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FORMULATION AND *IN VITRO* EVALUATION OF SUMATRIPTAN SUCCINATE FAST DISSOLVING TABLETS

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ABSTRACT

Recent development in Fast disintegration tablets have brought convenience in dosing to elderly and children who have trouble in swallowing tablets. The objective of the present study was to prepare the Fast disintegration tablets of sumatriptan succinate, an anti migrane drug. As precision of dosing and patient compliance become an important prerequisite for a migrane treatment, there is a need to develop a formulation for this drug which overcomes problems such as difficulty in swallowing, inconvenience in administration while travelling and patient's acceptability. Hence, the present work was undertaken with a view to develop a fast disintegration tablet of sumatriptan succinate which offers a new range of product having desired characteristics and intended benefits. Various techniques like direct compression and sublimation technique were used to formulate Fast disintegration tablets of sumatriptan succinate. In direct compression method and sublimation method the effect of various super disintegrants was studied, among these 4% cross povidone showed better drug release. The tablets were evaluated for hardness, friability, weight variation, wetting time, disintegration time and uniformity of content. Optimized formulations were evaluated for *in-vitro* dissolution test. Amongst all the techniques sublimation technique was found to be most successful and tablets prepared by this technique (F12) had disintegration time of 30 sec. and % CR 52.74±1.42 after 5 min.

KEYWORDS: Sumatriptansuccinate, superdisintegrants, directs compression technique, sublimation technique and, mouth disintegration tablets.

1. INTRODUCTION

1.1 ORAL DRUG DELIVERY

Oral drug delivery is the most desirable and preferred method of administering therapeutic agents for their systemic effects.

1.2 CLASSIFICATION OF TABLETS (USP CLASSIFICATION)[3]

A. According to drug release rate from the tablet (USP classification):

a) Immediate release (Conventional) tablet*:*

The tablet is intended to be released rapidly after administration, or the tablet is dissolved and administered as solution. It is the most common type and includes:

1. Disintegrating tablet
2. Chewable tablet
3. Sublingual tablet
4. Buccal tablet
5. Effervescent tablet

b) Modified-release tablet:

They have release features based on; time, course or location. They must be swallowed *intact.*

1. Extended-release tablet: Allowing the reduction in dosing frequency.
2. Delayed-release tablet: Drug release is delayed due to physiological conditions e.g. pH (a lag period followed by normal release).

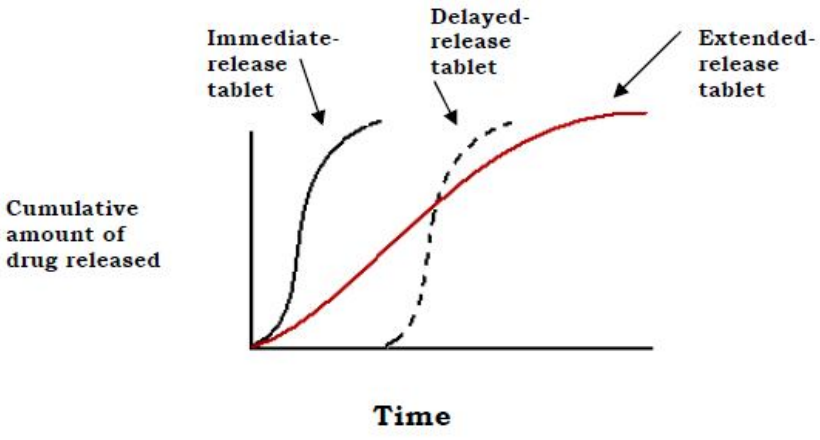

Fig.1: Comparative dissolution profiles of an immediate release and modified release tablet.

B) According to method of manufacturing:

a) Compressed tablet:

It is obtained by compressing uniform volume of particles using "Tablet compression machine". It is used for large-scale production.

b) Molded tablet:

Molding means shaping and hardening of semi-solid mixture of drug and excipients. It is obtained using "tablet mold". It is restricted for small-dose tablet and small-scale production.

Various classes of tablets are present in the market, each having their own advantages and disadvantages.

1.3 Advantages

1. Tablets are easy to use, handle and carry by the patient.
2. Tablets provide prolonged stability to medicament.
3. Tablets are attractive and elegant in appearance.

1.4 Disadvantages

1. Drugs that are amorphous in nature or have low density character are difficult to compress into tablet.
2. Hygroscopic drugs are not suitable candidate for compressed tablets.
3. Drugs having bitter taste and unpleasant odour requires special treatment like coating or encapsulation which may increase their production cost.

The Center for Drug Evaluation and Research (CDER), US FDA defined Oral Disintegrating Tablets (ODT) as “A solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue.”

1.5. Limitations of fast dissolving tablet[20,21]

1. The tablets usually have insufficient mechanical strength; hence, careful handling is required.
2. The tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly.
3. Drugs with relatively larger doses are difficult to formulate into MDT e.g. antibiotics like ciprofloxacin with adult dose tablet containing about 500 mg of the drug.

2. MATERIALS AND METHODS

2.1 MATERIALS

The following materials of Pharma grade or the best possible laboratory reagent were used as supplied by the manufacturer. The double distilled water was used in all the experiments.

Table No.3: LIST OF MATERIALS

S.NO	MATERIALS	CATEGORY	MANUFACTURED BY
1	SUMATRIPTAN	Anti migrane	Spectrum pharma research solutions, Mumbai
2	SODIUM STARCH GLYCOLATE	Super disintegrant	SD fine chemicals, Mumbai
3	CROSS CARMELLOSE SODIUM	Super disintegrant	SD fine chemicals, Mumbai
4	CROSS POVIDONE	Super disintegrant	SD fine chemicals, Mumbai
5	MAGNESIM STEARATE	Lubricant	Central drug house (p) ltd, New Delhi
6	TALC	Glidant	SD fine chemicals, Mumbai
7	CAMPHOR	Sublimating agent	Central drug house (p) ltd, New Delhi
8	ASPARTAME	Sweetening agent	SD fine chemicals, Mumbai
9	DI POTASSIUM HYDROGEN PHOSPHATE	Buffering agent	Finar chemicals ltd, Ahmedabad
10	SODIUM HYDROXIDE	Buffering agent	Finar chemicals ltd, Ahmedabad

2.2 METHODS

2.2.1 Preformulation studies

Preformulation testing is the first step in the rationale development of dosage form of a drug substance. It can be defined as an investigation of physical and chemical properties of a drug substance alone and when combined excipients. It gives extensive information to bring out good quality at high standard at which optimal dosage desired. Preformulation studies were performed on the drug (API), which included solubility and compatability studies.

The following preformualtion studies were performed for Sumatriptan succinate and polymers.

1) Determination of solubility

Solubility of sumatriptan succinate was performed in solvents like water, methanol and ethanol.

2) Determination of λmax of sumatriptan succinate

Principle: Sumatriptan succinate is reported to exhibit λ max at 282 nm.

Procedure

50 mg of Sumatriptan succinate was accurately weighed and dissolved in 50 ml methanol to get a stock solution of 1 mg/ml. Further, an aliquot was pipette out and diluted suitably to get the concentration in the Beer's range. The aliquot was scanned in the wavelength region of 250-350 nm to record the wavelength of maximum absorption (λ max).

3) Calibration curve for sumatriptan succinate

a) Preparation of standard graph of sumatriptan succinate in distilled water

Accurately weighed amount (25 mg) of the drug was dissolved in distilled water in 100 ml volumetric flask and the volume was made up to 100ml. from this stock solution 10ml is withdrawn in to volumetric flask, made the volume up to 100ml withdistilled water. From this 2nd stock solution (100mcg/ml), concentrations of 10,20,30,40,50, 60µg/ml solutions were prepared and the corresponding absorbance of the solutions was measured at 282 nm in a UV/Visible spectrophotometer.

b) Preparation of standard graph of sumatriptan succinate in pH 6.8 phosphate buffer

Accurately weighed amount (25 mg) of the drug was dissolved in pH6.8 phosphate buffer in 100 ml volumetric flask and the volume was made up to 100ml. From this stock solution 10ml is withdrawn in to volumetric flask, made the volume up to 100ml with pH 6.8 buffer.

From this 2nd stock solution (100mcg/ml), concentrations of 10,20,30,40,50, 60µg/ml solutions (Table No.12) were prepared and the corresponding absorbance was measured at 282 nm in a UV/Visible spectrophotometer (Fig No.3).

4) Drug - excipient compatability studies by FT-IR

Excipients are integral components of almost all pharmaceutical dosage forms. The successful formulation of a stable and effective solid dosage form depends on the careful selection of the excipients, which are added to facilitate administration, promote the consistent release and bioavailability of the drug and protect it from degradation.

FT-IR spectroscopy is one of the most powerful analytical techniques to identify functional groups of a drug.In the preparation of the tablet formulation, drug and polymer may interact as they are in close contact with each other, which could lead to instability of the drug.

Preformulation studies regarding the drug – polymer interaction are therefore very critical in selecting appropriate polymers. FT- IR spectroscopy was employed to ascertain the compatability between the sumatriptan succinate and the selected polymers.

Method: The pure drug and its formulation were subjected to Ft- ir studies. In the present study, the potassium bromide disc (pellet) method was employed.

2.2.2 FORMULATION OF FAST DISINTEGRATING TABLETS

a) Preparation of the tablet formulations by direct compression method

Each tablet (weight 100mg) consisted of sumatriptan succinate, superdisintegrants such as crospovidone, croscarmellose sodium, and sodium starch glycolate (SSG), micro crystalline cellulose, and aspartame, talc and magnesium stearate, prepared by direct compression method. The drug, diluent, superdisintegrant, sweetners, are passed through the sieve no.40. All the ingredients are mixed well in the motor. Then it was mixed with lubricant (2 mg) for 3 min in a motor. The mixer was compressed by using sixteen station rotary tablet compression machine (Table No.3).

Table No.3: General composition of formulation prepared by directcompression method

S.No	Ingredients	F1	F2	F3	F4	F5	F6
1.	Sumatrriptan succinate	25mg	25mg	25mg	25mg	25mg	25mg
2.	SSG	2mg	-	-	4mg	-	-
3.	CCS	-	2mg	-	-	4mg	-
4.	CP	-	-	2mg	-	-	4mg
5.	MCC	67mg	67mg	67mg	65mg	65mg	65mg
6.	Magnesium stearate	2mg	2mg	2mg	2mg	2mg	2mg
7.	Talc	2mg	2mg	2mg	2mg	2mg	2mg
8.	Aspartame	2mg	2mg	2mg	2mg	2mg	2mg

SSG = sodium starch glycolate; **CCS** =croscarmellose sodium

CP = Cross Povidone; **MCC** = Micro crystalline cellulose

b) Preparation of the tablet formulations by sublimation method

Each tablet (weight 25mg) consisted of Sumatriptan succinate, superdisintegrants such as crospovidone, croscarmellose sodium, and sodium starch glycolate (SSG), micro crystalline cellulose, camphor, and aspartame, talc and magnesium stearate, prepared by sublimation method. The drug, diluent, superdisintegrant, sweetners, are passed through the sieve no.40. All the ingredients are mixed well in the motor. Then it was mixed with lubricant (2mg) for 3 min in a motor. The mixer was compressed by using sixteen station rotary tablet compression machine. The compressed tablets were subjected to sublimation at 80^{o}C until a constant weight was obtained to the complete removal of sublimable agent (Table No.8).

Table No.4: General composition of formulation prepared by sublimation method

S.no	Ingredients	F7	F8	F9	F10	F11	F12
1.	Sumatrriptan succinate	25mg	25mg	25mg	25mg	25mg	25mg
2.	Camphor	10mg	10mg	10mg	10mg	10mg	10mg
2.	SSG	2mg	-	-	4mg	-	-
3.	CCS	-	2mg	-	-	4mg	-
4.	CP	-	-	2mg	-	-	4mg
5.	MCC	57mg	57mg	57mg	55mg	55mg	55mg
6.	Magnesium stearate	2mg	2mg	2mg	2mg	2mg	2mg
7.	Talc	2mg	2mg	2mg	2mg	2mg	2mg
8.	Aspartame	2mg	2mg	2mg	2mg	2mg	2mg

SSG = Sodium starch glycolate; CCS = Cross carmellose cellulose;

CP = Crospovidone; MCC = Micro crystalline cellulose

2.2.3EVALUATION OF FAST DISINTEGRATING TABLETS

A. PRE-COMPRESSION PARAMETERS

The quality of tablet is generally dictated by the quality of physicochemical properties of blends. There are many formulation and process variables involved in mixing step and all these can affect the characteristics of blends produced.

The various characteristics of blends tested are as given below:

1. Angle of Repose

The frictional force in a loose powder can be measured by the angle of repose θ. It is defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle θ, is in equilibrium with the gravitational force. The angle of repose was determined by the funnel method suggested by Newman. Angle of repose is determined by the following formula

$\tan \theta = h/r$

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

Where θ = Angle of repose

h = height of the cone

r = Radius of the cone base.

2. Bulk Density

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weight powder (passed through standard sieve#20) into a measuring cylinder and initial weight was noted.

Thisinitialvolumeiscalledthebulkvolume.Fromthisthebulkdensityiscalculated accordingtotheformulamentionedbelow.Itisexpresseding/mlandis givenby

$D_b = M/Vb$

Where,M is the mass of powder

Vbisthebulkvolumeofthepowder.

3. Tapped Density

It is the ratio of the total mass powder to the tapped volume of the powder. It was determined by placing a graduated cylinder, containing a known mass of drug-excipients blend. The cylinder was allowed to fall under its own weight onto a hard surface from the height of 10cm at 2- second intervals. The tapping was continued until no further change in volume was noted.

$D_t = M/Vt$

Where, M is the mass of powder

Vt is the tapped volume of the powder.

4. Compressability Index

In recent years, the compressibility index and the closely related Hausner's ratiohave become the simple, fast, and popular methods of predicting powder flowcharacteristics. The compressibility index has been proposed as an indirect measureof bulk density, size, shape, surface area, moisture content and cohesiveness ofmaterials because all of these can influence the observed compressibility index.

Carr's compressibility index(%)=[(D_t-D_b)X100]/ D_t

Where D_t is the tapped density

D_b is the bulk density

5. Hauser's ratio

Hausner's ratio is an indirect index of the ease of powder flow. It is calculated by the following formula.

Hausners ratio = D_t/D_b

Where, Dtis the tapped density,

Dbis the bulkdensity.

Lowerhausnerratio(<1.25)indicatesbetterflowpropertiesthanhigherones (>1.25).

Table No.4: Limits for flow properties

S.NO	Flow character	Carr's index	Hausner's Ratio	Angle of repose [°]
1	Excellent	≤ 10	1.00-1.11	25-30
2	Good	11-15	1.12-1.18	31-35
3	Fair (aid not needed)	16-20	1.19-1.25	36-40
4	Passable	21-25	1.26-1.34	41-45
5	Poor	26-31	1.35-1.45	46-55
6	Very poor	32-37	1.46-1.59	56-65
7	Very very poor	>38	>1.60	>66

B. Postcompression parameters

The tablets after punching of every batch were evaluated for in-process and finished product quality control tests i.e. thickness, weight variation, hardness, friability, drug content, *In Vitro*dispersion time, water absorption ratio, wetting time, and *In Vitro*drug release studies.

1) General appearance test

The general appearance of a tablet, its visual identity and over all "elegance" is essential for consumer acceptance. Include in are tablet's size, shape, colour, presence or absence of an odor, taste, surface texture, physical flaws and consistency and legibility of any identifying marking.

2) Tablet thicknesstest[63]

Randomly 10 tablets were taken from each formulation trial batch and their thickness was measured using a Verniercaliperse. The individual tablet was placed between two anvils and sliding knob was rotated until the tablet was tightly fitted. The digital reading displayed was noted.

3) Weight variation test[63]

Theweightvariationtestiscarriedoutinorderto ensureuniformityintheweightoftabletsinabatch. Thetotalweightof20tabletsfromeachformulation wasdeterminedandtheaveragewascalculated.The individualweightsofthetabletswerealsodetermined accurately and the weight variation was calculated.

Table No.5: **Limits foruniformity of weight**

S.NO	Average weight of Tablets (mg)	Maximum percentage difference allowed
1	80 or less	10
2	80 – 250	7.5
3	More than 250	5

4) Measurement of tablet hardness[63]

The hardness of tablet is an indication of its strength. Measuring the force required to break the tablet across tests it. The force is measured in kg and the hardness of about 3-5 kg/cm2 is considered to be satisfactory for uncoated tablets. Hardness of 10 tablets from each formulation was determined by Monsanto hardness tester.

5) Friabilitytest[63]

It is measured of mechanical strength of tablets. Roche fribalator is used to determine the

friability by following procedure. Twenty tablets were weighed and placed in Roche Friabilator where the tablets were exposed to rolling and repeated shocks resulting from free falls within the apparatus. After 100 revolutions, tablets are removed, dedusted and weighed again. The friability was determined as the percentage loss in weight of the tablets.

% Friability = (loss in weight / Initial weight) X 100

6) Disintegration Time

The USP device to rest disintegration was six glass tubes that are "3 long, open at the top, and held against 10" screen at the bottom end of the basket rack assembly. One tablet is placed in each tube and the basket rack is positionedin 1 liter beaker of distilled water at 37±2^{o}C, such that the tablets remain below the surface of the liquid on their upward movement and descend not closer than 2.5cm from the bottom of the beaker.

7) *In-Vitro* Dispersion Time[64]

In-vitro dispersion time was measured by dropping a tablet in a measuring cylinder containing 6ml of phosphate buffer pH 6.8 (simulated saliva fluid). The time for the tablet to completely disintegrate into fine particles was noted. Three tablets from each batch were randomly selected and *In- vitro* dispersion time was performed.

8) Wetting time[65]

The method reported by yunixia et al., was followed to measure tablet wetting time. A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in a small petridish (ID= 6.5 cm) containing 6 ml of Sorenson's buffer pH 6.8. A tablet was put on the paper, and the time for complete wetting was measured. Three trials for each batch and the standard deviation were also determined.

9) Water absorption ratio

A small culture Petri dish can be taken containing 6ml of water and a piece of tissue paper folded twice is placed. A tablet is placed gently on itand the time for complete wetting is measured. The wetted tablet is reweighed.

Water absorption ratio R was determined according the following equation:

R = (Wa - Wb) / Wb x100

Where Wa is the weight of tablet after water absorption

Wb is the weight of tablet before absorption.

10) Content uniformity

From each batch of prepared tablets, ten tablets were collected randomly and powdered. A quantity of powder equivalent to weight of one tablet was transferred in to a 100 ml volumetric flask, to this 50 ml pH 6.8 buffer of was added and then the solution was subjected to sonication for about 2 hrs. The solution was made up to the mark with pH 6.8 buffer. The solution was filtered and suitable dilutions were prepared with pH 6.8 buffer. Same concentration of the standard solution was also prepared. The drug content was estimated by recording the absorbance at 282 nm by using UV-Visible spectrophotometer.

11) *In-vitro* dissolution

Freshly prepared phosphate buffer(pH 6.8) of 900 ml was placed in each dissolution vessels of dissolution test apparatus (USP, II paddle method). The tablets were placed in the dissolution medium. The temperature of the dissolution medium was maintained at 37± 0.5^0C and the paddle was rotated at 50 rpm. 5 ml samples were withdrawn. The sample volume was immediately replaced with the same volume of fresh media as when a sample was taken. The samples withdrawn were filtered, diluted and estimated spectrophotometrically at 282 nm. Cumulative amount of the drug released at each interval was calculated by using standard graph of sumatriptan succinate.

12) Stability studies of fast dissolving tablets

It is the responsibility of the manufacturers to see that the medicine reaches the consumer inan active form. So the stability of pharmaceuticals is an important criteria. Stability of medicinalproducts may be defined as the capability of a particular formulation in a specific container to remain within its physical, chemical, microbial, therapeutic and toxicological specification, i.e.stability of drug is its ability to resists detoriation. 90% of labelled potency is generally recognized as the minimum acceptable potency level. Detoriation of drug may take several forms arising from changes in physical, chemical and microbiological properties. The changes may affect the therapeutic value of preparation or increase its toxicity.

Accelerated stability testing

Since the period of stability testing can be as long as two years, it is time consuming andexpensive. Therefore it is essential to devise a method that will help rapid prediction of long-termstability of drug.

The accelerated stability testing is defined as the validated method by which the product stability may be predicted by storage of the product under conditions that accelerate the change in defined and predictable manner. The stability studies of formulated tablets were carried out at 40^{o}Cand at room temperature for onemonth. The effects of temperature and time on thephysical characteristics of the tablet were evaluated for assessing the stability of the prepared formulations. The stability studies were carried out when the room temperature was 20 to25^{o}C. The different parameters that were studiedare *in- vitro* disintegration time, wetting time, drugcontent and *In-vitro* dissolution rate.

3. RESULTS ANDDISCUSSION

3.1 PREFORMULATION STUDIES

1) Determination of solubility

Sumatriptan succinate was found to be freely soluble in water and methanol.

2) UV Spectrophotometric analytical method for sumatriptan succinate

A) UV Scanning

When sumatriptan succinate was scanned in the wavelength region of 180-380nm, peak was observed at 282nm as shown in fig. No.5:

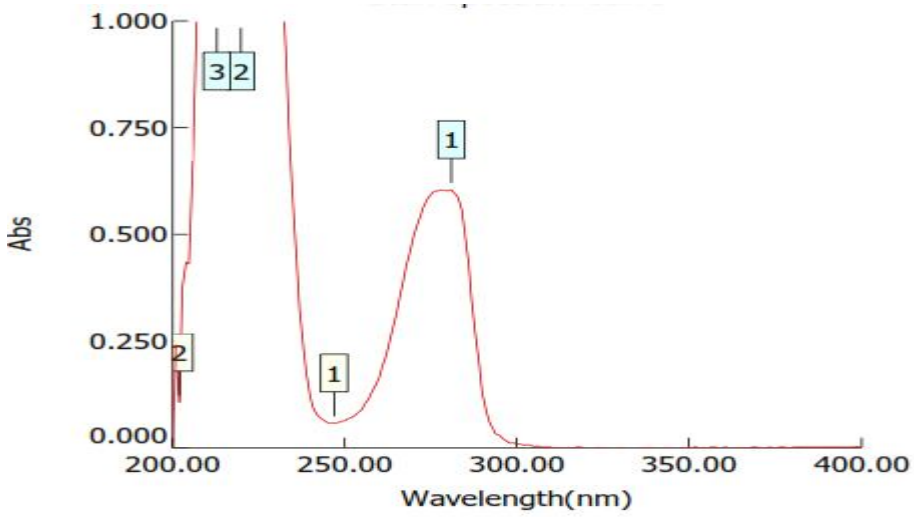

Fig No.5: UV spectrum of Sumatriptan succinate

B) Preparation of reagents

Preparation of 0.2M Potassium dihydrogen phosphate

Dissolve 27.218gm of potassium dihydrogen in distilled water and diluted the volume to 1000ml with distilled water.

Preparation of 0.2M Sodium Hydroxide

Dissolve 8.0gm of sodium hydroxide in distilled water and diluted to 1000ml with distilled water.

Preparation of pH 6.8 phosphate buffer (simulated saliva pH)

Place 50ml of 0.2M Potassium dihydrogen phosphate in a 200ml volumetric flask, added 22.4ml of 0.2M sodium Hydroxide, mixed and volume was made upto 200ml with distilled water.

C) Preparation of standard graph of sumatriptan succinatein distilled water

Sumatriptan succinate has the maximum absorbance at 282 nm. Standard graph of sumatriptan succinate in water was plotted by taking concentration ranging from 10 to 60 µg/ml and a good correlation was obtained with R^2 value of 0.9994(Fig No. 6).

Table No.6: Preparation of standard graph of sumatriptan succinate in distilled water

S.NO	Concentration(mcg/ml)	Absorbance(nm)
1	0	0
2	10	0.022
3	20	0.07
4	30	0.118
5	40	0.17
6	50	0.23
7	60	0.286

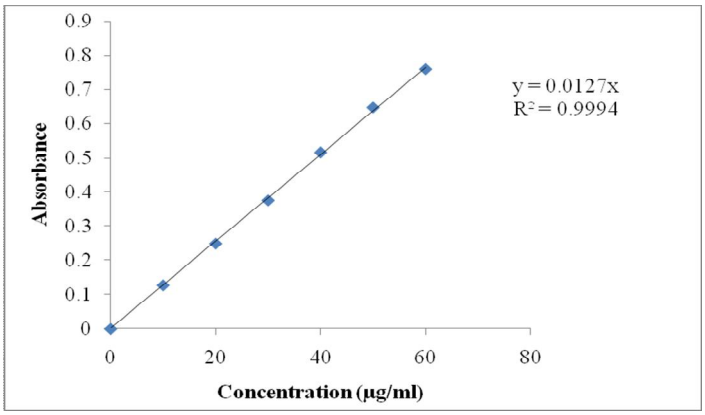

Fig No.6: Standard graph of sumatriptan succinate in distilled water.

D) Preparation of standard graph of sumatriptan succinate in pH 6.8 buffer

Standard graph of sumatriptan succinate in pH 6.8 buffer was plotted by taking concentration ranging from 10 to 60 µg/ml and a good correlation was obtained with R^2 value of 0.999(Figure 7).

Table No.7: Preparation of standard graph of sumatriptan succinate in pH 6.8 phosphate buffer

S.NO	Concentration(mcg/ml)	Absorbance(nm)
1	0	0
2	2	0.21
3	4	0.38
4	6	0.56
5	8	0.75
6	10	0.93
7	12	1.1

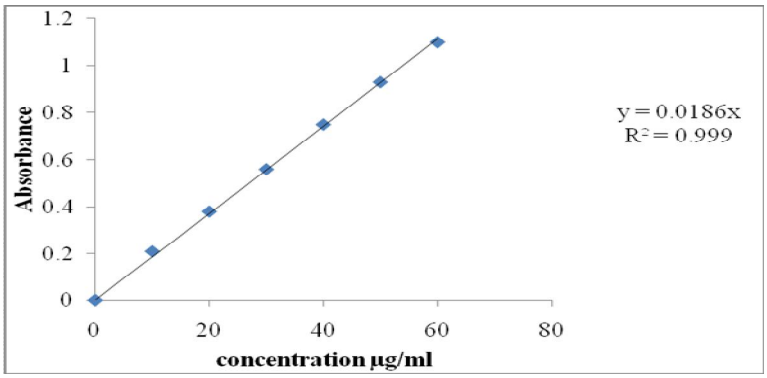

Figure No.7: Standard graph of sumatriptan succinate in pH 6.8 buffer.

3.2 Evaluation parameters of sumatriptan succinate tablets Drug – polymer compatability study by FT- IR

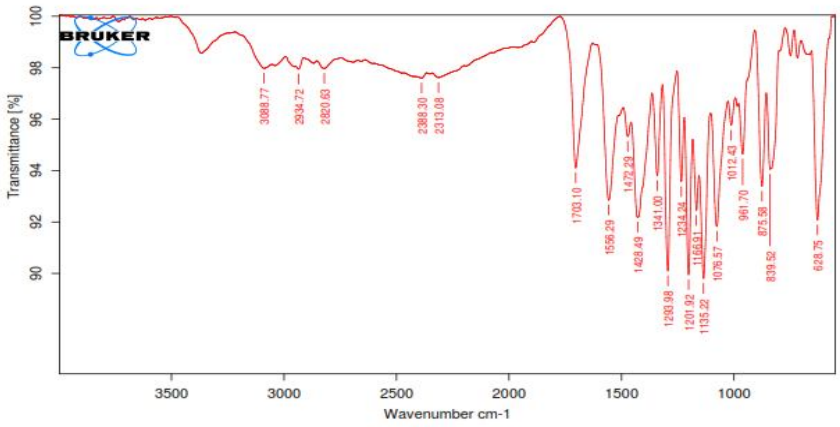

Fig No.8: FT-IR spectra of pure Sumatriptan succinate

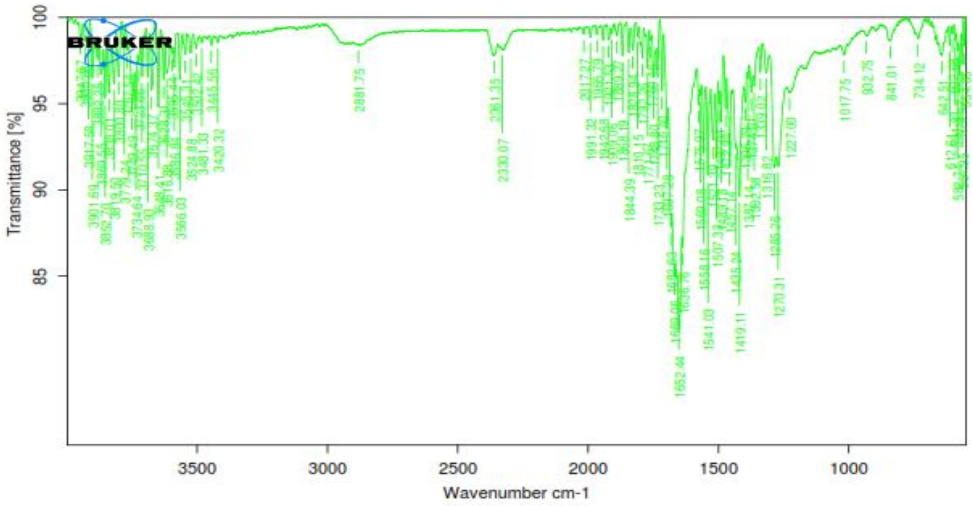

Fig No.9: FT-IR spectra of Crospovidone

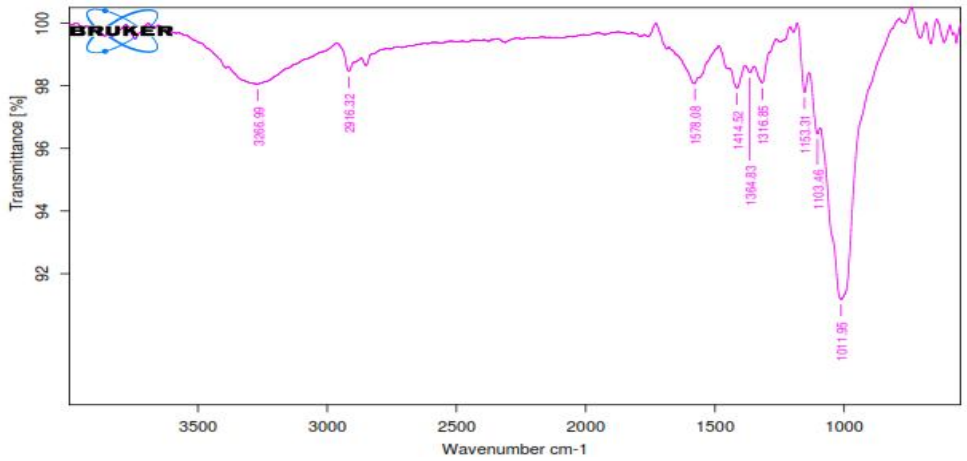

Fig No.10: FT-IR of Cross carmellose sodium

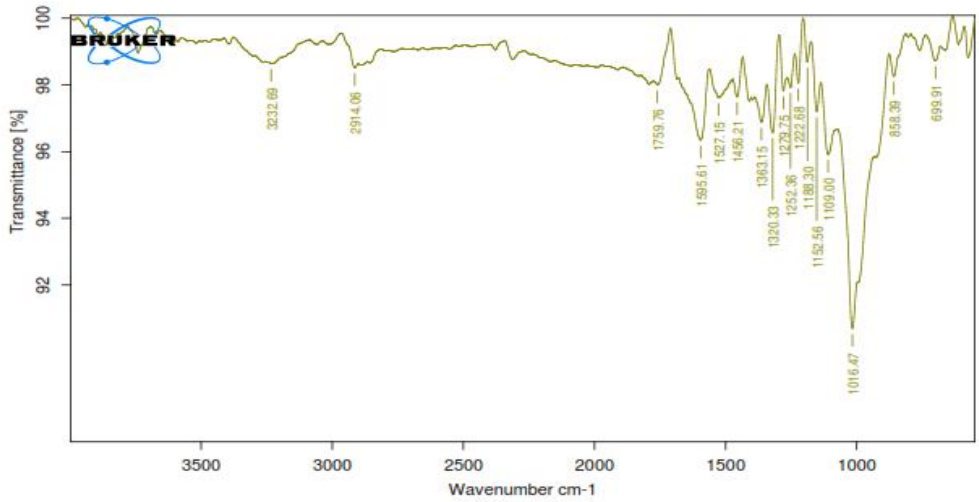

Fig No.11: FT-IR spectra of Sodium starch glycolate

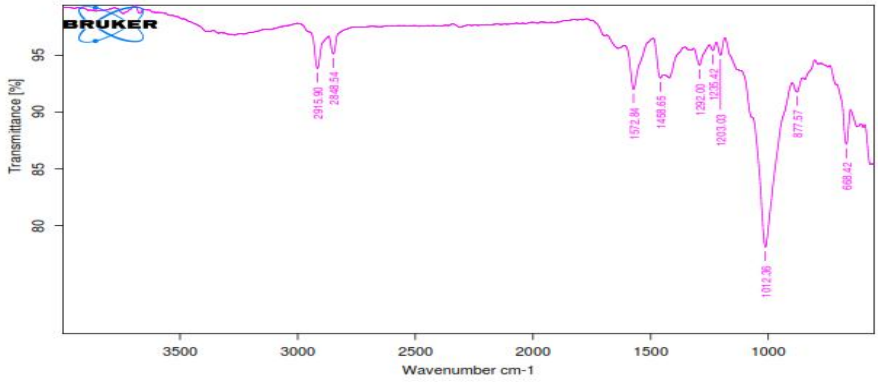

Fig No. 12: FT-IR spectra of optimized formula (F12)

3.3. EVALUATION OF SUMATRIPTAN SUCCINATE TABLETS

1) Pre-compression parameters

Blend was evaluated for bulk density, tapped density, compressibility index, hausner's ratio, angle of repose (Table No.8 and 9).All the formulation show angle of repose below 30^0 that mean they show free flowing property. All the formulation has hausner's ratio between the 1.19 to1.26. It indicates all the formulation show better flow property.

Table No.8: Results of flow properties of fast dissolving tablets which were prepared by direct compression method

S.NO	Formula	Angle of repose(θ)	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Compressibility index (I)	Hausner's ratio
1	**F1**	25.16	0.512	0.647	20.86	1.26
2	**F2**	23.74	0.549	0.673	18.42	1.22
3	**F3**	28.70	0.532	0.650	18.15	1.22
4	**F4**	26.65	0.545	0.651	16.28	1.19
5	**F5**	24.72	0.541	0.655	17.40	1.21
6	**F6**	22.89	0.535	0.668	19.91	1.24

Table No.9:Results of flow properties of fast dissolving tablets which were prepared by sublimation method

S.NO	Formula	Angle of repose(θ)	Bulk density (gm/cm^3)	Tapped density (gm/cm^3)	Compressibiliy index (I)	Hausner's ratio
1	**F7**	30.01	0.541	0.682	20.67	1.26
2	**F8**	29.72	0.532	0.670	20.59	1.25
3	**F9**	27.54	0.529	0.665	20.45	1.25
4	**F10**	28.45	0.532	0.667	20.23	1.24
5	**F11**	27.89	0.530	0.661	19.81	1.24
6	**F12**	24.13	0.533	0.650	18.50	1.22

2) Post compression parameters

The total weight of each formulation was not maintained constant however; the weight variation of the tablets was within the permissible limits of 5%, as specified for tablet weighing more than 100 mg(Table No.10 and 11).

The hardness of tablets was tested using hardness tester to findout whether they could retain their physical shape. The hardness of the prepared tablets was within the limits.

Tablet thickness was also used to assess the quality of tablets. Under uniform conditions of manufacture, the total weight of tablet and thickness were linearly related. The friability loss of less than 0.5 – 1% in weight is generally considered acceptable.

Table No.10: Uniformity of thickness, Hardness, Friability, and Weight variation of fast disintegrating tablets prepared by direct compression method.(F1-F6)

S.NO	Formulation code	Weight Variation (n=10) (mg)	Uniformity of Thickness (n=3) (mm)	Hardness (n=3) (kg/cm^3)	Friability %
1	**F1**	101.6±0.20	2.71±0.04	3.62±0.17	0.15
2	**F2**	102.3±0.75	2.73±0.03	3.79±0.34	0.27
3	**F3**	101.5±0.89	2.76±0.03	3.76±0.25	0.16
4	**F4**	100.1±0.23	2.83±0.04	3.84±0.20	0.18
5	**F5**	101.1±0.2	2.53±0.01	3.53±0.15	0.24
6	**F6**	101.0±0.25	2.65±0.01	3.96±0.12	0.37

± S.D, † **n=3** average ofthree Observations, ‡mm- Millimetre

Table No.11: Uniformity of thickness, Hardness, Friability, and Weight variation of fastdisintegrating tablets prepared by sublimation method.(F7-F12)

S.NO	Formulation code	Weight Variation (n=10) (mg)	Uniformity of Thickness (n=3) (mm)	Hardness (n=3) (kg/cm^3)	Friability %
1	**F7**	100.1±0.20	2.79±0.06	3.43±0.22	0.14
2	**F8**	100.5±0.75	2.68±0.07	3.36±0.31	0.23
3	**F9**	98.3±0.89	2.88±0.05	3.71±0.26	0.16
4	**F10**	99.71±0.23	2.75±0.07	3.67±0.14	0.18
5	**F11**	102.1±0.2	2.79±0.04	3.46±0.15	0.24
6	**F12**	101.0±0.25	2.81±0.01	3.86±0.25	0.23

± S.D, † **n=3** average ofthree Observations, ‡mm- Millimetre

Disintegration test was conducted for all the formulation. From the results the tablets which have cross povidone they show less disintegration time when compared with other disintegrants, in addition to its unique particle size and morphology,disintegrant properties of CP are not affected by pH and consequently being non-ionic does not bind to ionic drug moieties. The probable reason for delayed disintegration of the tablets with cross carmellose sodium, sodium starch glycolate, might be due to their tendency to gel more than cross povidone.

So, it may be assumed that 4% concentration is optimum for cross povidone. 4%concentration is optimum for cross carmellose and sodium starch glycolate, disintegration occurs as a result of uptake of water followed by rapid and enormous swelling (Table No 12 and13).

Water absorption study conducted for all batches. Crospovidone shows more water absorption ratio. All the formulations were checked for content uniformity as per IP. All the formulations passed the test and the % of active ingredient ranged from 98.0-101.2% (Table No 12 and 13).

Table No.12: Wetting Time, Water Absorption Ratio, *In-vitro* Disintegration Time, *In-vitro* Dispersion Time,Drug Content Uniformity (F1 to F6)

S.NO	Formulation code	Wetting Time (n=3)	Water Absorption Ratio (n=3)	In-vitro Disintegration Time (sec)	In-vitro Dispersion Time (sec)	Drug Content(%)
1	**F1**	42.76±1.56	39.30±1.25	52.40±0.46	74.57±1.23	98.0
2	**F2**	35.52±1.73	37.16±1.41	50.71±0.67	72.74±1.36	99.1
3	**F3**	34.38±1.75	36.92±1.25	48.07±1.20	70.12±1.20	98.7
4	**F4**	34.19±1.85	38.64±1.51	51.81±1.03	71.71±1.51	98.57
5	**F5**	33.38±1.58	29.45±1.20	48.13±1.06	68.17±1.43	98.32
6	**F6**	31.46±1.25	27.10±1.02	42.19±0.96	66.12±1.15	99.15

***** ± S.D,† **n=3** average ofthree Observations

Table No.13: Wetting Time, Water Absorption Ratio, *In-vitro* Disintegration Time, *In-vitro* Dispersion Time,Drug Content Uniformity (F7to F12)

S.NO	Formulation code	Wetting Time (n=3)	Water Absorption Ratio (n=3)	In-vitro Disintegration Time (sec)	In-vitro Dispersion Time (sec)	Drug Content(%)
1	**F7**	38.66±0.99	38.01±1.30	48.19±0.15	70.17±1.51	99.9
2	**F8**	33.72±0.12	35.31±1.11	41.91±1.24	65.18±1.62	101.2
3	**F9**	32.65±1.72	33.71±1.01	39.46±0.97	63.16±1.19	98.4
4	**F10**	36.87±1.01	35.46±1.12	44.12±1.12	69.16±1.03	99.9
5	**F11**	30.76±1.02	29.02±0.52	38.72±0.15	62.19±1.24	98.7
6	**F12**	29.74±1.00	26.71±1.10	30.17±1.21	59.21±1.05	99.79

***** ± S.D,† **n=3** average ofthree Observations

Comparison of dissolution profiles for F1 to F6 batches prepared by direct compression method.

In vitro dissolution study of formulations F1 batch drug release within 10 min 62.66±1.10, with in 10 min F2 batch drug release 67.14±1.12, with in 10 min F3 batch release the drug 71.81±1.20, with in 10 min F4 batch drug release is 76.09±1.52, with in 10 min F5 batch drug release is78.05± 1.10, within 10 mins F6 batch drug release is 82.71±1.06 (Table No.14). Among these formulations F6 batch shows good dissolution property (Fig No. 13). F6 batch contain 4% of cross povidone.

Table No.14:Comparison of dissolution profiles for F1 to F6 batches which were prepared by direct compression method.

S.NO	Time (mins)	F1 Cumulative % drug release	F2 Cumulative % drug release	F3 Cumulative % drug release	F4 Cumulative % drug Release	F5 Cumulative % drug Release	F6 Cumulative % drug Release
1	0	0	0	0	0	0	0
2	5	34.05±1.25	38.34±0.98	42.62±1.24	43.01±1.64	44.56±1.52	48.85±1.13
3	10	62.66±1.10	67.14±1.12	71.81±1.20	76.09±1.52	78.04±1.10	82.71±1.06
4	15	81.15±0.95	82.32±1.15	86.02±0.85	87.77±0.98	89.33±0.99	90.88±0.92
5	20	90.88±0.86	91.66±0.97	93.22±0.97	93.41±1.19	95.75±1.51	96.53±1.02

Data represents mean ± SD, n=3

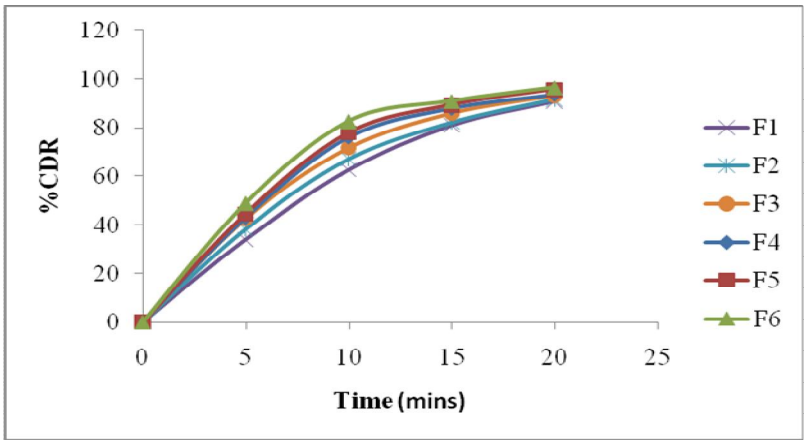

Fig No.13: Dissolution profiles for F1 to F6 batches

Comparison of dissolution profiles for F7 to F12 batches prepared by sublimation method.

In vitro dissolution study of formulation F7 batch release the drugWithin 10 min 65.00±1.53, with in 10 min F8 batch release the drug is 71.23±1.14, F9 batch release the drug is 76.29±1.27 in 10 min. F10 batch release the drug 79.01±1.19 within 10 min, F11 batch release the drug is 84.07±1.24in 10 min, F12 batch release the drug is 85.82±1.03. Among these formulations F12 batch shows good dissolution property (Fig No.14). It contains4% of cross povidone (Table No. 15).

Table No.15: Comparison of dissolution profiles for F7 to F12 batches which were prepared by sublimation method.

S.NO	Time (mins)	F7 Cumulative % drug release	F8 Cumulative % drug Release	F9 Cumulative % drug release	F10 Cumulative % drug release	F11 Cumulative % drug release	F12 Cumulative % drug Release
1	0	0	0	0	0	0	0
2	5	36.39±1.12	40.28±1.52	44.95±1.31	47.09±1.24	49.82±1.14	52.74±1.42
3	10	65.00±1.53	71.23±1.14	76.29±1.27	79.01±1.19	84.07±1.24	85.82±1.03
4	15	83.88±1.24	84.33±1.58	87.19±1.16	90.5±1.36	92.64±1.04	93.03±1.18
5	20	91.66±1.29	93.41±1.35	95.56±0.96	96.72±1.23	97.89±1.33	99.64±1.05

Data represents mean ± SD, n= 3

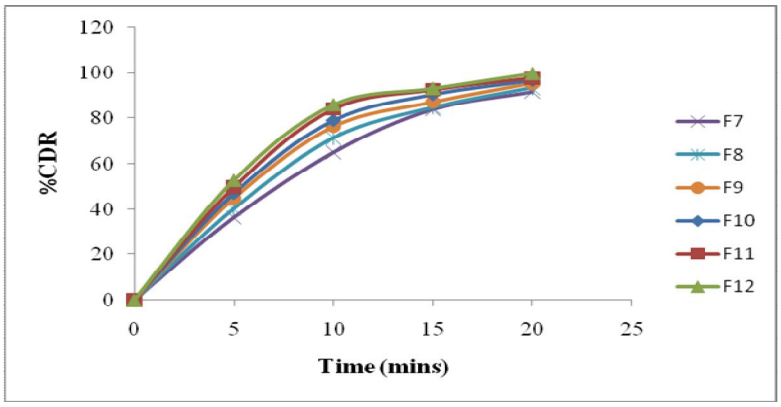

Fig No.14: Dissolution profiles for F7 to F12 batches.

Comparison of dissolution profiles for F6, F12 batches

*In vitro*dissolution study of formulation F12 batch release the drug 91.17±1.24with in 10 min and other batches showed (Fig No.15) less percentage of drug release than F12 batches (Table No. 16).

Table No.16: Comparison of dissolution profile for F6, F12 batches.

S.NO	TIME	F6 Cumulative % drug release	F12 Cumulative %drug release
1	0	0	0
2	5	48.85±1.13	52.74±1.42
3	10	82.71±1.06	85.82±1.03
4	15	90.88±0.92	93.03±1.18
5	20	96.53±1.20	99.64±1.04

Data represents mean ± SD, n=3

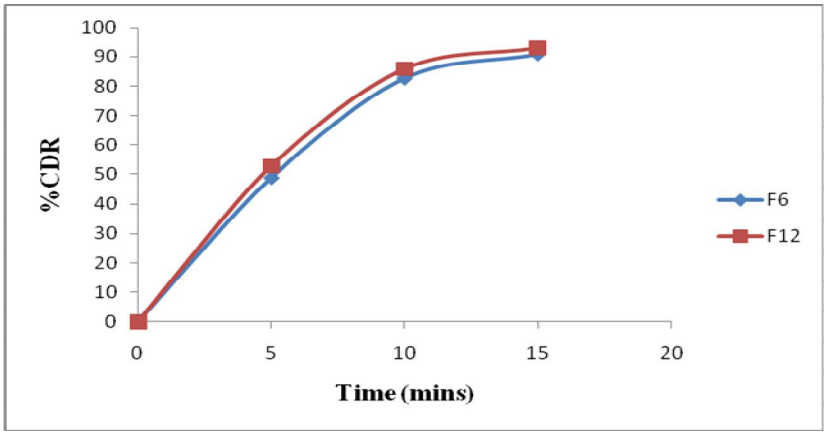

Fig No.15: Comparison of dissolution of F6, F12 batches.

3.4 Accelerated stability studies of fast dissolving tablets.

Stability studies for all the formulation were carried out as per the procedure in the methodology. The results shown below

Table No.17: Stability study of tablet properties of optimized formulations (F6 & F7)

S.NO	PARAMETERS	CONTROLLED		F6		F12	
		F6	F12	AFTER 15 DAYS	AFTER ONE MONTH	AFTER 15 DAYS	AFTER ONE MONTH
1	Hardness (Kg/cm)	3.96±0.12	3.86±0.25	3.95±0.29	3.92±0.16	3.85±0.21	3.83±0.78
2	Drug content (%)	99.15	99.75	99.01	98.56	99.12	99.01
3	In-vitro disintegration time (sec)	42.19±0.96	30.17±1.21	42.76±0.94	43.07±0.91	31.32±1.26	32.12±1.52
4	Wetting time (sec)	31.46±1.25	29.74±1.00	31.99±1.25	32.04±1.06	30.12±1.23	31.52±1.15

Table No.18:Stability study of in-vitro dissolution for formulations F6 & F12 stored at Room Temperature

S.NO	TIME (MINS)	CUMULATIVE %DRUG RELEASE					
		CONTROLLED		F6		F12	
		F6	F12	After 15 days		After 1 month	
1	0	0	0	0	0	0	0
2	5	48.85±1.13	52.74±1.42	48.62±1.26	44.12±1.52	52.63±1.72	51.96±1.63
3	10	82.71±1.06	85.82±1.03	82.06±1.23	81.99±1.02	84.69±1.56	84.01±1.26
4	15	90.88±0.92	93.03±1.18	90.24±0.85	89.95±1.63	92.86±0.96	91.56±1.35
5	20	96.53±1.02	99.64±1.05	95.96±1.26	94.29±1.36	99.01±1065	98.56±1.14

4. DISCUSSION

The UV Spectrophotometric scan of the sumatriptan succinate showed a peak exhibits at 282nm which was found to be same as that of the reported value. Since the dissolution medium for sumatriptan succinate tablets as indicated in USP is degassed water, the calibration curve was made accordingly. The calibration curve was found to be linear over concentration range of 10-70µg/ml with R^2value 0.999.

The present work was to formulate Fast disintegration tablets of sumatriptan succinate using two techniques.

The first approach was to formulate the tablets by direct compression method which is reported to be simple and cost effective.The tablets were prepared using crospovidone, cross Carmel lose sodium and sodium starch glycolate as a superdisintegrants, and micro crystalline cellulose as diluent. The pre-compression parameters were found to be satisfactory. The tablets exhibited a disintegration time in the range of 42.19-52.40 sec and wetting time in the range of 31.46-42.76 sec and *In vitro* dissolution study of formulation of F6, (which gave least disintegration time of 42.19±0.96) showed a cumulative release of 48.85±1.13 after 5 min. This method was found to give a low disintegration time and a good release after 5 min.

In the next approach the tablets were formulated by sublimation technique using camphor as subliming agent. Sublimation technique is reported to yield porous tablets with low disintegration time and hence this technique was also used in present study. The tablets were prepared using crospovidone, cross Carmel lose sodium, sodium starch glycolate as a superdisintegrants, micro crystalline cellulose as diluent and camphor as a subliming agent. The pre-compression parameters were found to be satisfactory. The tablets exhibited a disintegration time in the range of 30.17-48.19sec and wetting time in the range of 29.74-38.66 sec. *In vitro* dissolution study of formulation of F12, (which gives least disintegration time of 30.17±1.21 sec) showed a cumulative releaseof 52.74±1.42 after 5 min. The sublimation technique was thus found to be suitable to obtain the target disintegration time and a good % cumulative release after 5 min.

The two techniques used for fast disintegration tablets of sumatriptan succinate were compared. It was found that the sublimation technique was more beneficial compared to direct compression method inobtaining the target disintegration time.

The sublimation technique though beneficial, involves an additional step of adding a volatile subliming agent and at a subliming it constant temperature. This could be considered as one of the drawbacks of the technique compared to direct compression technique. However this technique would definitely be beneficial for drugs with a higher dose where low disintegration time cannot be achieved using super disintegrate alone.

Formulations which gave target disintegration time were selected for stability studies. The report of study indicated that the tablets were found to be stable without any significant change in the disintegration time and *in-vitro* release.

5. CONCLUSION

From the present work, it can be concluded that among the various techniques used,sublimation is best suitable in the preparation of Fast disintegration tablets of sumatriptan succinate. The developed formulations have suitable characteristics. Among the three superdisintegrants, Crosspovidone (F12) showed good disintegrants property. It has also shown good water absorption ratio.

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