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# FORMULATION AND EVALUATION OF SUBLINGUAL TABLETS OF TERAZOSIN HYDRO-CHLORIDE

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**Keywords:**

Sublingual, Wetting time, Water absorption ratio, *In-vitro* dissolution study

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**ABSTRACT:** The objective of the current study was to develop and optimize sublingual tablets of Terazosin Hydrochloride, which is an effective drug in the treatment of Benign Prostate Hyperplasia, Hypertension. Sublingual tablets of Terazosin Hydrochloride were prepared by direct compression method using different superdisintegrating agents such as Crosspovidone, Sodium starch glycolate and Crosscarmellose sodium. The tablets were evaluated for pre-compression studies like Bulk density, Tapped density, Carr's index, Hausner's ratio and post-compression studies like Thickness, Hardness, Weight variation, Friability, drug content, Wetting time, Water absorption ratio, *in-vitro* disintegration time, *in-vitro* dispersion time, *in-vitro* dissolution study and also drug release kinetic study. The Hardness, Weight variation, Thickness, Friability and Drug content of tablets were found to be acceptable according to pharmacopoeial limits. An optimized formulation i.e. F6 was found, which provided short wetting time of 67sec, water absorption ratio of 39.01 , *in-vitro* disintegration time of 61sec and *in-vitro* dispersion time of 112sec. From the above results It indicated that the amount of superdisintegrant i.e. Crosspovidone was significantly affected the dependent variables like Wetting time, Water absorption ratio, *in-vitro* disintegration time and *in-vitro* dispersion time. The best *in-vitro* drug release was found to be in formulation F6 i.e. 102% during the end of 15min. The *in-vitro* drug release data of all Terazosin Hydrochloride tablets were subjected to goodness of fit test by linear regression analysis according to Zero order reaction, 1st order equation, Higuchi's equation and Korsemeyer-Peppas equation to ascertain the mechanism of drug release. Hence the drug release followed the first order release kinetics with diffusion mechanism.

**INTRODUCTION:** Tablets that disintegrate or dissolve rapidly in the patient's mouth are convenient for young children, especially elderly and patients who are unable to swallow and in some cases where potable liquids are not available. The drug can be easily disintegrated in the presence of small volume of saliva in oral cavity. Then the medication can be absorbed partially or entirely into the systemic circulation from blood vessels in the sublingual mucosa, or it can be swallowed as a solution to be absorbed from gastrointestinal tract. The sublingual route usually produces a faster onset of action than orally administered tablets and the amount absorbed through sublingual blood vessels bypass the hepatic first- pass metabolic processes [1-3].

Terazosin Hydrochloride is a selective alpha1-antagonist used for treatment of symptoms of Benign Prostatic Hyperplasia (BPH). It also acts to lower blood pressure, so it is a drug of choice for men with hypertension and prostate enlargement.

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It works by blocking the action of adrenaline on smooth muscle of the bladder and the blood vessel walls. The bioavailability of Terazosin Hydrochloride is 90%, Molecular Weight 459.9, Half - Life is12hrs [4]. It can be absorbed rapidly on oral administration; the drug undergoes hepatic first pass metabolism. Various techniques can be used to formulate rapidly disintegrating or dissolving tablets [5-6].

Direct compression is one of these techniques which require incorporation of a superdisintegrant into the formulation, or the use of highly water-soluble excipients to achieve fast tablet disintegration. Extremely rapidly disintegration of the sublingual tablets would be required to enhance the release of Terazosin Hydrochloride from tablets for rapid absorption by the sublingual mucosa blood vessels. It was confirmed that Terazosin Hydrochloride formulated as rapidly disintegrating tablets for sublingual administration.

**MATERIALS AND METHODS:** Terazosin Hydrochloride was obtained as gift sample from Mylan laboratories, Hyderabad. Crosspovidone, Sodium starch glycolate and Crosscarmellose sodium were obtained from Amit Cellulose Products. Pune. Microcrystalline cellulose pH 102 grade was obtained from Wei Ming Pharmaceutical Mfg.Co.Ltd, Taiwan. Sodium saccharine, Mannitol, Talc and Magnesium stearate were obtained from S.D. Fine Chemicals. Pvt Ltd, Mumbai, India. All chemicals and solvents used were of analytical grade.

**Drug-Excipient compatibility studies:** The drug polymer and polymer-polymer interaction was studied by the FTIR spectrometer using Shimadzu 8400-S, Japan. Two percent (w/w) of the sample with respect to a potassium bromide disc was mixed with dry KBr. The mixture was grind into a fine powder using an agate mortar and then compressed into a KBr disc in a hydraulic press at a pressure of 1000psi. Each KBr disc was scanned 16 times at 2 mm/sec at a resolution of 4 cm-1 using cosine apodization. The characteristic peaks were recorded.

**Formulation of sublingual tablets:** Terazosin Hydrochloride sublingual tablets were prepared by the direct compression method using different excipients. The excipients used were Micro crystalline cellulose (binding agent), mannitol (diluents), sodium saccharine (sweetening agent), Crosspovidone, Sodium starch glycolate and Crosscarmellose sodium (super disintegrants). Different concentrations of excipients were used to prepare different formulations of sublingual tablets. Compositions of various formulations are shown in **Table 1**. All the ingredients of the sublingual tablets of Terazosin Hydrochloride were weighed and mixed in mortar with the help of pestle. Then the blended material was slightly compressed on the 6mm flat–biconvex punch using a Rimek MINI PRESS-I MT tablet machine (Karnawati Engg. Ltd., Mehsana, India).

**Pre-compression studies of formulated sublingual tablets of Terazosin Hydrochloride:** The evaluations of Pre-compression studies of formulated sublingual tablets of Terazosin Hydrochloride were done as per standard procedures The following parameters were evaluation.

**TABLE 1(A): FORMULATION COMPOSITION OF MUCOADHESIVE SUBLINGUAL TABLETS OF TERAZOSIN HYDROCHLORIDE**

| INGREDIENTS | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 | F10 | F11 | F12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Drug | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| Cross PVP | 2 | 4 | 6 | 8 | 10 | 12 | - | - | - | - | - | - |
| Sodium starch glycolate | - | - | - | - | - | - | 2 | 4 | 6 | 8 | 10 | 12 |
| Crosscarmellose sodium | - | - | - | - | - | - | - | - | - | - | - | - |
| Microcrystalline cellulose | 45 | 40 | 35 | 30 | 25 | 20 | 45 | 40 | 35 | 30 | 25 | 20 |
| Mannitol | 53 | 56 | 59 | 62 | 65 | 68 | 53 | 56 | 59 | 62 | 65 | 68 |
| Sodium saccharine | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 |
| Talc | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
| Magnesium stearate | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| Total wt. (mg) | 125 | 125 | 125 | 125 | 125 | 125 | 125 | 125 | 125 | 125 | 125 | 125 |

**TABLE 1(B): FORMULATION COMPOSITION OF MUCOADHESIVE SUBLINGUAL TABLETS OF TERAZOSIN HYDROCHLORIDE**

| INGREDIENTS | F13 | F14 | F15 | F16 | F17 | F18 |
|---|---|---|---|---|---|---|
| Drug | 10 | 10 | 10 | 10 | 10 | 10 |
| Cross PVP | - | - | - | - | - | - |
| Sodium starch glycolate | - | - | - | - | - | - |
| Crosscarmellose sodium | 2 | 4 | 6 | 8 | 10 | 12 |
| Microcrystalline cellulose | 45 | 40 | 35 | 30 | 25 | 20 |
| Mannitol | 53 | 56 | 59 | 62 | 65 | 68 |
| Sodium saccharine | 10 | 10 | 10 | 10 | 10 | 10 |
| Talc | 2 | 2 | 2 | 2 | 2 | 2 |
| Magnesium stearate | 3 | 3 | 3 | 3 | 3 | 3 |
| Total wt.(mg) | 125 | 125 | 125 | 125 | 125 | 125 |

**Bulk density [7-10]:** It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder (passed through standard sieve #20) in to a measuring cylinder and the initial volume was noted, it is bulk volume. The results are presented in **Table 2**. The bulk density is calculated by given formula

Bulk density ($\rho_b$) = Mass of the powder (M) / Bulk volume ($V_B$)

**Tapped density [7-10]:** It is the ratio of total mass of powder to the tapped volume of powder. The volume was measured by tapping the powder for 500 times. The results are presented in Table 2. It is expressed by given formula

Tapped density ($\rho_T$) = Mass of the powder (M) / Tapped volume ($V_T$)

**Carr's Index [7-10]:** It is the simple test to evaluate the bulk density and tapped density of a powder and the rate at which it packed down. The results are presented in Table 2. It is expressed by the given formula

Carr's Index (%) = [(Tapped density – Bulk density) × 100] / tapped density

**Hausner's Ratio [7-10]:** It is the ratio of tapped density to the bulk density. The results are presented in Table 2. .

Hausner's Ratio = Tapped density / Bulk density

**Angle of repose [7-10]:** Angle of repose of powdered blend was determined by the funnel method. The accurately powdered blends were taken in the funnel. The height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powdered blend was allowed to through the funnel freely on to the surface .the diameter of the powder cone was measured and angle of repose was calculated by using the following formula and The results are presented in Table 2. .

$\tan \Theta = h/r$

h = height of the powder cone, r = radius of the powder cone

**Post-compression studies formulated sublingual tablets of Terazosin Hydrochloride:** The evaluations of Post-compression studies of formulated sublingual tablets of Terazosin Hydrochloride were done as per standard procedures The following parameters were evaluation.

**Hardness [11]:** The test was done as per the standard methods. The hardness of three randomly selected tablets from each formulation (F1 to F4) was determined by placing each tablet diagonally between the two plungers of tablet hardness tester (with the nozzle) and applying pressure until the tablet broke down into two parts completely and the reading on the scale was noted down in $Kg/cm^2$. The results are presented in **Tables 3**.

**Thickness [11]:** The thickness of three randomly selected tablets from each formulation was determined in mm using a Vernier caliper (Pico India). The average values were calculated. The results are presented in Table 3.

**Weight variation (or) Uniformity of Weight [11]:** Weight variation test was done as per standard procedure. Ten tablets from each formulation (F1 to F18) were weighed using an electronic balance and the average weight was calculated. The results are shown in Table 3.

**Friability [11]:** The friability of tablets using 10 tablets as a sample was measured using a Roche Friabilator. Tablets were rotated at 25 rpm for 4 minutes or up to 100 revolutions. The tablets were taken out, dedusted and reweighted. The percentage friability was calculated from the loss in weight as given in equation below. The weight loss should not more than 1%. The results are shown in Table 3.

%Friability = (Initial weight – Final weight) x 100 (Initial weight)

**Drug Content [11]:** Ten randomly selected tablets from each formulation (F1 to F18) were finely powdered and powder equivalent to 10mg of Terazosin Hydrochloride was accurately weighed and transferred to 100 ml volumetric flasks containing 50 ml of phosphate buffer( pH 6.8). The flasks were shaken to mix the contents thoroughly. The volume was made up to the mark with phosphate buffer pH 6.8 and filtered. One ml of the filtrate was suitably diluted and Terazosin Hydrochloride content was estimated at 245nm using a double beam UV-Visible Spectrophoto-meter. This procedure was repeated thrice and the average value was calculated. The results are presented in **Table 4**.

**Wetting Time [12]:** The tablets wetting time was measured by a procedure modified from that reported by Bi *et al*. The tablet was placed at the centre of two layers of absorbent paper fitted into a dish. After the paper was thoroughly wetted with distilled water, excess water was completely drained out of the dish. The time required for the water to diffuse from the wetted absorbent paper throughout the entire tablet was then recorded using a stopwatch. The results are presented in Table 4 and **Fig. 4**.

**Water absorption ratio [12]:** A piece of tissue paper folded twice was placed in a small Petri dish Containing 6 ml of water. A tablet was put on the tissue paper and allowed to completely wet. The wetted tablet was then weighted.

Water absorption ratio, R was determined using following equation.

$$R = 100 \times Wa - Wb/Wa$$

Where, Wa = Weight of tablet after water absorption, Wb = Weight of tablet before water absorption

The results are presented in Table 4 and **Fig. 5**.

***In- vitro* Disintegration Time [12]:** *In- vitro* Disintegration times for sublingual tablets were determined using USP tablet disintegration apparatus with phosphate buffer of pH 6.8 as medium. The volume of medium was 900 ml and temp was 37±2°C. The time in seconds taken for complete disintegration of the tablets with no palatable mass remaining in the apparatus was measured. The results are presented in Table 4 and **Fig. 6**.

***In-vitro* Dispersion Time [13, 14]:** *In- vitro* dispersion time was measured by dropping a tablet in a10ml measuring cylinder containing 6ml of buffer solution simulating saliva fluid (pH 6.8). The results are presented in Table 4 and **Fig. 7**.

***In- vitro* drug release study [12]:** *In-vitro* release rate of Terazosin Hydrochloride sublingual tablets was carried out using United State Pharmacopoeia (USP) dissolution testing apparatus (Paddle method). The dissolution test was carried out using 900 ml of 6.8 pH phosphate buffer, at 37±2$^{o}$C and 50 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus at 2, 5, 7, 10, 12 and 15 min. The samples were replaced with fresh dissolution medium of same quantity. The samples were filtered through Whatman filter paper No 40 and analyzed for Terazosin Hydrochloride after appropriate dilution by UV spectrophotometer at 245 nm. The percentage drug release was calculated using an equation obtained from the calibration curve. The results are presented in **Fig. 8-10**.

**Drug release kinetics:** To examine the release mechanism of Terazosin Hydrochloride from the prepared sublingual tablets, the results were analyzed according to the following equation;

$$\frac{M_t}{M} = k.t^n$$

Where $M_t$ / M is the fractional drug released at time *t*, *k* is a kinetic constant incorporating structural and geometrical characteristics of the drug/polymer

system [device] and *n* is the diffusional exponent that characterizes the mechanism of drug release. It is known that for non-swelling tablets, the drug release can generally be expressed by the Fickian diffusion mechanism, for which *n* = 0.5, whereas for most erodible matrices, a zero-order release rate kinetics is followed, for which *n* = 1. For non-Fickian release, the *n* value falls between 0.5 and 1.0 [0.5 < *n* < 1.0]; whereas in the case super case II transport *n* > 1.

The data of the *in-vitro* release was fit into different equations and kinetic models to explain the release kinetics of Terazosin Hydrochloride from sublingual tablets. The kinetic models used were Zero-order equation[15] (eq. 1), First-order equation [16] (eq. 2), Higuchi equation [17] (eq. 3) and Korsemeyer-Peppas equation [18] (eq. 4).

$Q_t = K_0 t$ ---------- (1)

$Q_t = Q_0 (1- e^{-k1}t)$ ---------- (2)

$Q_t = K_H.t^{1/2}$ ---------- (3)

$Q_t / Q_\infty = K_k\, t^n$ ---------- (4)

Where,

$Q_t$ ------- Is the amount of drug release in time t;

$Q_0$ ------- Is the initial amount of the drug;

n ------- Exponent value

and $K_0$, $K_1$, $K_H$, and $K_k$ are release rate constants for Zero-order, First-order, Higuchi, and Korsemeyer-Peppas model respectively.

Data of the *in-vitro* release was fit into different equations and kinetic models to explain the release kinetics of Terazosin Hydrochloride from sublingual tablets. The data are presented in **Table 5**.

## RESULTS AND DISCUSSION:

**Compatibility studies:** The incompatibility between the Drug and Excipients were studied by FTIR spectroscopy. The spectral data of pure drug and various drug-excipient mixtures are presented in **Fig. 1- 3**. The results indicate that there was no chemical incompatibility between drug and excipients used in formulation.

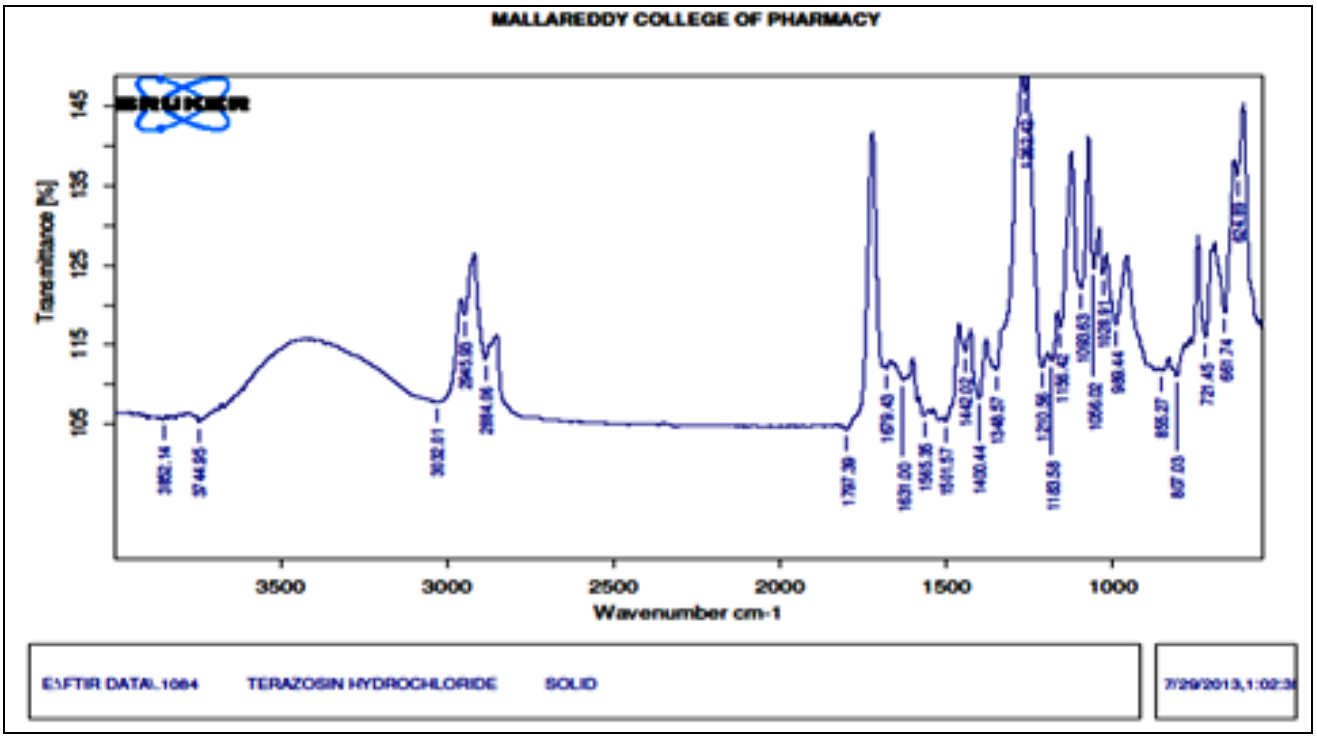


**FIG. 1: FTIR SPECTRUM OF SUCCESSFUL FORMULATION F6**

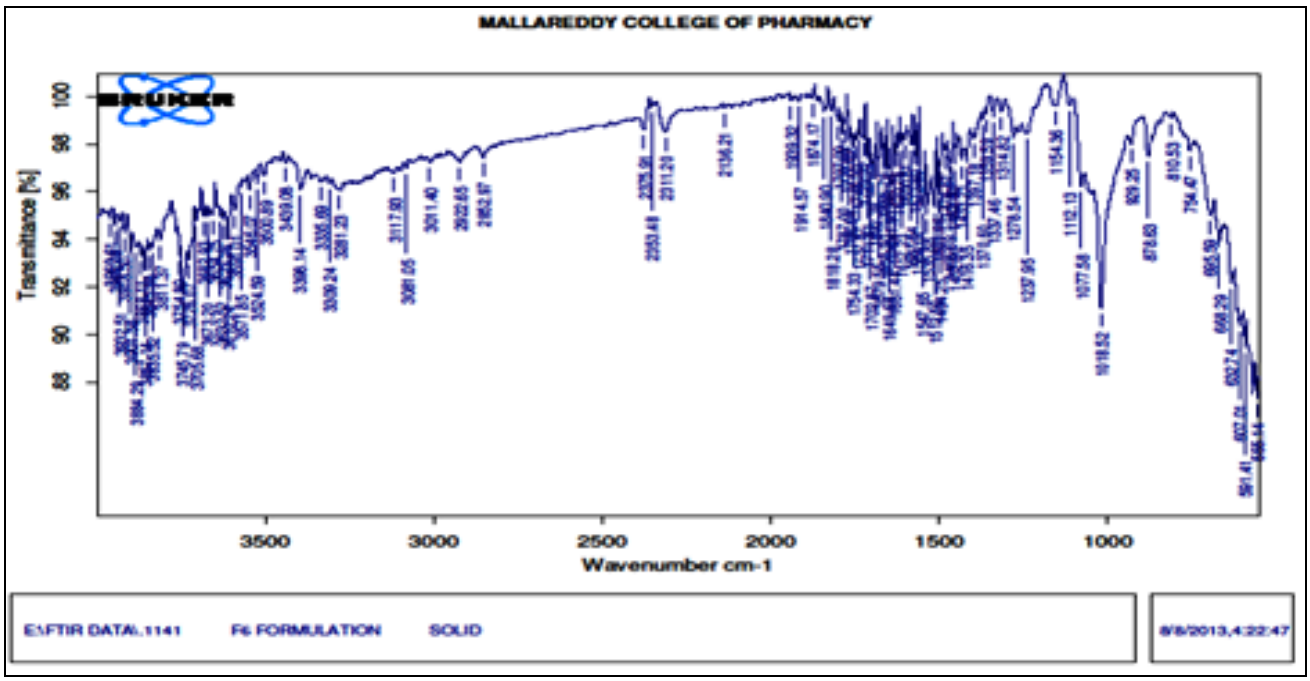


**FIG. 2: FTIR SPECTRUM OF SUCCESSFUL FORMULATION F6**

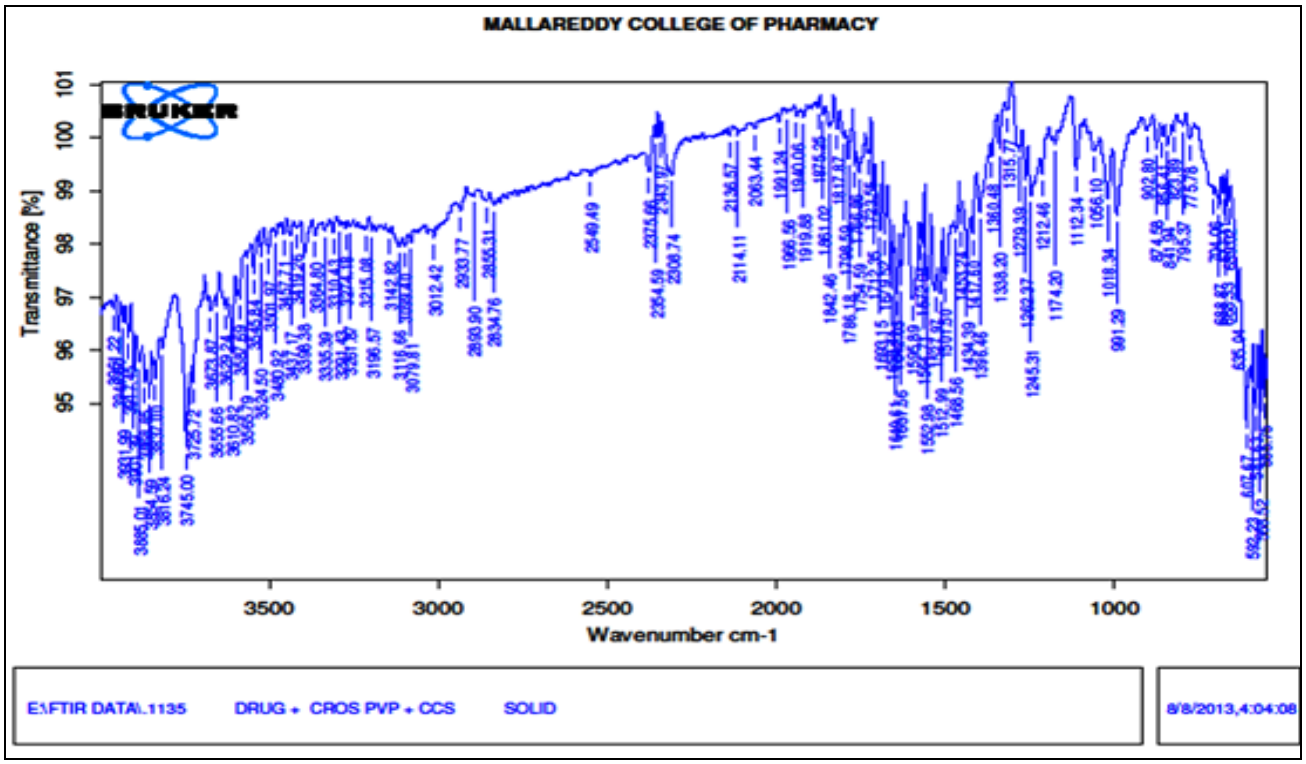


**FIG. 3: FTIR SPECTRUM OF DRUG - EXCIPIENTS**

**Preformulation studies:** Preformulation parameters of all formulations F01 to F18 are satisfactory. Bulk density, Tapped density, Angle repose, %compressibility (or) Carr's index, Hausner's ratio are within the limits. The results are shown in Table 02.

| | | |
|---|---|---|
| Bulk density (gm/ml) | : | 0.52 to 0.56 |
| Tapped density (gm/ml) | : | 0.62 to 0.65 |
| Angle of repose | : | 18.98 to 24.34 |
| %compressibility | : | 13.84 to 16.12 |
| Hausner's ratio | : | 1.16 to 1.19 |

The results obtained confirm that the batches which exhibit good flow properties have good packing characteristics.

**TABLE 2: PRECOMPRESSION STUDIES**

| Formulation code | Angle of Repose | Bulk density | Tapped density | Carr's index (%) | Hausner's ratio |
|---|---|---|---|---|---|
| **F1** | 22.38 | 0.53 | 0.62 | 14.51 | 1.16 |
| **F2** | 24.26 | 0.56 | 0.65 | 13.84 | 1.16 |
| **F3** | 19.68 | 0.54 | 0.63 | 14.28 | 1.16 |
| **F4** | 20.04 | 0.52 | 0.62 | 16.12 | 1.19 |
| **F5** | 20.67 | 0.55 | 0.65 | 15.38 | 1.18 |
| **F6** | 24.37 | 0.56 | 0.65 | 13.84 | 1.16 |
| **F7** | 23.87 | 0.54 | 0.63 | 14.28 | 1.16 |
| **F8** | 21.56 | 0.52 | 0.62 | 16.12 | 1.19 |
| **F9** | 24.34 | 0.55 | 0.65 | 15.38 | 1.18 |
| **F10** | 22.92 | 0.52 | 0.62 | 16.12 | 1.19 |
| **F11** | 23.46 | 0.53 | 0.62 | 14.51 | 1.16 |
| **F12** | 21.11 | 0.54 | 0.63 | 14.28 | 1.16 |
| **F13** | 19.52 | 0.55 | 0.64 | 14.06 | 1.16 |
| **F14** | 18.98 | 0.54 | 0.63 | 14.28 | 1.16 |
| **F15** | 21.38 | 0.55 | 0.65 | 15.38 | 1.18 |
| **F16** | 20.09 | 0.54 | 0.64 | 15.62 | 1.16 |
| **F17** | 23.59 | 0.55 | 0.64 | 14.06 | 1.16 |
| **F18** | 23.64 | 0.55 | 0.65 | 15.38 | 1.18 |

**Evaluation of sublingual tablets of Terazosin Hydrochloride:** The parameters of all formulations F01-F18 was found to be satisfactory and all were within pharmacopeias limits.

The Hardness for all formulations found to be 2.7kg/cm$^2$ to 3.3 kg/cm$^2$

The Thickness of tablet was found to be between 2mm to 2.2 mm.

The Friability was found to between 0.29% to 0.69 %.

The Weight variation was found to between 125±0.18 % to 125±0.67 %.

Assay values of the formulations were observed in the range of 97% to 102%.The results are shown in Table 3.

**TABLE 3: WEIGHT VARIATION, HARDNESS, THICKNESS, FRIABILITY OF MUCOADHESIVE SUBLINGUAL TABLETS OF TERAZOSIN HYDROCHLORIDE**

| Formulation code | Weight variation | Hardness (kg/ cm$^2$) | Thickness (mm) | Friability (%) |
|---|---|---|---|---|
| **F1** | ±0.33 | 3.1 | 2.1 | 0.63 |
| **F2** | ±0.37 | 2.9 | 2 | 0.31 |
| **F3** | ±0.62 | 3.2 | 2.1 | 0.69 |
| **F4** | ±0.58 | 3.2 | 2.2 | 0.29 |
| **F5** | ±0.45 | 3.3 | 2.1 | 0.46 |
| **F6** | ±0.18 | 3.1 | 2 | 0.39 |
| **F7** | ±0.53 | 3.3 | 2.1 | 0.47 |
| **F8** | ±0.67 | 3.1 | 2.2 | 0.39 |
| **F9** | ±0.29 | 2.9 | 2.1 | 0.60 |
| **F10** | ±0.65 | 3.3 | 2 | 0.39 |
| **F11** | ±0.51 | 3.2 | 2.2 | 0.56 |
| **F12** | ±0.26 | 3.0 | 2 | 0.37 |
| **F13** | ±0.62 | 3.1 | 2.2 | 0.69 |
| **F14** | ±0.39 | 2.7 | 2.2 | 0.34 |
| **F15** | ±0.58 | 3.3 | 2.1 | 0.67 |
| **F16** | ±0.43 | 3.0 | 2.0 | 0.62 |
| **F17** | ±0.31 | 3.3 | 2.1 | 0.55 |
| **F18** | ±0.23 | 3.2 | 2.0 | 0.32 |

**Water absorption ratio and Wetting time:** The wetting time and water absorption ratio which are the important criteria for determining the capacity of disintegrates to swell in presence of little water. By using different superdisintegrant the water absorption ratio and wetting time in the formulations F01 to F18 were found to be in the range of 32.10% to 39.01% and 67sec to 95 sec

respectively. The results are shown in **Table 4 and Fig. 4 and 5**. The best result has been shown by batch F6 tablets, it showed the water absorption ratio and wetting time was 39.01% and 67 seconds. Thus the results indicated that the preparation was more water absorption ratio and minimum wetting time, so it will take less time for disintegrating.

***In- vitro* disintegration time:** The disintegration time of sublingual tablets should be less because in a very short time it should be totally disintegrates. By using different superdisintegrant, disintegration time in the formulations F01 to F18 were found to be in the range of 61sec to 87 sec. The results are shown in Table 4 and **Fig. 6**. The best result has been shown by batch F6 tablets, it showed the disintegration time was 61seconds.In conclusion, with increase in concentration of superdisintegrant, disintegration time decreases.

***In- vitro* dispersion time:** The dispersion time of sublingual tablets should be less because in a very short time it should be totally dispersed. By using different superdisintegrant, dispersion time in the formulations F01 to F18 were found to be in the range of 112sec to 132 sec. The results are shown in Table 4 and **Fig. 7**. The best result has been shown by batch F6 tablets, it showed the dispersion time was 112 seconds. In conclusion, with increase in concentration of superdisintegrant, dispersion

**TABLE 4: WETTING TIME, WATER ABSORPTION RATIO, DISINTEGRATION TIME, *IN- VITRO* DISPERSION TIME AND DRUG CONTENT ASSAY OF TERAZOSIN HYDROCHLORIDE SUBLINGUAL TABLETS**

| Formulation Code | Wetting time (sec) | Water absorption ratio | Disintegration time (sec) | *In-vitro* Dispersion Time (sec) | Drug content Assay (%) |
|---|---|---|---|---|---|
| **F1** | 92 | 32.10 | 76 | 126 | 104 |
| **F2** | 89 | 35.58 | 75 | 122 | 102 |
| **F3** | 82 | 33.84 | 73 | 119 | 103 |
| **F4** | 76 | 37.03 | 69 | 115 | 97 |
| **F5** | 73 | 33.84 | 64 | 117 | 103 |
| **F6** | 67 | 39.01 | 61 | 112 | 102 |
| **F7** | 97 | 37.03 | 87 | 147 | 102 |
| **F8** | 87 | 32.10 | 83 | 141 | 98 |
| **F9** | 84 | 33.84 | 81 | 137 | 101 |
| **F10** | 72 | 35.58 | 79 | 132 | 102 |
| **F11** | 81 | 37.03 | 76 | 128 | 104 |
| **F12** | 86 | 33.84 | 72 | 124 | 98 |
| **F13** | 95 | 33.84 | 81 | 132 | 99 |
| **F14** | 86 | 32.10 | 78 | 129 | 104 |
| **F15** | 81 | 37.03 | 75 | 126 | 102 |
| **F16** | 76 | 32.10 | 72 | 122 | 98 |
| **F17** | 73 | 37.03 | 69 | 118 | 104 |
| **F18** | 72 | 35.58 | 67 | 115 | 101 |

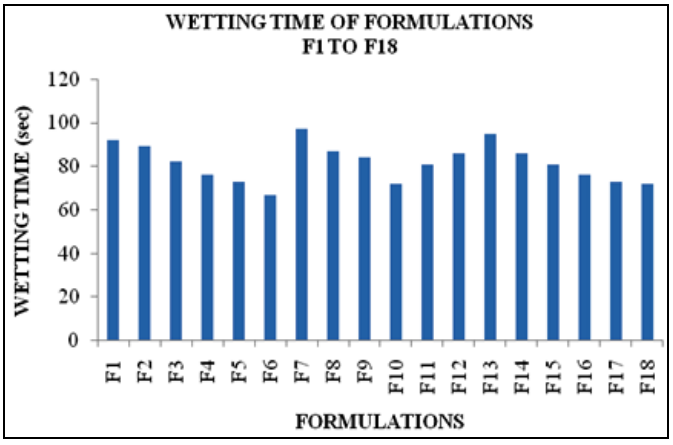


**FIG. 4: WETTING TIME PROFILE OF TERAZOSIN HYDROCHLORIDE FORMULATIONS F1 TO F18**

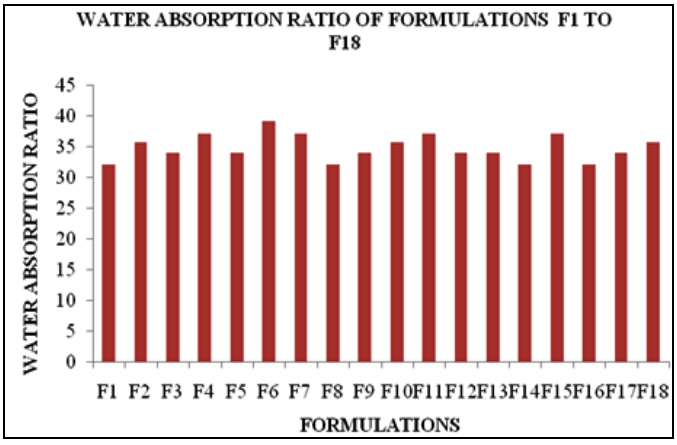


**FIG. 5: WATER ABSORPTION RATIO OF TERAZOSIN HYDROCHLORIDE FORMULATIONS F1 TO F18**

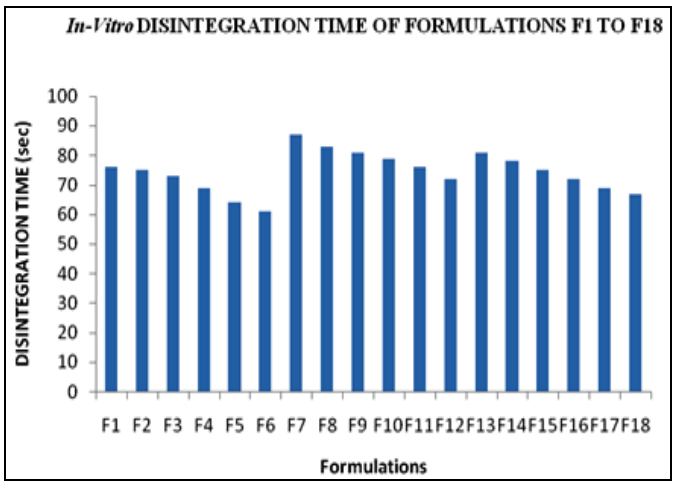


**FIG. 6: *IN-VITRO* DISINTEGRATION TIME OF TERAZOSIN HYDROCHLORIDE FORMULATIONS F1 TO F18**

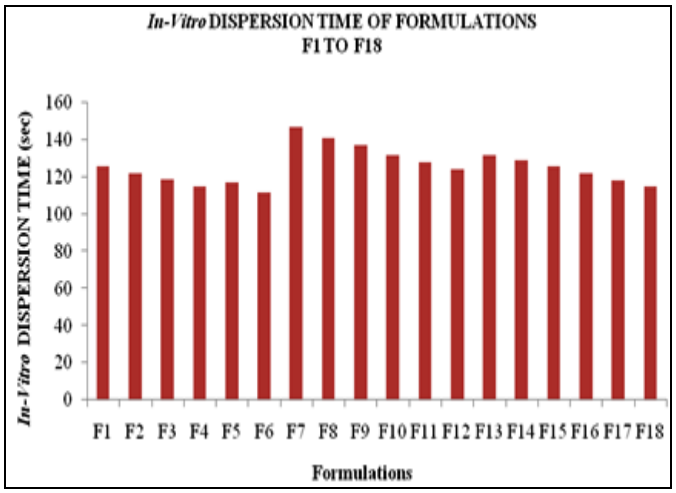


**FIG. 7: *IN-VITRO* DISPERSION TIME OF TERAZOSIN HYDROCHLORIDE FORMULATIONS F1 TO F18**

***In-vitro* dissolution study:** The *in-vitro* dissolution studies of all formulations (F1 to F18) were conducted and the results are shown in **Fig. 8-10**. The percentage of drug release for formulations, F1to F18 was found to be 11.14 % to 102% during 5min to 25 min. The maximum percentage of drug release was found to be 102% in formulation, F6 during 15 min.

From the above studies, it was observed that increase in concentration of superdisintegrant i.e. Crosspovidone, the percentage of drug release increased. Among the all formulations (F1 to F18), the best *in-vitro* drug release observed in formulation, F6 was found to be 102%, as increase the concentration of Crosspovidone that is due to result of rapid disintegration. During the dissolution studies, it was observed that the tablets were initially swelled and erodible over period of time.

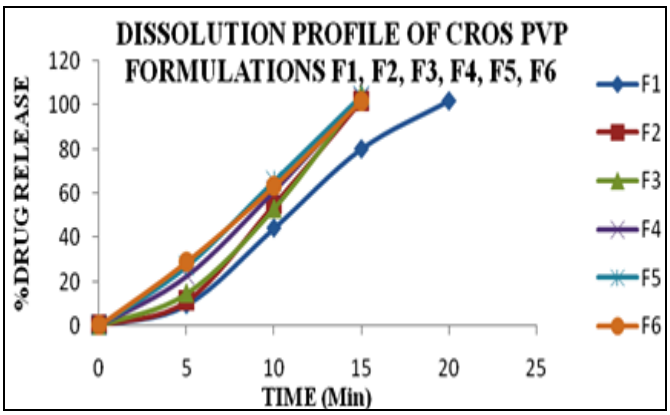


**FIG. 8: DISSOLUTION PROFILE OF CROSS-POVIDONE FORMULATIONS F1-F6**

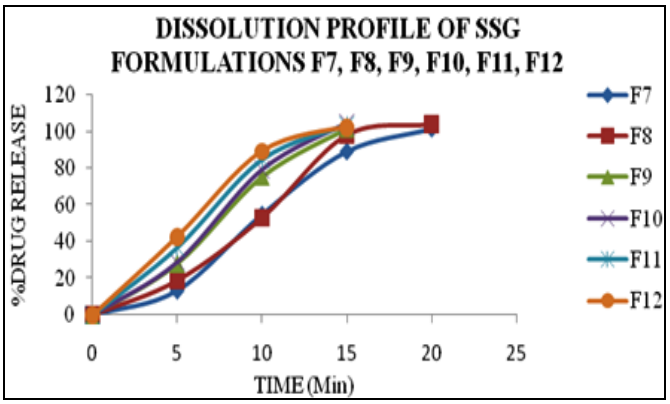


**FIG. 9: DISSOLUTION PROFILE OF SSG FORMULATIONS F7-F12**

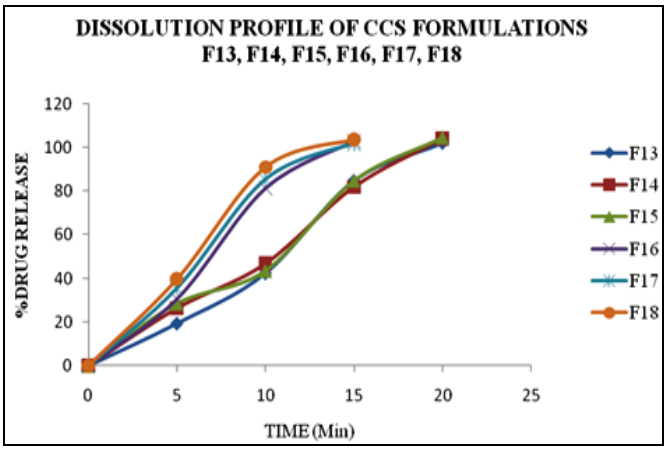


**FIG. 10: DISSOLUTION PROFILE OF CCS FORMULATIONS F13-F18**

**Drug release kinetic studies**: The *in-vitro* drug release data of all Terazosin Hydrochloride sublingual tablets were subjected to goodness of fit test by linear regression analysis according to Zero order equation, 1st order equation, Higuchi's equation and Korsemeyer-Peppas equation to ascertain the mechanism of drug release. The results of linear regression analysis including regression coefficient are presented in **Table 5**.

Among the regression correlation co-efficient ($R^2$) values of zero order equation was found to be higher, similarly among the Higuchi's equation and Korsemeyer-Peppas equation, the ($R^2$) values of Higuchi's equation was found to be higher. Hence the drug release followed the zero order release kinetics with diffusion mechanism.

**TABLE 5: REGRESSION ANALYSIS OF FORMULATIONS F1 TO F18**

| S. No. | Formulation Code | Release Kinetics | | | |
|---|---|---|---|---|---|
| | | Zero Order($R^2$) | First Order ($R^2$) | Higuchi ($R^2$) | Korsemeyer Peppas ($R^2$) |
| **1** | **F1** | 0.973 | 0.866 | 0.823 | 0.972 |
| **2** | **F2** | 0.943 | 0.858 | 0.755 | 0.990 |
| **3** | **F3** | 0.946 | 0.898 | 0.762 | 0.999 |
| **4** | **F4** | 0.982 | 0.934 | 0.840 | 0.999 |
| **5** | **F5** | 0.993 | 0.946 | 0.876 | 0.999 |
| **6** | **F6** | 0.995 | 0.967 | 0.888 | 0.999 |
| **7** | **F7** | 0.951 | 0.880 | 0.911 | 0.968 |
| **8** | **F8** | 0.960 | 0.938 | 0.867 | 1.000 |
| **9** | **F9** | 0.986 | 0.914 | 0.899 | 0.977 |
| **10** | **F10** | 0.983 | 0.903 | 0.899 | 0.972 |
| **11** | **F11** | 0.975 | 0.919 | 0.939 | 0.963 |
| **12** | **F12** | 0.956 | 0.923 | 0.959 | 0.949 |
| **13** | **F13** | 0.979 | 0.984 | 0.857 | 0.986 |
| **14** | **F14** | 0.994 | 0.999 | 0.899 | 0.979 |
| **15** | **F15** | 0.983 | 0.989 | 0.888 | 0.924 |
| **16** | **F16** | 0.9784 | 0.903 | 0.910 | 0.964 |
| **17** | **F17** | 0.968 | 0.910 | 0.933 | 0.910 |
| **18** | **F18** | 0.898 | 0.942 | 0.942 | 0.939 |

**CONCLUSION:** An optimized formulation of Terazosin Hydrochloride sublingual tablets was found and prepared in this study by direct compression method. The best *in-vitro* drug release observed in formulation F6 was found to be 102% which contain the drug Terazosin Hydrochloride and Crospovidone as superdisintegrant agent with other excipients. The formulation F6 was found to be best among all other formulations because it has exhibited good wetting time, water absorption ratio, faster disintegration time and *in-vitro* dispersion time when compared to other formulations.

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