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# FORMULATION AND EVALUATION OF ALMOTRIPTAN ORAL DISINTEGRATING TABLETS

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## ABSTRACT

Over the past three decades, orally disintegrating tablets(ODTs) have considerable attention as a preferred alternative to conventional tablets and capsules due to better patient compliance. United States Food and Drug administration (FDA) defined ODT as " A Solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually with in a matter of seconds when placed upon the tongue". Almotriptan is an extremely potent member of triptan class drugs which is widely used in the treatment of migraine. It shows high bioavailability, rapid action with fewer side effects when compared to other drugs of the same class. The present study is aimed to develop an oral disintegrating solid dosage form of Almotriptan which disintegrates rapidly without the need of water or chewing and release its drug instantaneously showing rapid action for sudden attacks of migraine with good patient compliance for all age groups. Crosspovidone & SSG were selected as super disintegrants. FTIR studies were carried out to confirm the drug excipients compatability. Pre compression evaluation tests and post compression evaluation tests were also carried out as the tablets are ODTs wetting time and water absorption studies were also carried out. The evaluation results confirmed that the crosspovidone is more suitable to SSG and Almotriptan can be best formulated as ODT using crosspovidone.

**KEYWORDS:** Over the past three decades, ODT using crosspovidone.

## INTRODUCTION

Orally disintegrating tablets have been developed and new ODT technologies compensate many pharmaceuticals and patients needs, ranging from enhanced life-cycle management to convenient dosing for pediatric, geriatric, and psychiatric patients with dysphasia.[1] Over the past three decades, orally disintegrating tablets(ODTs) have considerable attention as a preferred alternative to conventional tablets and capsules due to better patient compliance[2] Orally disintegrating tablets are similar to melts and are designed to disperse in the mouth and to be washed down with saliva. United States Food and Drug administration (FDA) defined ODT as " A Solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually with in a matter of seconds when placed upon the tongue"[3,4] Orally disintegrating tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people. The disintegration time for ODTs generally ranges from several seconds to about a minute. As like sub-lingual, buccal and melts, orally disintegrating tablets require an adequate amount of saliva production.[5,6]

Almotriptan is an extremely potent member of triptan class drugs which is widely used in in the treatment of migraine. It shows high bioavailability, rapid action with fewer side effects when compared to other drugsof the same class. The present study is aimed to develop an oral disintegrating solid dosage form of Almotriptan which disintegrates rapidly without the need of water or chewing and release its drug instantaneously showing rapid action for sudden attacks of migraine with good patient compliance for all age groups.

### Advantages[7,8]

1. Pregastric absorption leading to increased bioavaibility/rapid absorption of drugs from mouth, pharynx and oesophagus as saliva passes down to stomach, also avoids hepatic metabolism.
2. Convenient for administration to traveling patients and busy people who do not have accesses to water.
3. Excellent mouths feel property produced by use of flavours and sweetners help to change the perception of "medication as bitter pill" especially in pediatric population.
4. Fast disintegration of tablets leads to quick dissolution and rapid absorption which may produce rapid onset of action.
5. ODTs offer all the advantages of solid dosage forms and liquid dosage forms.
6. Convenience of administration and accurate dosing compared to liquids.

## MATERIALS

Almotriptan was obtained from Chandra labs, Hyd. Remaining All the chemicals were purchased from S.D fine chemicals.

## METHODS

Compatibility studies: The compatibility of Almotriptan with different excipients was tested using FT-IR Spectrophotometer.

### Solubility

Solubility studies were carried out to select a suitable solvent like water, Dichloromethane, Methanol to dissolve the drug and to select the dissolution medium.

### Calibration Curve of Almotriptan in 0.1n Hcl

### Preparation of Stock solution

The standard stock solution containing 1 mg/ml of Almotriptan drug was prepared.

The absorbances on x-axis were plotted against the concentrations on y-axis and $r^2$ value was obtained.

**Table 1: Formulations of Almotriptan oral disintegrating tablets by Direct compression method formulation design.**

| | Formulations Code | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Ingredients (mg) | **F1** | **F2** | **F3** | **F4** | **F5** | **F6** | **F7** | **F8** | **F9** |
| Almotriptan | 6.25 | 6.25 | 6.25 | 6.25 | 6.25 | 6.25 | 6.25 | 6.25 | 6.25 |
| Crospovidone | - | 3 | 5 | 7 | 9 | - | - | - | - |
| SSG | - | - | - | - | - | 3 | 5 | 7 | 9 |
| Mannitol | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 | 50 |
| Avicel PH 102 (MCC) | 37.25 | 34.25 | 32.75 | 30.25 | 28.25 | 34.25 | 32.75 | 30.25 | 28.25 |
| Magnesium stearate | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 |
| Aspartame | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 | 5 |
| Total weight (mg) | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |

The Almotriptan oral disintegrating tablets were prepared by Direct compression technique, All ingredients are passed through sieve no.40. Required quantity of each ingredient is taken for each specified formulation and all ingredients were mixed. the powder blend was subjected to dying for removal of moisture content if any and then subjected to tablet compression by using Round and flat faced 8mm punches in CADMACH 16 punches tablet punching machine.

**Precompression parameters of tablet blend**

**Angle of repose:** A funnel with 10 mm inner diameter of stem was fixed at a height of 2 cm. over the platform. About 10 gm of sample was slowly passed along the wall of the funnel. A rough circle was drawn around the pile base and the radius of the powder cone was measured.

$\text{Tan } \theta = h / r$

$\theta = \text{Tan}^{-1} h / r$

Where θ = angle of repose,

h = height, r = radius

**Untapped density:** Untapped density of the drug was determined by pouring (pre seived 40-mesh) gently 25 gm of sample through a glass funnel into a 100 ml graduated cylinder. Then after pouring the powder bed was made uniform without disturbing. Then the volume was measured directly from the graduation marks on the cylinder in ml. The volume measured was called as the untapped volume and the untapped density was calculated by following formula.

**Untapped density** = weight of sample in gram /volume occupied by the sample

**Bulk density:** Bulk density of the drug was determined by pouring gently 25 gm of sample through a glass funnel into a 100 ml graduated cylinder. The cylinder was tapped for 10 times from height of 1 inches and the volume obtained was noted, Bulk volume and the Bulkdensity was calculated by following formula.

**Bulk density** = Wt. of sample in gm / bulk volume

**4. Measures of Powder Compressibility (Carr's compressibility index)**

$$\text{Carr's index} = \frac{\text{Tapped desnity} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

**5. Hausne's ratio:** Hausner's ratio provides an indication of the degree of densification which could result form vibration of the feed hopper. A lower value of indicates better flow and vice versa.

Hausner Ratio = Bulk Density / Untapped Density

**Table 2: Compressibility Index and Hausner's ratio.**

| Compressibility Index (%) | Flow Character | Hauser's Ratio |
|---|---|---|
| 10 | Excellent | 1.00–1.11 |
| 11–15 | Good | 1.12–1.18 |
| 16–20 | Fair | 1.19–1.25 |
| 21–25 | Passable | 1.26–1.34 |
| 26–31 | Poor | 1.35–1.45 |
| 32–37 | Very poor | 1.46–1.59 |
| >38 | Very, very poor | >1.60 |

**Relation of flow property with HR & CI:** ***C.I=tapped-untapped*100/tapped***

**Post compression parameters evaluation** The Formulated ODT's were evaluated for weight variation, Hardness, Friability, Thickness, Content uniformity, Disintegration time, Water absorption ratio, and *in-vitro* drug release.

**1. Weight variation:** 20 tablets were weighed individually and average weight of tablet was calculated, then % weight varaiation was calculated.

**2. Hardness:** 20 tablets were selected randomly from each formulation and Hardness was measured using Monsanto hardness tester.

**3. Friability:** 10 tablets were selected randomly from each formulation and fraiability test was performed using Roche friabilator.

**4. Content uniformity test:** 5 tablets were powdered and dissolved in 100ml 0.1NHcl, filtere and dilute sample were taken and measured for its absorbance at 232nm using a UV-Visible spectrophotometer.

**5. Disintegration Time:** 6 Tablets were placed in the disintegrating apparatus or a disintegrator having pH 6.8 phosphate buffer solution at 37±.0.5$^0$c Time required for complete dispersion of a tablet was measured.

**6. Wetting time and Water Absorption Ratio:** A small volume (8ml) of water containing the water soluble dye, Rhodamine B (0.1g) was taken in a petridish. A Whatman filter paper disk folded once diametrically was placed in that petridish. The tablet was carefully placed on the filterpaper. The time for complete wetting of the tablet was measured. The appearance of the dye on the surface of the tablet was taken as a sign for complete wetting. The Wetted tablet was then weighed and Water absorption ratio, R, was determined.

**7. In-vitro Release Studies**: The *in-vitro* drug release studies were carried out in an USP Type I (Basket) dissolution apparatus using 0.1N HCl as dissolution medium. The volume of the medium in the dissolution apparatus was maintained at 900ml. The stirring rate was 50

rpm and the temperature was maintained at 37±0.5oC. Aliquots of dissolution medium were withdrawn at predetermined time intervals and the same volume of medium was replaced maintain the constant volume.

## RESULTS AND DICUSSIONS

### UV-Spectroscopy - Analysis of drug

### Ultraviolet Visible (UV-visible) spectroscopy

Drug sample showed wavelength of maximum absorption (λ-max) 232 nm.

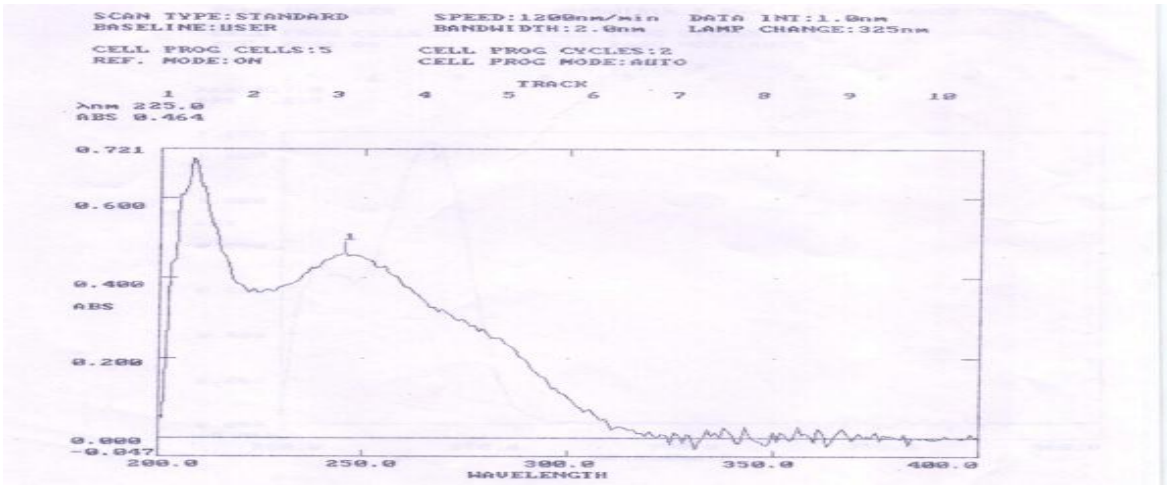


**Fig. 1: Ultraviolet Visible Spectroscopy Almotriptan graph.**

### Calibration Curve Data of Almotriptan in 0.1n Hcl

Wavelength of maximum absorption: 232 nm.

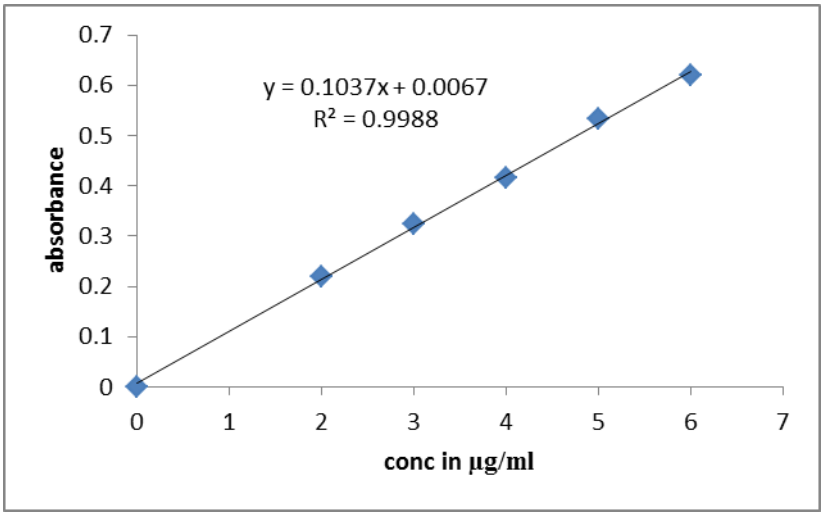


**Fig. 2: Calibration curve graph.**

**Drug-excipients Compatibility studies**

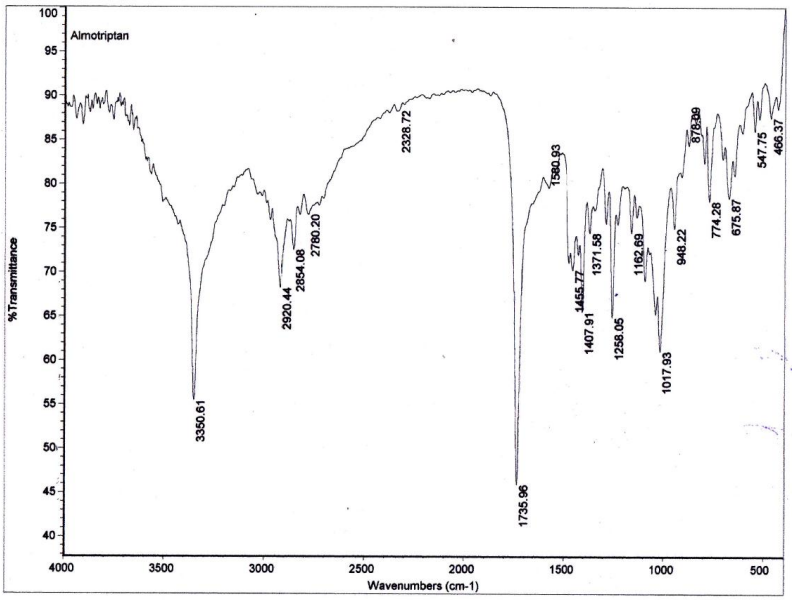


**Fig. 3: FT-IR Spectra of Almotriptan pure drug.**

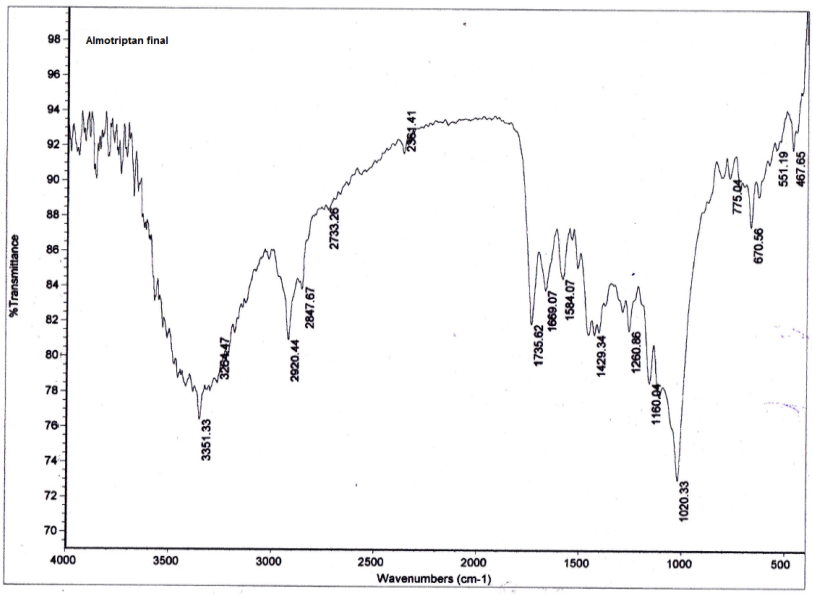


**Fig. 4: FT-IR Spectra of Almotriptan with excipients.**

**Micromeritic Properties: (Pre-compression)**: Almotriptan powder blends were evaluated for untapped density (0.22 to 0.28 gm/cc), Bulk density (0.313 to 0.393 gm/cc), Hausner's ratio (1.10 to 1.28), Compressibility index (15.4 to 19.5%) and the Angle of repose ranged from ($25.54^0$ to $29.82^0$). this values are given in table no:3.

**Table 3: Evaluation of Pre-compression Parameter of Tablet blend.**

| Formulation | Untapped Density* (g/cc) ±SD | Bulk Density* (g/cc)±SD | Hausner ratio* ±SD | Compressibility index* (%)±SD | Angle of repose(ɵ) ±SD |
|---|---|---|---|---|---|
| **F1** | 0.223±0.063 | 0.381±0.057 | 1.25±0.155 | 18.1±0.556 | 27.47±0.688 |
| **F2** | 0.251±0.043 | 0.324±0.040 | 1.23±0.253 | 15.4±0.305 | 25.63±0.287 |
| **F3** | 0.262±0.066 | 0.359±0.049 | 1.27±0.212 | 18.2±0.208 | 27.54±0.168 |
| **F4** | 0.242±0.068 | 0.356±0.061 | 1.10±0.221 | 16.7±0.401 | 28.23±0.425 |
| **F5** | 0.285±0.064 | 0.393±0.053 | 1.21±0.389 | 19.5±0.251 | 27.21±0.458 |
| **F6** | 0.250±0.068 | 0.338±0.059 | 1.28±0.120 | 17.2±0.386 | 25.38±0.446 |
| **F7** | 0.268±0.050 | 0.313±0.049 | 1.22±0.293 | 18.8±0.256 | 26.46±0.541 |
| **F8** | 0.287±0.087 | 0.367±0.067 | 1.19±0.250 | 17.6±0.258 | 29.71±0.181 |
| **F9** | 0.236±0.068 | 0.318±0.055 | 1.26±0.096 | 15.8±0.287 | 28.82±0.510 |

**DISCUSSION**

All blends were having almost same bulk density and Angle of repose values. The values of the compressibility index and angle of repose were well correlated to the free flow of the blends.

**Post compression parameters**

**Table 4: Evaluation of post-compression parameters.**

| Formulation | Hardness ($kg/cm^2$)±SD | Friability (%)±SD | Weight varaiation %±SD | Thickness (mm)±SD | Drug content(%)±SD |
|---|---|---|---|---|---|
| **F1** | 3.5±0.286 | 0.39±0.030 | 0%±0.95 | 2.20±0.098 | 98.60±0.981 |
| **F2** | 3.0±0.280 | 0.36±0.040 | 1%±0.78 | 2.21±0.017 | 97.36±0.844 |
| **F3** | 3.5±0.248 | 0.40±0.062 | 2%±0.47 | 2.16±0.050 | 98.18±0.745 |
| **F4** | 3.9±0.246 | 0.38±0.025 | 2%±0.89 | 2.11±0.090 | 99.17±0.947 |
| **F5** | 3.5±0.486 | 0.35±0.061 | 0%±0.35 | 2.19±0.030 | 99.58±0.743 |
| **F6** | 2.5±0.173 | 0.31±0.045 | 2%±0.74 | 2.13±0.050 | 98.26±0.823 |
| **F7** | 2.5±0.115 | 0.36±0.026 | 1%±0.53 | 2.20±0.070 | 97.35±0.935 |
| **F8** | 3.3±0.218 | 0.35±0.047 | 0%±0.87 | 2.18±0.068 | 98.16±0.896 |
| **F9** | 3.5±0.162 | 0.42±0.052 | 1%±0.98 | 2.14±0.101 | 99.05±0.974 |

**DISCUSSION**

The weight varation test results indiacate that all formulation were with in the USp weight varaiation test tolerance limit. Hardness of all the tablets was found to be between 2.5 to 4.0 $kg/cm^2$, indiacting optimum hardness of all formulations while the friability of the tablets ranged from 0.31 to 0.42% indiacting the tablets had enough hardness and friability to withstand stress and were mechanically stable during handling and transportation. The content uniformity of all the formulations were ranged 97.35% to 99.58% w/w the values are given in table: 4.

The Disintegration time of all the formulations ranged from 13 to 35 seconds, the wetting time values ranged from 18 to 25 seconds the values are given in table 5.

**Table 5: Wetting & Disintegrating Time (Sec).**

| Formulation | Wetting time(sec) | Disintegration time(sec) |
|---|---|---|
| **F1** | 23 | 35 |
| **F2** | 19 | 18 |
| **F3** | 24 | 16 |
| **F4** | 25 | 13 |
| **F5** | 23 | 19 |
| **F6** | 21 | 26 |
| **F7** | 24 | 19 |
| **F8** | 20 | 18 |
| **F9** | 18 | 21 |

**Table 6: % Cummulative Drug release profile *In-vitro* drug release.**

| | Percentage Drug Release | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Time in min** | **F1** | **F2** | **F3** | **F4** | **F5** | **F6** | **F7** | **F8** | **F9** |
| 0 | 0 | 0 | 0 | **0** | 0 | 0 | 0 | 0 | 0 |
| 5 | 4.89 | 60.93 | 61.72 | **65.47** | 62.12 | 48.51 | 52.24 | 50.23 | 48.61 |
| 10 | 9.12 | 71.20 | 78.65 | **83.02** | 80.45 | 50.12 | 66.61 | 62.82 | 60.10 |
| 15 | 16.89 | 83.96 | 105.81 | **101.03** | 100.30 | 78.82 | 85.26 | 84.68 | 83.83 |
| 30 | 21.08 | 89.06 | 105.90 | **101.01** | 100.80 | 89.42 | 94.61 | 90.28 | 89.54 |

## DISCUSSION

It was observed that as the super disintegrant concentration increases % of drug release with in 5 min was increased. This result was followed upto 7% of the super disintegrant concentration only, Beyond which the % dreug dissolved got reduced. F1 formulation without super disintegrant shown only 21.08% drug release in 30min, F2 to F5 formulations crosspovidone as the superdisintegrant at a concentration of 3,5,7 and 9% shown *in-vitro* dissolution values ranged from 60.93-89.06%, 61.72 -105.90%, 65.47 -101.03% and 62.12 – 100.80% respectively F6 to F9 formulation having SSG as the superdisintegrant at a concentration of 3,5,7,9% shown *in-vitro* dissolution values ranged from 48.51-89.42%, 52.24 – 94.61%, 50.23 -90.28%, and 48.61-89.54% respectively. Among all F4 formulation containing 7% crosspovidone as super disintegrant shown faster release with in 5min and 100% release with in 15min. hence F4 can be considered as optimum formulation showing better dissolution profile.

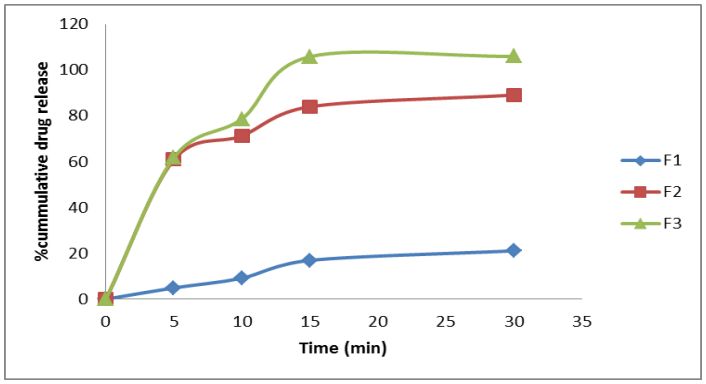


**Fig: 5 % Cummulative Drug Release (F1,F2,F3).**

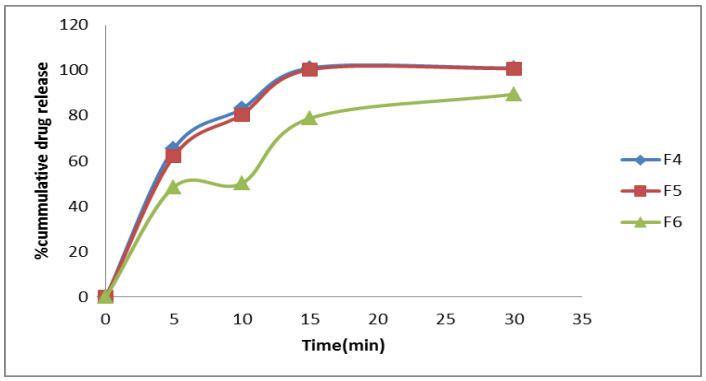


**Fig: 6 % Cummulative Drug Release (F4,F5,F6).**

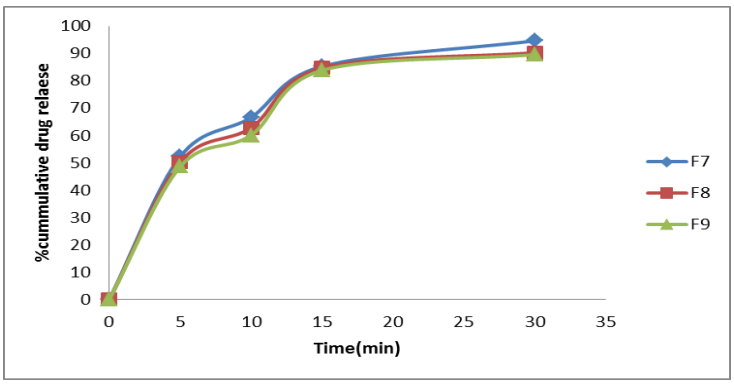


**Fig: 7 % Cummulative Drug Release (F7,F8,F9).**

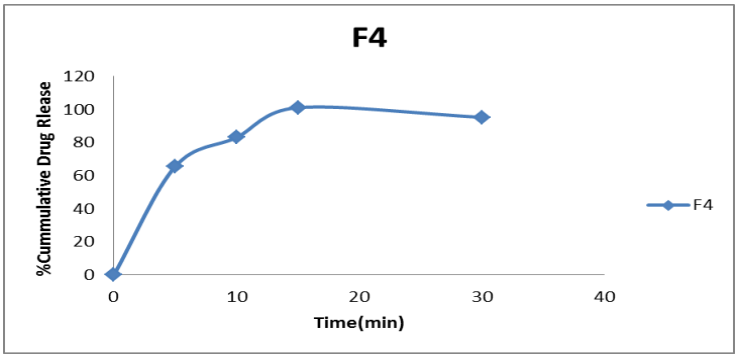


**Fig: 8 % Cummulative Drug Release (F4).**

## CONCLUSION

In the present study 9 formulation were prepared where F1 have no disintegrant, F2 to F5 were having crosspovidone as super disintegrant at the concentration of 3%, 5%,7%,9% respectively. F6 to F9 were having SSG as super disintegrant at the concentration of 3%, 5%, 7%,9% respectively. The results indicate that super disintegrants showed concentration dependent disintegration upto 7%. Among all F4 formulation showed least disintegrantion time and faster and higher amount of drug release and complete release of drug with in 15min indicating among Crosspovidone and SSG, the super disintegrant Cross povidone is more preferable at the concentration of 7% beyond which as the results for not improved. The concentration of 7% was optimised, hence formulation F4 is considered as optimum formulation as Almotriptan ODT.

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