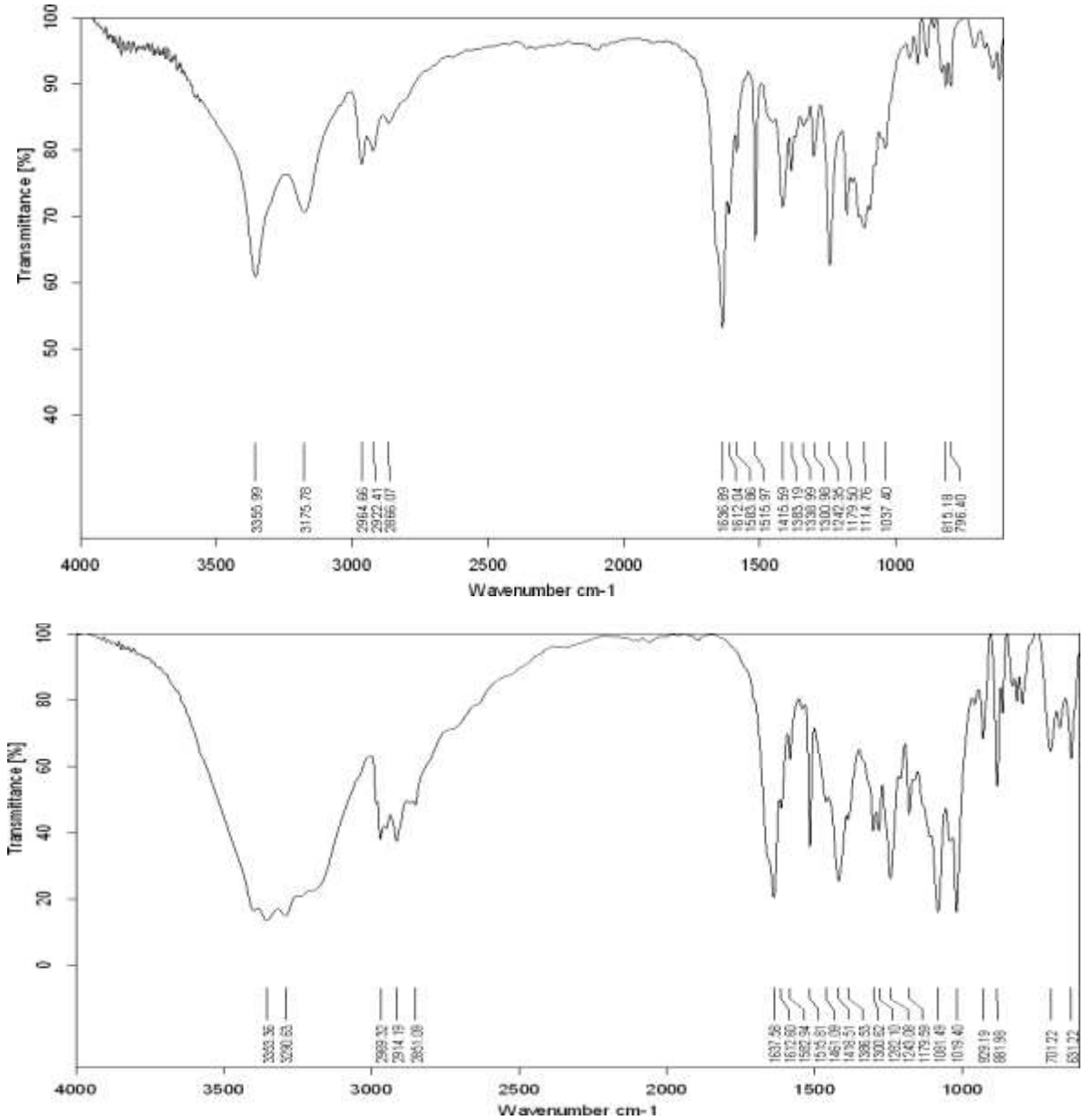

Fig. 2- IR spectra of physical mixture of final formulation

The characteristics peaks of atenolol and polymer were present in the physical mixture, thus indicating no significant evidence of chemical interaction between drug and polymer which confirms the stability of drug. peaks N – H stretching at 3353.36 cm-1 , C –N stretching at 1243.09 cm-1, C=C stretching at 1515.81cm-1, aromatic C – H stretching at 2969.32 cm-1 which were present in pure drug atenolol were also found in physical mixture indicating that there is no interaction between drug and polymer[32].

4.2.2 DSC study:

One of the most classic applications of DSC analysis is the determination of the possible interactions between a drug entity and the excipients in the formulation. Supporting evidence for compatibility between drug and excipients was obtained from DSC studies. As shown in the figure 3, the DSC thermogram of atenolol showed endothermic peak at 153.74^0 C which is close to the

International Journal of Pharmaceutical Research and Applications
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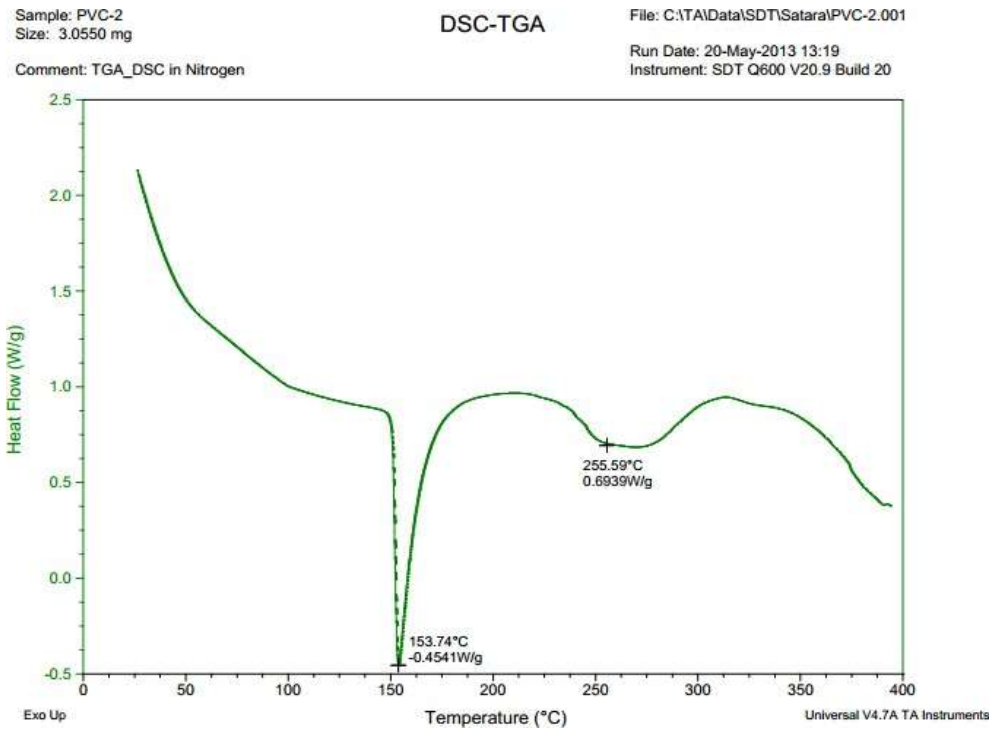
melting point of drug. As observed in DSC thermogram of representative

Fig.3-DSC thermogram of Atenolol.



formulation, figure 4, no significant shift in the endothermic peaks of drug was found (endothermic peak at 148.78^0 C). This indicated the absence of any interaction between drug and excipients. Hence from the DSC thermograms, it could be concluded that there was compatibility between drug andexcipients.

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 1 Jan-Feb 2022, pp: 135-148 www.ijprajournal.com ISSN: 2249-7781

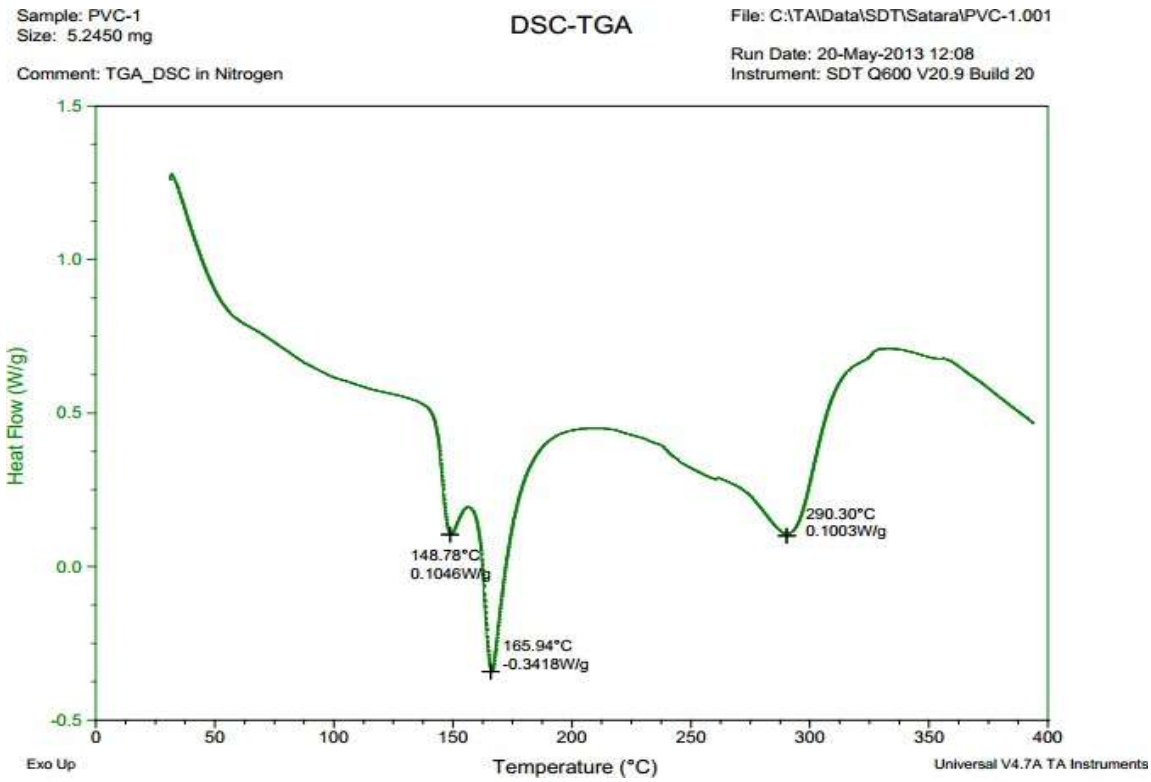


Fig. 4–DSC thermogram of representative formulation.

EVALUATION OF ATENOLOLTABLETS

Formulation Code	*Angle of repose(θ)	*Bulk density (g/cc)	*Tapped density (g/cc)	*Carr's index	*Hausner's ratio
A1	25.43±0.02	0.52±0.005	0.625±0.001	16.8±0.01	1.20±0.001
A2	24.72±0.47	0.52±0.001	0.625±0.001	16.8±0.02	1.20±0.001
A3	28.05±0.56	0.52±0.001	0.625±0.005	16.8±0.05	1.20±0.002
A4	28.43±0.70	0.52±0.001	0.625±0.001	16.8±0.08	1.20±0.001
A5	27.68±0.10	0.54±0.005	0.625±0.001	13.6±0.02	1.15±0.005
A6	29.79±0.11	0.52±0.005	0.56±0.001	7.14±0.01	1.07±0.002
A7	28.43±0.60	0.52±0.001	0.625±0.001	16.8±0.01	1.20±0.001

*Value expressed as mean±SD, n=3

Table 2 -Precompression parameters of Atenolol tablets

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 1 Jan-Feb 2022, pp: 135-148 www.ijprajournal.com ISSN: 2249-7781

Formulation Code	*Thickness (mm)	*Hardness (kg/cm$^{2)}$	*Friability (%)	*Weight variation
A1	2.47±0.01	3.14±0.02	0.399±0.04	249.33±1.15
A2	2.49±0.01	3.19±0.02	0.480±0.04	251.19±0.33
A3	2.44±0.02	3.25±0.03	0.44±0.07	249.66±0.28
A4	2.49±0.01	3.69±0.02	0.43±0.07	250.33±0.10
A5	2.46±0.03	3.68±0.03	0.20±0.01	248.74±0.34
A6	2.47±0.01	3.40±0.03	0.64±0.03	249.10±0.71
A7	2.49±0.02	3.52±0.02	0.40±0.04	250.31±0.48

Table 3- Results of thickness, hardness, friability and weight variation of Atenolol tablets

Formulation Code	*In vitro disintegration time (sec.)	*Wetting time (sec.)
A1	26.43±0.51	34±1.10
A2	27.83±0.76	36±0.91
A3	22±0.62	24.86±0.96
A4	23.76±0.25	25.76±0.46
A5	16.13±0.70	20.03±0.97
A6	19.2±0.36	22.46±0.87
A7	29.56±0.65	38.06±0.20

*Value expressed as mean±SD, n=3

Table 4 - Results of in vitro disintegration time and wetting time of Atenolol tablets

Determination of drug content of Atenololtablets is shown in table 5.

Formulation	% Drug content
A1	96.15±0.14
A2	96.03±0.16
A3	97.42±0.35
A4	97.25±0.11
A5	99.61±0.11
A6	99.06±0.10
A7	97.89±0.12

*Value expressed as mean±SD, n=3

Table 5- drug content of Atenololtablets

In vitro drug release profile of Atenololtablet

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 1 Jan-Feb 2022, pp: 135-148 www.ijprajournal.com ISSN: 2249-7781

Sr. No.	Time (min)	% cumulative drug release						
		A1	A2	A3	A4	A5	A6	A7
1	0	0	0	0	0	0	0	0
2	2	16.67 ±0.31	14.50±1.2 5	18.34±0. 41	16.89±0. 66	21.67±0. 87	23.23±0.5 7	16.12±0.7 4
3	4	36.39 ±0.51	26.85±0.7 8	43.89±0. 80	41.03±0. 58	43.22±0. 60	46.68±0.6 8	25.73±0.4 3
4	6	67.21 ±0.60	56.39±0.8 5	69.78±0. 27	63.18±0. 66	68.15±0. 60	73.16±1.4 4	49.51±0.9 3
5	8	78.23 ±1.10	71.70±0.2 6	79.83±1. 05	75.82±0. 75	83.16±0. 26	85.78±0.4 2	73.71±0.8 6
6	10	92.15 ±0.90	89.38±0.5 6	94.89±0. 73	91.90±0. 51	99.62±0. 99	94.60±0.6 6	86.68±0.6 0

Table 6-In vitro drug release data of Atenolol tablets

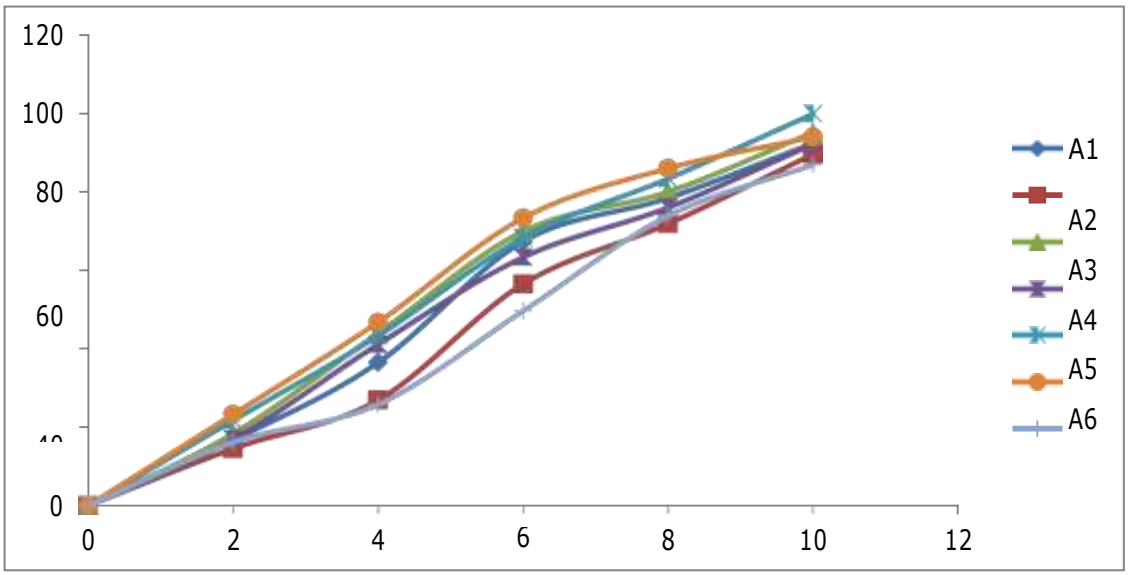


Fig. 5- In vitro drug release profile of Atenolol tablets

V. DISCUSSION

In the present study, an attempt was made to develop and evaluate mouth dissolving tablets of Atenolol (75 mg.) for better treatment of antihypertensive condition. In general Atenolol having only 40-50% oral bioavailability because of high first pass metabolism rate. Thus, formulated mouth dissolving tablets of Atenolol prevents or avoids first pass metabolism and their absorption directly takes place into the saliva which results in better oral bioavailability compared to conventional Atenolol tablets.

5.1 PREFORMULATIONSTUDIES

The solubility of Atenolol reveals that it was freely soluble in methanol and soluble in acetic acid and dimethyl sulfoxide. It is sparingly soluble in 96% ethanol, slightly soluble in water andisopropanol. Melting point of Atenolol was determined by capillary method. The melting point of Atenolol was found to be in the range 152^{o} C to 155^{o} C, which complied with BP standards thus indicating purity of the drugsample. In Preformulation studies, it was found that, the λmax of Atenolol by UV spectroscopic method was found at 225 nm in pH6.8 buffer. A standard calibration curve of Atenolol was made in phosphate buffer pH6.8 by taking absorbance V/S concentration between 2-20µg/ml ranges. This complied with BP standards thus indicating purity of obtaineddrug.

International Journal of Pharmaceutical Research and Applications
Volume 7, Issue 1 Jan-Feb 2022, pp: 135-148 www.ijprajournal.com ISSN: 2249-7781

5.2 Evaluation of Atenolol mouth dissolvingtablets

5.2.1 Drug –polymer compatibility by FTIR studies

FTIR of drug-polymers interaction studies are shown in Figure 1 and Figure 2. It was found that Atenolol was compatible with super disintegrants used in the formulation and there were no extra peaks observed.

5.2.2 Pre-compressionparameters

Pre-compression parameters play an important role in improving the flow properties of pharmaceuticals especially in tablet formulation. These include angle of repose, bulk density, tapped density, carr's index and haunser ratio. Before formulation of tablets the drug and superdisintegrants mixture were evaluated for all the above said parameters and it was found that all the observations were within the prescribed limits of IP.

Angle of repose of all the formulations was found to be raging from 24.72-29.79, bulk density was found to be 0.52-0.54 g/cc, tapped density was in between 0.56- 0.625g/cc, Carr's index was found to be within 7.14-16.80 and haunser ratio was found to be within 1.07-1.20 indicating compressibility of the tablet granules is good as reported in Table2.

5.2.3 Post-compressionparameters

5.2.3.1 Tablet thickness andhardness

The thickness of the tablet indicates that die fill was uniform. The thickness depends upon the size of the punch (9 mm) and the weight of the tablet (250 mg). The thickness of the batch from A1-A7 was found to be 2.46-2.49 mm and hardness was found to be 3.14- 3.69 kg/cm^2 as reported in Table 3 and thus tablets were having good mechanical strength.

5.2.3.2 Friability

Friability is needed for tablets to withstand force of compression applied during the manufacture of tablets. The friability of all the formulated tablets of Atenolol was found to be between 0.20-0.64 % are reported in Table 3 and all the formulated tablets of Atenolol were shown the % friability within the official limits.(i.e. not more than 1%).

5.2.3.3 Weightvariation

Prepared tablets were evaluated for weight variation and percentage deviation from the average weight are reported in Table 3 and was found to be within (±7.5) the prescribed officiallimits.

5.2.3.4 In vitro disintegrationtime

All the formulated tablets (A1-A7) have shown in vitro disintegration time of less than 30 seconds, showing that formulated Atenolol tablets were better and effective than conventional tablets. Among all the formulations, tablets prepared with crospovidone had shown less than 20 sec. of disintegration time. The obtained results were showed in Table4.

5.2.3.5 Wettingtime

The wetting time of all the formulations (A1-A7) were found to be within 20-38 seconds, which complies with the official specifications. The results were showed in Table 4.

5.2.3.6 Drugcontent

The drug content of all the seven formulations of Atenolol tablets were found to be within the range of 96.03-99.64% which were within the limits of IP specifications. The drug content of all the formulations of Atenolol tablets is shown in Table 5.

5.2.3.7 In vitro dissolutionstudy

Total seven formulations were formulated A1 to A7 by using three different superdisinegrants in varying concentrations. The formulations A1-A6 were formulated with the help of sodium starch glycolate, crospovidone and crosscarmellose sodium in concentration 8% to 4% respectively. The formulation A7 were formulated with the help of sodium starch glycolate, crospovidone and crosscarmellose sodium in concentration 2% respectively. The formulations A1-A7 showed more than 86.68 to 99.62% drug release. Among those seven formulations A5 showed highest drug release of 99.62%. The data for in vitro drug release of formulations was shown in Table 6the in vitro drug release profile in figure 5.

VI. CONCLUSION

The conclusion drawn from the present investigation is given below;

Preformulation studies of Atenolol were performed. From the FTIR and DSC studies the interference was verified and found that Atenolol did not interfere with the polymers used.

Seven batches of mouth dissolving tablets of Atenolol were successfully prepared using sodium starch glycolate, crosscarmellose and crospovidone by direct compression method.

Thetabletswereevaluatedforparameterslikethickness ,hardness,friability,invitro disintegration time, wetting time, % drug content and in vitro drug release studies.

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Based on the results, formulation containing 8% crospovidone (A-5) was identified as ideal and better formulation among all formulations developed for Atenololtablets.

In vitro release of optimized formulation of Atenolol mouth dissolving tablets of A-5 was found to be 99.62% drug release within 10 min. with in vitro disintegration time being 16.13sec.

VII. SUMMARY

Atenolol a β_1 selective antagonist acting selectively and competitively on β- adrenoreceptor and by blocking the actions of catecholamines used in the treatment of diverse cardiovascular diseases like hypertension, angina pectoris, cardiac arrhythmias and myocardial infarction. The drug is also indicated in the prophylactic treatment of migraine. Administration of conventional tablets of Atenolol has been reported to exhibit fluctuations in the plasma drug levels resulting in either manifestation of side effects or reduction in drug concentration at the receptor site. The present study is an attempt to develop and formulate mouth dissolving tablets of Atenolol with superdisintegrants which disintegrates in matter of seconds in the oral cavity, thereby reducing the time of onset of pharmacological action and to prevent the first pass metabolism ofAtenolol.

The identification characterstics of drug like solubility, melting point, λ_{max} were performed to find out the purity of drug. All the parameters observed were satisfactory and were within the prescribed official limits.

In this system direct compression method was used. Microcrystalline cellulose (MCC) is used as a diluent, sodium starch glycolate (SSG), crosscarmellose sodium and crospovidone (CP) were used as superdisintegrants, talc is used as flow promoter, magnesium stearate was used as lubricant and aspartame as sweetener.

The drug-polymer compatibility was confirmed by FTIR and DSC studies. The results obtained by FTIR and DSC studies revealed that there was no chemical interaction between the pure drug and excipients. Direct compression method was employed to formulate the tablets, because of its cost effectiveness and due to reduced number of manufacturing steps.

The pre-compression parameters like bulk density, tapped density, Carr's index and angle of repose were determined. The final formulation showed acceptable flow properties. The post-compression parameters like the thickness, hardness, friability and in vitro disintegration time, wetting time and in vitro drug release were carried out and the values were found to be within IP, BP limits.

The optimized formulation of Atenolol tablets containing 8% crospovidone (A-5) showed 99.62% release in 10 min. Hence, the results revealed that formulated mouth dissolving tablets of Atenolol is effective and better to meet patient compliance

Prepared tablets were evaluated for weight variation and percentage deviation from the average weight are reported in Table 3 and was found to be within (±7.5) the prescribed officiallimits.

In vitro disintegrationtime

All the formulated tablets (A1-A7) have shown in vitro disintegration time of less than 30 seconds, showing that formulated Atenolol tablets were better and effective than conventional tablets. Among all the formulations, tablets prepared with crospovidone had shown less than 20 sec. of disintegration time. The obtained results were showed in Table4.

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