FORMULATION AND EVALUATION OF FAST DISSOLVING TABLETS OF SUMATRIPTAN SUCCINATE

By Dry-Granulation Method

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Abstract *:*In this study, Fast dissolving tablets of Sumatriptan Succinate has been prepared by dry granulation to improve dissolution rate of drug in oral cavity for better patient's compliance & effective therapy. Sumatriptan Succinate is widely used in the treatment of migraine and cluster headache. Migraine caused by temporary swelling of blood vessels in head. The main objective of this study was to formulate fast dissolving tablets of Sumatriptan succinate to achieve a better dissolution rate and further improvement in the bioavailability of the drug. It has low oral bioavailability due to first pass metabolism and incomplete absorption. Fast dissolving tablets of Sumatriptan succinate were prepared with combination of superdisintegrants like Kollidon CL (crospovidone), AC-DI-SOL (croscarmellose sodium), and Starch-1500 (Pregelatinised starch) by using the dry granulation and compression method. The all (formulations) compressed tablets were evaluated for thickness, uniformity of weight, drug content, hardness, friability, wetting time, in vitro and in vivo disintegration time, in vitro drug release and microbial evaluation. It has been evaluated that formulation batch F3 contains superdisintegrants i.e. Kollidon-CL (4%), Ac-di-sol (1.5%), which exhibit the promising results in term of enhanced dissolution rate, wetting time and disintegration time and leads to improved bioavailability, effectiveness and better patient's compliance. In this study, Fast dissolving tablets (F1-F8) has also been subjected to microbial contamination study, as that presence of microbial flora may affect the quality, safety and efficacy of the product's activity. It has been evaluated that the presences of total aerobic bacterial counts were found less than 100cfu while fungal colonies were found nil.ration time, *in vitro drug release.*

Keywords -Sumatriptan Succinate, FDTs**,** Dry Granulation, *In-vitro* & *In-vivo* disintegration time, *in vitro drug release.*

I. INTRODUCTION

Fast dissolving tablets is gained fast popularity as a novel drug delivery system. When, it is placed orally in the mouth, rapidly absorb the small quantity of available saliva and quickly dispersed in about 10-45 sec. FDTs demonstrate unique advantages by addressing patient compliance issues with paediatric, geriatric and uncooperative patient unable to swallow tablets. They also allow administration of medication without any need of water. To date a variety of FDTs with their own claim of advantages have been developed using technologies ranging from as wet granulation or direct compression (www.drugdeliverysystem).

In recent year, rapidly disintegrating tablet dosage forms have become extremely popular (Fu *et al.,* 2004). These dosage forms have particular advantage in certain group of patients like geriatric, paediatric and psychiatric patient (Bonger *et al.*, 2002, Prakash *et al.,* 2003). These dosage forms have more beneficial to certain medical conditions such as pain, migraine, nausea, panic attack, allergic conditions, cough/cold, and Alzheimer's diseases.

The fast dissolving tablets have good taste and can be taken anywhere, any time. Many patients have difficulty swallowing solid dosage forms and consequently unable to medications as prescribed. The demand for solid dosage form that can be dissolved and suspended in water or chewed. It is rapidly dissolved in mouth is particularly strong in the paediatric and geriatric markets, with further application to other patients prefer the convenience of a readily administered dosages form because of the increase in the average human life span and the decline with age in swallowing ability.

Oral tablets administered to patients are a significant problem and has become the object of public attention. The problem can be resolved by the creation of rapidly dispersing or dissolving oral dosage form, which do not required water to aid swallowing. The dosage forms are placed in mouth, allowed to dispersed or dissolved in saliva, swallowed in normal way. Less frequently, they are designed to be absorbed through the buccal and oesophageal mucosa as the saliva passes into the stomach. In case, the bioavailability of a drug from fast dispersing formulation may be even greater than that observed for standard dosage form. Furthermore, side effect may be reduced if they are caused by first pass metabolites (Okuda *et al.,* 2009).

II. MATERIALS AND METHODS

Materials

Sumatriptan succinate, Kollidon-CL (crospovidone), Ac-di-sol (Croscarmellose), Microcrystalline cellulose (Avicel PH-102), Pregelatinized starch (Starch-1500), Mannitol (Pearlitol SD-200), Pineapple, Tartrazine color were used & gifted by the Natco Pharma, Uttarakhand. Analytical grade solvents & reagents were used.

Experimental Methods

Fast dissolving tablets containing sumatriptan succinate (50mg) were prepared by dry granulation & compression operation; granules were prepared by direct compression of powders as slug of Sumatriptan Succinate (API), Kollidon CL, Ac-di-sol, Modified Starch 1500 (superdisintegrants), Avicel PH-102 (Binder/Diluent), Mannitol (Pearlitol SD-200) (diluent/flow promoter), Magnesium Stearate, Talc (Lubricating agent), Aspartame (sweetening agent), pineapple (flavoring agent) and Tartrazine yellow lake as colouring agent which make elegant product to quality.

III. PREFORMULATION STUDIES

Pre-formulation studies is the first step, rationally to development the dosage form of a drug substance. Pre-formulation study is useful for drug substance informations, to develop formulation portfolio for investigation of the physical and chemical properties of drug substance alone and combined with excipients. It is designed to identify those physicochemical properties and pharmacokinetic-biopharmaceuticals properties of ingredient/ excipients with drugs that may influence the pharmacokinetic-biopharmaceuticals properties of the resulting product (Lachmann, 2003) ,*www.drugindex.com/sumatriptan succinate*).

a. Organoleptic characteristics: Sumatriptan succinate is odourless, white to off-white powder in colour, bitter in taste and hygroscopic.

b. **Determination of melting range:** Sumatriptan succinate melting point determined by digital melting point apparatus (by the Thiele's tube with light paraffin) melting point was found 169°C which is approximate nearer to reference value (*IP 2010, USP 2011, BP 2010*).

c. Determination of solubility: An excess of drug was taken and added into separates test tubes, containing 5 ml of each solvent. The test tubes were shaken for 5-10 minute (IP 2010, USP 2011). Sumatriptan succinate freely soluble in distilled water, methanol, chloroform, phosphate buffer pH 6.8.

d. Determination of partition coefficient ($P_{o/w}$): Partition coefficient is the measurement of drug lipophilicity and indication of its ability to cross the lipoidal cell membrane. Partition coefficien was determined in n-octane phase, After appropriate dilutions, the aqueous phase was analyzed for drug against reagent blank solution using Shimazdu 1700-E UV-Visible spectrophotometer..The drug partition coefficient of Sumatriptan sucinate was found 0.90, which matched with reference values 0.92 (BP 2010, USP 2011, IP 2010, www.drugindex/sumatriptan succinate) indicated that drug is highly hydrophilic in nature.

e. Determination of Absorption maxima (λ-max): Absorption maxima were determined by comparison between Reference solution and Test Solution.

- **Reference solution:** Accurately weighed 50mg reference drug (USP vial) dissolved in methanol up to 100ml, sonicated and prepared the stock solution of 100µg/ml. Further 2ml solution was diluted in 100ml methanol, filtered (0.45µfilter) and make solution of 10µg/ml.
- **Test solution:** Accurately weighed 50mg sumatriptan succinate dissolved in methanol up to 100ml, sonicated and prepared the stock solution of 100µg/ml. Further 2ml solution was diluted in 100ml methanol, filtered (0.45µfilter) and make solution of 10µg/ml.

The standard and test solution of sumatriptan succinate (10µg/ml dilution) in methanol were prepared and scanned between 200 nm to 400 nm using double beam UV/Visible spectrophotometer. The maximum absorbance of standard and test dilution was found at wavelength (λ-max) as 281.10nm and 281.51nm which correlate to 282±1nm (*Reference value as per USP 2011, IP 2010*). The maximum absorption of sumatriptan succinate standard (Fig.1) and test are given in the Fig.2.

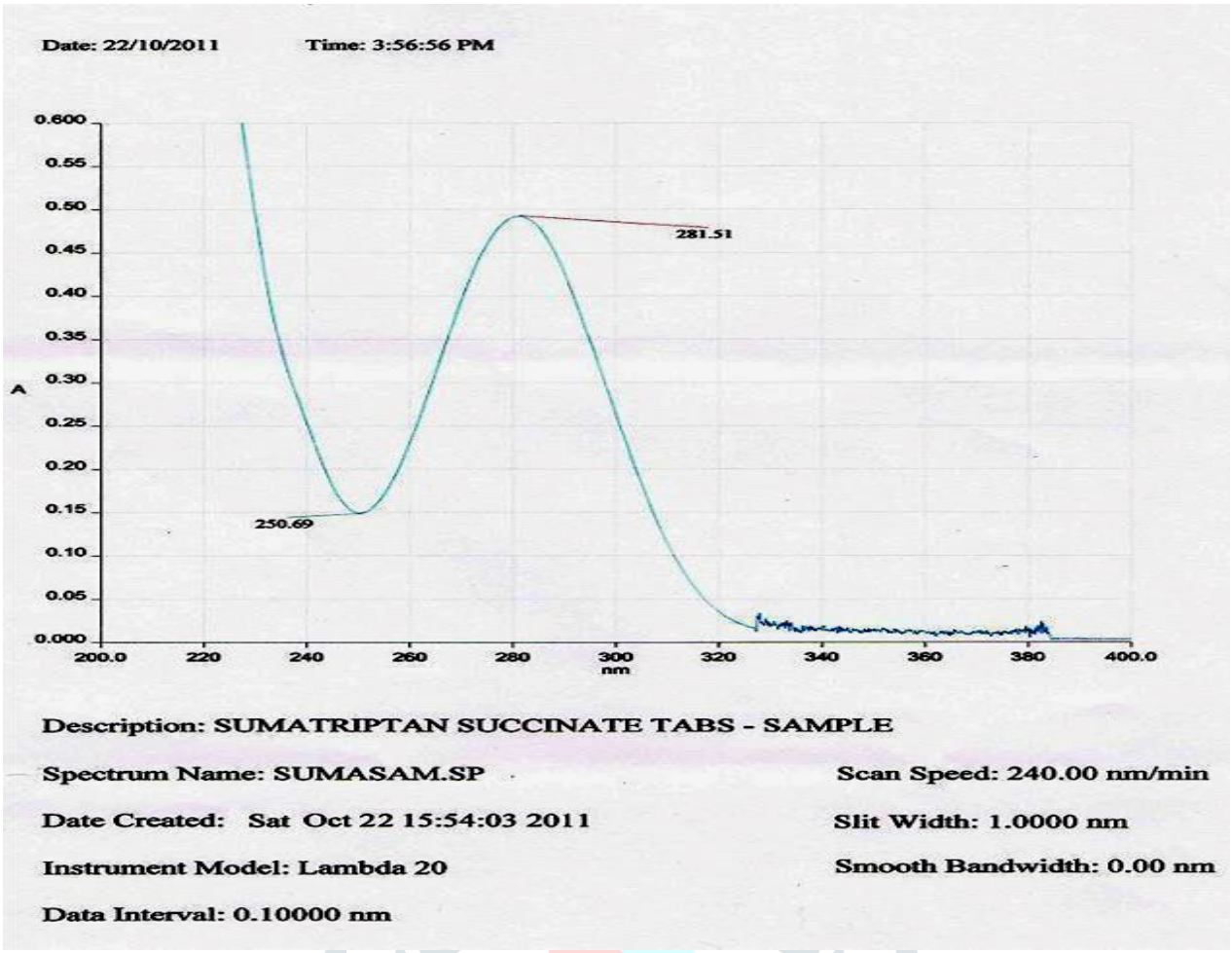

Fig.1: The Absorbtion Maxima of Reference Standard of Sumatriptan Succinate in Methanol (λ max 282±1 nm)

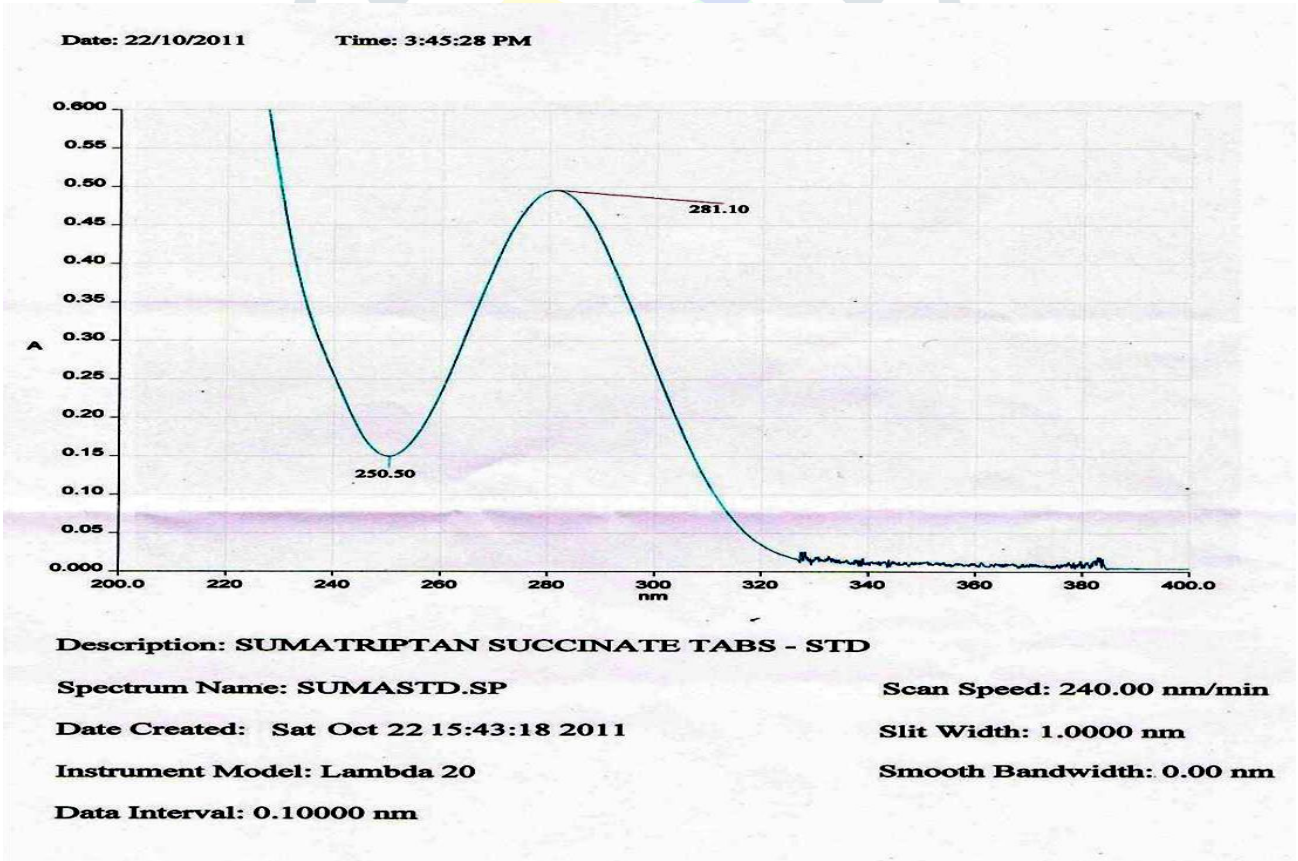

Fig.2: The Absorbtion Maxima of Test Sample of Sumatriptan Succinate In Methanol (λ max 282±1 nm)

f. Preparation of calibration curve

Standard solution: accurately weighed 50mg sumatriptan succinate powder dissolved in methanol and diluted up to 100ml, prepared dilution of 100µg/ml, filter (0.45µ) and the filtrate was used as standard solution.

Test solution: Twenty tablets were crushed & accurately weighed 265mg powder containing 50mg of sumatriptan succinate dissolved in methanol, diluted up to 100ml, prepared dilution of 100µg/ml, filter (0.45µ) and filtrate was used as sample solution.

Test solution of drug (100µg/ml) was prepared in methanol by gentle shaking. The test solution of appropriate concentration (2-16µg/ml) were made by further dilution of methanol. The absorbances of test solution of different concentration (2-16µg/ml) were analyzed by UV spectrophotometry. Similarly, the calibration curve of test solution sumatriptan succinate was made in methanol. The absorbances of sumatriptan succinate were found linear at various concentrations of test solution (for linearity). The calibration curve was plotted with concentration of drug on x-axis and absorbance on y-axis. The concentration of standard and test solution of drug was measured the absorbances at 282 nm by UV/Visible spectrophotometer (USP 2011, IP 2010).

The standard curve was plotted between the absorbance (Y-Axis) and concentration X-axis (2-16µg/ml) of test solution. This method had reproducibility R^2 =0.999 and followed the Beer's lambert law in the range 1-16 µg/ml. The absorbance data are given in Table-1 and Fig.3 shows the standard curve of sumatriptan succinate in methanol at λ-max 282 nm.

Table -1: Absorbance data of Sumatriptan Succinate in methanol

S. No.	Conc. (µg/ml)	Absorbance (282±1nm)
1	0	0
2	2	0.096
3	4	0.189
4	6	0.273
5	8	0.362
6	10	0.454
7	12	0.551
8	14	0.648
9	16	0.741

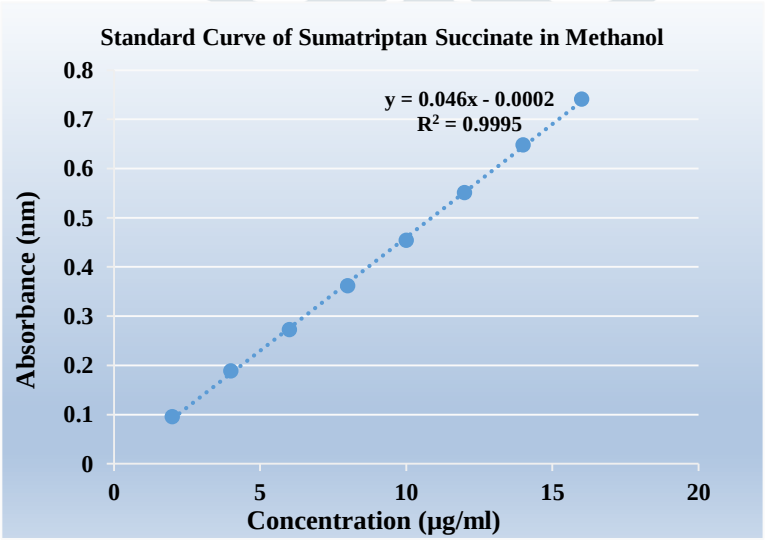

Fig. 3: Standard Curve of Sumatriptan Succinate in Methanol

g. **Infra red Spectroscopy (FTIR):** Taken 1mg suatriptan succinate mixed with 100mg dried potassium bromide (KBr), mixture was compressed by hydroulic press in to transparent thin pellet**.** Then thin pellet was put on pellet disc to get IR spectra of the drug. The IR spectrum exhibits main bands for identification of sumatriptan succinate at or near wave numbers (cm^{-1}) 3380, 1708, 1567, 1339, 1300, 1235, 1207, 989, 844, 767 (IP 2010). Identification of drug is illustrated in Fig.4.

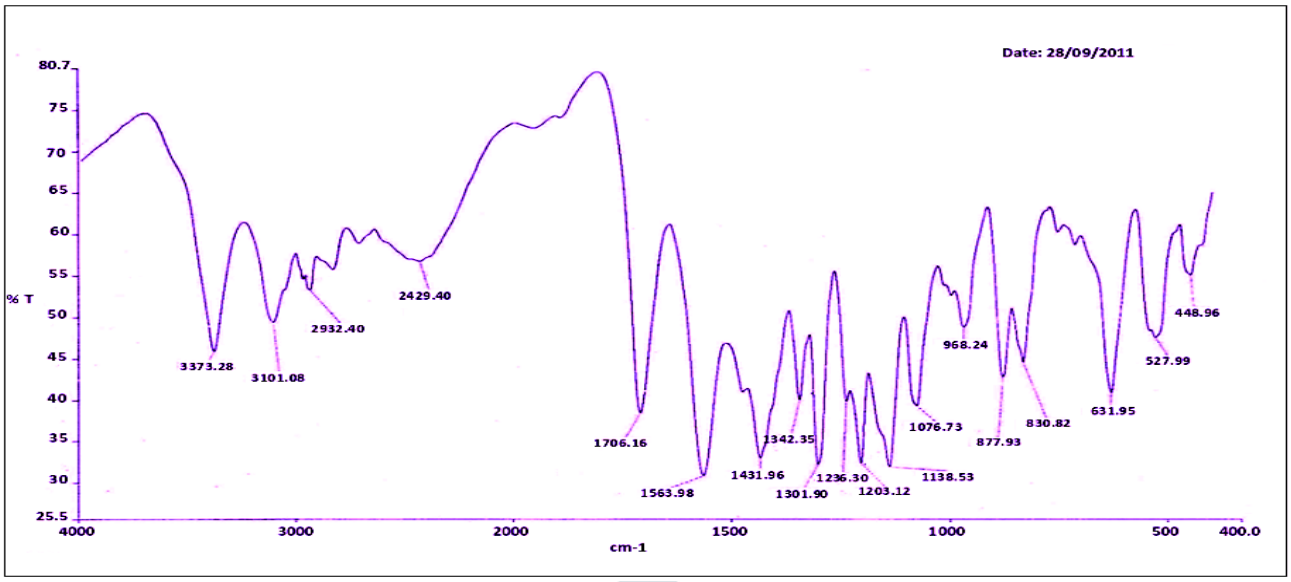

Fig. 4 : IR Spectra of Sumatriptan Succinate

IV. DRUG EXCIPIENTS COMPATIBILITY STUDIES

Compatibility studies used to detect physical, chemical interaction between drug and excipients. Drug and excipients were mixed thoroughly in a ratio at which use in the formulation. Mixtures of drug and excipients were stored 20°C, 40°C, 60°C and at room temperature in closed vials. After four weeks samples were scanned through FTIR spectrophotometer (Model-Paragon-500 Spectrum BX, Perkin Elmer). The spectra were compared to observe any incompatibility.

The spectra of pure sumatriptan succinate (Fig.4). The spectra of sumatriptan succinate with Kollidon CL, Ac-di-sol and pregelatinized starch, compared to observe any incompatibility The spectra of sumatriptan succinate with Kollidon CL, Ac-di-sol figure-5 and Avicel PH 102, compared to observe any incompatibility.

No significant changes were found in the peak behaviour of functional group in pure drug and drug excipients mixture. The following characteristic peaks were observed with Sumatriptan succinate, given in Table.2.

Table -2: Interpretation of IR spectra of Sumatriptan Succinate with excipients (Sharma, B.K., 2002, USP, IP 2010)

S.No	Characteristic group	Range [cm^{-1}]	Observed Peak (cm^{-1})
1	Aromatic C=C	1600-1425	1508.02
2	Carboxylic acid C=O	1725-1700	1701.04
3	Carboxylic acid C-O	1300-1000	1238.96
4	Carboxylic acid O-H	3400-2400	2931.75
5	N-H stretching	3500-3100	3384.57
6	N-H bending	1640-1550	1559.94
7	Secondary amine C-N stretching	1350-1000	1299.49
8	Sulphonamide S=O	1375-1300	1339.51
9	Aromatic C-H bending	850-700	844.57
10	C-S stretching	850-600	609.59

The results revealed no considerable changes in the IR peaks of Sumatriptan succinate when mixed with polymers such as Kollidon CL, Ac-di-Sol, Pregelatinized starch with Avicel PH 102.

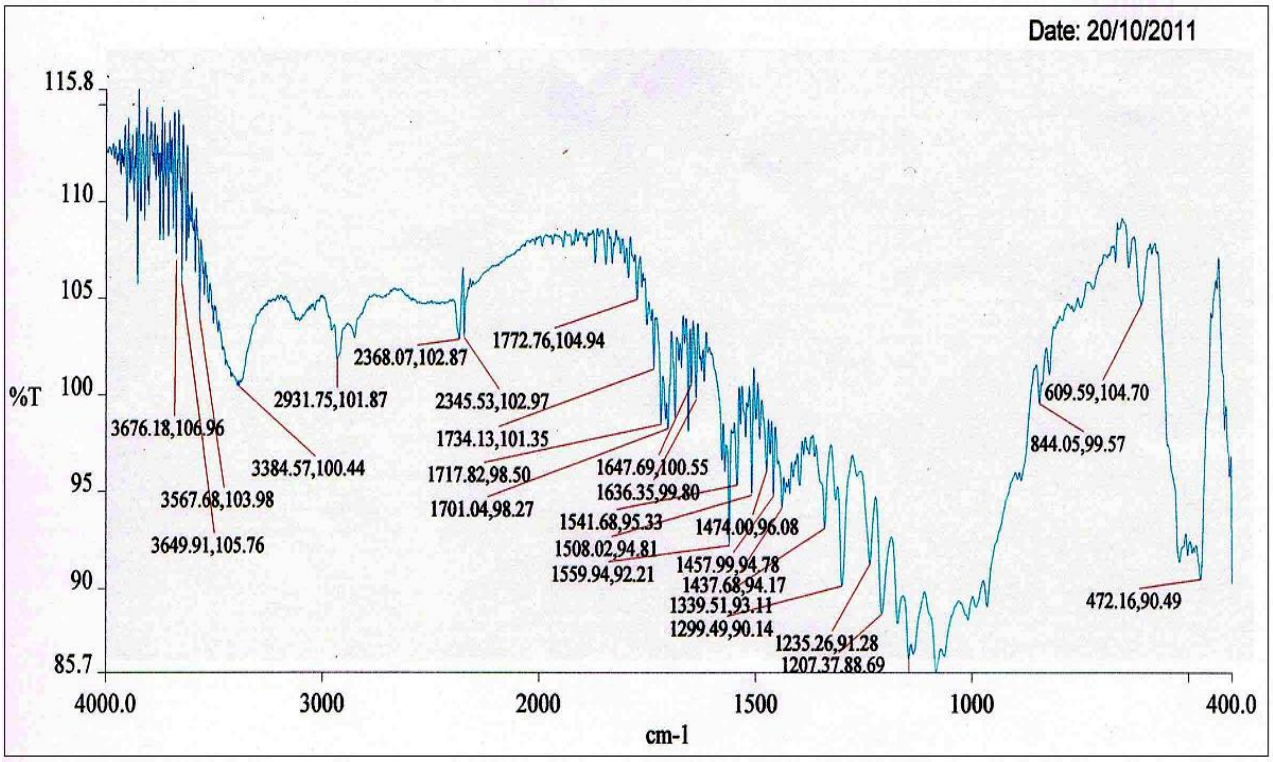

Fig. 5: IR spectra of Sumatriptan Succinate Mixture (i.e Kollidon CL, Ac-di-sol, Avicel PH 102 and others excipients)

V. FORMULATION AND DEVELOPMENT OF FAST DISSOLVING TABLETS BY DRY-GRANULATION & COMPRESSION METHOD

Fast dissolving tablets were prepared by three steps operation i.e Dry-granulation, Blending and compression. All ingredients were accurately weighed and passed through mesh individually.

I. ***Dry-Granulation operation:*** Sumatriptan succinate and Avicel PH-102 sieved through #30SS mesh. Aspartame and Pearlitol SD 200 sieved through #60SS mesh. Tartrazine color and Pineapple flavor sieved through#100SS Mesh. All sifted materials were transfer (individually mixed in geometrically mixing order) in double cone blender and mixed for 30 minute. The mixed material was slugged in to slug-tablets (hardness 5-6 kp). The slugged-tablets was resized through (#14SS Mesh) oscillating granulator in to sized granules. The sized granules increase particle density, improves powder flow and captures fines.

II. ***Blending operation:*** Kollidon CL, Ac-di-sol, Starch 1500, Magnesium Stearate and Talc ***were*** sieved through #60SS mesh and sized granules were sieved through #30SS Mesh. The whole mass were mixed for 15 minutes blending in to double cone blender.

III. ***Compression operation:*** the blended granules were used to compressed fast dissloving tablets by compression machine (Cadmach).

Table -3: Basic Quantity of Ingredients Used in FDT of Sumatriptan Succinate

API/Ingredients/Batch	Batch Quantity/tablets							
	F1	F2	F3	F4	F5	F6	F7	F8
Sumatriptan Succinate	50.0	50.0	50.0	50.0	50.0	50.0	50.0	50.0
Avicel PH-102	164.0	156.0	149.4	156.0	148.0	156.0	148.0	149.4
Ac-Di-Sol	-	-	4.0	-	-	-	-	-
Pearlitol SD 200	40.0	40.0	40.0	40.0	40.0	40.0	40.0	40.0
Aspartame	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Pineapple flavor	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Tartrazine yellow lake	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Kollidon CL	-	8.0	10.6	-	-	-	-	10.6
Ac-Di-Sol	-	-	-	8.0	16.0	-	-	-
Starch 1500	-	-	-	-	-	8.0	16.0	4.0
Magnesium stearate	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Talc	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0
Total weight (mg)	**265.0**	**265.0**	**265.0**	**265.0**	**265.0**	**265.0**	**265.0**	**265.0**

VI. EVALUATION OF PRE -COMPRESSION PARAMETERS

a. **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 into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume (Bhowmik *et al.*, 2009). It is expressed in g/ml.

BD = M/ Vb Where: M- the mass of powder,

V_b- the bulk volume of the powder (ml)

The result of bulk density is shown in table 4.

b. **Tapped density:** It is the ratio of total mass of the powder to the tapped volume of the powder. It is expressed in g/ml and calculated by formula no 2.4.

Dt = M / Vt, Where: M- the mass of powder (gm),

V_t- the tapped volume of the powder

The result of tapped density is shown in table 4.

c. **Angle of repose:** It is defined as maximum angle possible between the surfaces of the pile of powder and the horizontal plane. The flow properties of angle of repose given in table4.

$\theta = \tan^{-1} h/r$ Where: θ- the angle of repose, h- the height in (cm),

r- the radius of powder cone (cm)

The result of angle of repose is shown in table 4.

d. **Carr's index (compressibility index):** It reflects the relationship between powder flow properties and compressibility. It is expressed in percentage and is given by

I = Dt – Db× 100/Dt Where: D_t- the tapped density of the powder,

D_b- the bulk density of the powder

The percentage compressibility results is shown in table 4.

e. **Housner's ratio:** Hausner's ratio is an indirect index of ease of powder flow. It was calculated by.

Hausner's ratio = Dt / Db Where: D_t - the tapped density,

D_b- the bulk density

The Results for hausner ratio is shown in table 4.

The pre-compression results of formulations (F1-F8) were found within limits and comply with specific standards.

Table-4; Pre-compression parameter's results of blended granules

Parameters / Formulation	F1	F2	F3	F4	F5	F6	F7	F8
Bulk density (g/ml)	0.4430	0.4570	0.4340	0.4490	0.4450	0.4490	0.4220	0.4510
Tapped density (g/ml)	0.4930	0.5100	0.5200	0.5010	0.5170	0.5280	0.4750	0.5380
Angle of Repose	24.050	23.240	23.390	23.130	24.230	24.150	24.340	23.890
Carr's index (%)	10.141	10.392	15.538	12.375	13.926	14.962	11.157	13.538
Housner's Ratio	1.1120	1.1150	1.1980	1.1410	1.1610	1.1750	1.1250	1.1520

VII. COMPRESSION SPECIFICATIONS FOR MODEL TABLETS

Specifications/Test	Characteristics/Limits
Description	Round, flat, scored, plain, dispersed tablets
Weight variation	±5% (Range 251.75mg-278.25mg)
Punch/Die	Punch round 9.8 mm size , Embossed with score line.
Thickness/ Hardness	2.9 -3.3 mm, / NLT 3.0 Kp

DT/ Friability	NMT 1 minute / NMT 1.0%

VIII. Evaluation of Post-Compression Parameters

a. **Weight variation test:** 20 tablets were randomly selected from each batch and calculated the average weight. Then individual tablets were weighed (digital balance) and the individual weight was compared with an average weight, the variation in the weight was expressed in terms of % deviation and weight variation specification (IP1996). The results are mentioned in table-5.

Average weight	≤80 mg	≥ 80 mg but≤250 mg	≥250 mg
Deviation	±10%	±7.5%	±5%

b. Thickness: Thickness of tablet was measured by using digimatic caliper (mitutoyo). Five tablets were selected at randomly from each batch. It is expressed in mm. The results are mentioned in table-5.

c. **Hardness:** Hardness or tablet crushing strength (the force required to break a tablet in a diametric compression) was **measured** using Dr. Schleunizer hardness tester. It is expressed in kp and data for hardness of tablet. The results are mentioned in table-5.

d. **Friability:** Friability of tablet determined using electrolab friabilator. Tablets is subjects to the combined effect of abrasion and stock in a plastic chamber revolving at 25 rpm and dropping a tablet at height of 6 inches in each revolution.

20 tablets of each batch were weighed, placed into the friabilator and enter the initial weight subjected to the 100 revolutions. After completion 100 revolution in 4 minute, tablets were de-dusted using a soft muslin cloth and reweighed and enter weight to friability apparatus get % of friability automatically. The results are mentioned in table-5.

e. ***In-vitro* disintegration time:** The disintegration test is same as conventional dosage forms. The disintegration test was setup and placed one tablet in each of the basket and discs was added to each tube and operate the apparatus, using water maintained at 25±1°C as the immense fluid, for three minutes. At the end of the time limits, the basket was lifted from the fluid and time was noted when tablets were complete disintegrates (BP 2010, USP 2011). The results are mentioned in table-5.

f. ***In-vitro* dispersion time:** Two tablets were placed into 100 ml of water containing beaker and stir until completely dispersed. A smooth dispersion was produced which passes through a sieve screen with normal mesh aperture. The complete dispersion time of a tablet were noted in sec (as per BP). The *in-vitro* dispersion is shown in fig.6. The results are mentioned in table-5.

Fig. 6: *In-vitro* dispersion of fast dissolving tablet.

g. **Water absorption ratio and wetting time:** A piece of tissue paper folded twice was placed in a small petri-dish containing 6 ml of water. A tablet of known weight was placed on the paper and the time required for complete wetting of tablet was measured. The wetted tablet was then weighed, water absorption ratio R was determined using the following formula. The results are mentioned in table-5.

$R=(Wa-Wb/Wa)x100$ Where: W_b- the weight of tablet before water absorption

W_a- the weight of tablet after water absorption

h. Drug Content Uniformity Study

Standard Solution: 50 mg of reference standard (USP Vial) was accurately weighed and dissolved in 100 ml volumetric flask. The sufficient quantity of methanol was added. And volume was made up to 100 ml with same solvent. Take 2 ml of this solution was transferred to 100 ml volumetric flask and volume made up to 100 ml with same solvent. Solution was sonicated for 5 minute and filtered through 0.45µ filter paper and filterate was used to determine the absorbances of reference standard solution.

Test Solution: 10 tablets of each formulation were crushed in mortar pestle. Accurately weighed 265 mg (equivalent to 50 mg of drug) was dissolved in 100 ml volumetric flask, added sufficient quantity of methanol to dissolve the powder. Volume was made up to 100 ml with same solvent. 2 ml of this solution was taken and transferred to 100 ml volumetric and then make up volume up to 100 ml with same solvent. Solution was sonicated for 5 minute and filtered through 0.45µ filter paper and filterate were used to determine the absorbance of test solution. The content of drug was calculated by the formula no. 2.10. The results are given in table-5.

$$\textbf{Content uniformity}\ (\%) = \frac{\mathbf{AT}}{\mathbf{AS}} \times \frac{\mathbf{SW}}{\mathbf{100}} \times \frac{\mathbf{2}}{\mathbf{100}} \times \frac{\mathbf{100}}{\mathbf{265mg}} \times \frac{\mathbf{100}}{\mathbf{2}} \times \frac{\mathbf{P}}{\mathbf{100}} \times \mathbf{100} \qquad (\mathbf{2.10})$$

Where: AT -Absorbance of test solution, AS -Absorbance of standard sample

AW -Average weight (mg), P -Potency of working standard

SW -Standard weight (mg), TW -Test weight (mg)

Table 5 Physical Parameters of Fast Dissolving Tablets of Sumatriptan Succinate

Parameter \ Batch	F1	F2	F3	F4	F5	F6	F7	F8
Weight (Mg)	266±5	264±6	265±4	267±6	264±5	263±7	265±4	266±5
Thickness (Mm)	2.99 ±0.16	2.98±0.22	3.01±0.27	3.08±0.2	2.96±0.3	3.09±0.2	3.05±0.15	2.99±0.3
Hardness (Kp)	3.55±0.65	3.42±0.78	3.70±0.8	3.49±0.27	3.50±0.27	3.48±0.11	3.51±0.12	4.05±0.5
Friability (%)	0.47	0.51	0.38	0.49	0.40	0.39	0.46	0.42
Disintegration Time (Sec.)	54±1.45	28±1.15	19±1.35	35±1.73	41±1.26	52±1.11	47±0.96	28±1.35
Dispersion Time (Sec.)	59.2±1.02	37.4±1.76	26.2±0.97	42.2±1.45	48.2±1.23	55.1±0.87	51.4±1.05	47.4±1.0
Wetting Time (Sec.)	69±2.13	41±0.88	35±1.65	51±2.13	57±1.04	68±0.89	62±1.89	45±1.05
Water Absorption (Sec.)	64.1±1.88	75.3±1.95	82.5±2.04	72.0±1.45	68.3±1.78	61.6±2.15	72.0±1.75	86.5±2.0
Drug Content (%)	98.78±0.31	99.41±0.29	99.81±0.10	98.24±0.24	99.23±0.38	99.44±0.17	98.92±0.4	98.5±0.9

IX. *IN-VITRO* DRUG RELEASE OF SUMATRIPTAN SUCCINATE TABLETS

The fast dissolving tablets of sumatriptan succinate were prepared by dry granulation method using various superdisintegrants like crospovidone (Kollidon CL), croscarmellose sodium (Ac-di-sol) and pregelatinized starch (Starch 1500) with microcrystalline cellulose phosphate (Avicel PH-102). All formulations batches (F1-F8) were subjected for *in-vitro* drug release. The release of drug was found within range 90.54 to 99.78 %. Based on drug release batch F3 containing the combination of Kollidon CL (4%) and Ac-di-sol (1.5%) which displayed better release rate in comparison to other formulations batches. Hence, results are concluded that fast dissolving tablets of sumatriptan succinate exhibit faster dissolution rate which leads to improved oral bio-availability and effective therapy of dry granulation method. Therefore, formulation batch F3 given the best promising results for formulation. The Results are given in table 6 and Fig.7.

Dissolution parameters

Apparatus : USP II (Paddle type), 30 RPM

Temperature: 37±0.5°C

Medium : 0.01N HCL (Mixed well Hydrochloric acid 8.5ml in 10 liter purified water)

Standard Solution: Accurately weighed 50mg of working standard (USP Vial) was dissolved in 70 ml of 0.01N HCL, sonicated for 5min, made up to 100ml in volumetric flask. Withdrawn 2ml solution transferred to volumetric flask further made up to 100 ml with 0.01N hydrochloric acid, filtered (0.45µ) the solution. Used the solution as blank (at 282nm).

Drug Dissolution Procedure: Taken 6 tablets from each batch and placed into each dissolution vessel containing 900ml of 0.01N HCL solution, equilibrated at temperature (37±0.5°C). paddle were rotated at 30 RPM for 15 min, withdrawn 10ml sample from each vessel. Then each vessel quantity were replenished 10ml 0.01NHCL. Aliquot of dissolution medium was withdrawn at 5, 10, 15 minute interval. Each interval's, withdrawn volume 10 ml were mixed with again 25ml of 0.01NHCL and filtered (0.45µ). filtered solution were used to measure the absorbance (at 282nm) (USP 2011). Dissolution rate were studied for all formulations (IHS). The % drug release results are given in table -6 and Fig.7.

$$\%\ \textbf{Drug release} = \frac{\mathbf{AT}}{\mathbf{AS}} \times \frac{\mathbf{SW}}{\mathbf{100}} \times \frac{\mathbf{5ml}}{\mathbf{100}} \times \frac{\mathbf{900}}{\mathbf{1Tablet}} \times \frac{\mathbf{25ml}}{\mathbf{10ml}} \times \frac{\mathbf{P}}{\mathbf{100}} \times \mathbf{100} \qquad (\mathbf{2.11})$$

Where: AT- Absorbance of test solution, AS- Absorbance of Standard solution,

SW- Standard weight (mg), P-Potency of working standard, T- Test weight (mg)

Table 6: Dissolution profile of batch F1-F8

Batch	*In-vitro* % drug release (Min.)			
	0	5	10	15
F1	0	47.20	74.42	90.54
F2	0	79.78	95.72	96.22
F3	0	81.50	98.14	99.78
F4	0	78.84	95.48	96.04
F5	0	74.23	94.79	96.75
F6	0	71.78	93.19	95.46
F7	0	75.06	95.58	96.01
F8	0	77.46	96.21	96.58

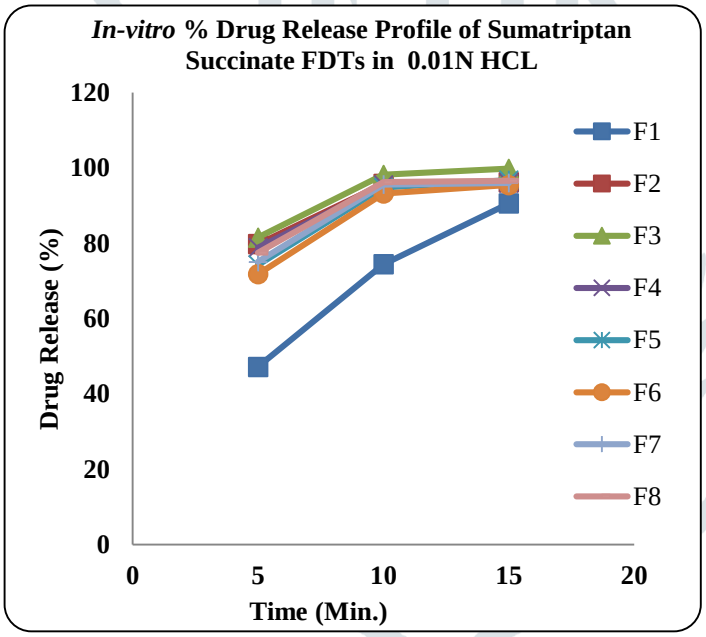

Fig. 7: *In-vitro* drug release of Sumatriptan Succinate FDTs in 0.01N HCL

X. MICROBIAL EVALUATION OF SUMATRIPTAN SUCCINATE TABLETS

The microbial flora presence may affect the quality, safety, efficacy and product activity and gram negative micro-organisms also like E.coli can cause serious food poisoning in humans. Salmonella can cause diarrhea, typhoid. Staphylococcus aureus can cause illnesses, skin infections, such as pimples, impetigo, boils, carbuncles, scalded skin syndrome (Nakajima,et.al.2005). Pseudomonas aeruginosa may cause the burns, urinary and respiratory tracts infection (Wiki).

The formulated batch's (F1-F8) were subjected to evaluate the microbial contamination i.e. TABC, TMC & Specified micro organism. Plate count method (SCDM, FTM) were used to estimate the total number of viable & specified micro-organisms presence in species in pharmaceutical substances. Microbial test were carried out aseptically under the laminar air flow.

Test Sample Preparation: Accurately weighed 10g powdered tablets were dissolved in 90ml of sterile buffered sodium chloride peptone solution (pH 7.0), made 100 ml volume.

Total Aerobic Bacterial Count: Two petri plates were prepared. first, 1ml of test sample and 20ml of molten and tempered Soyabeen Casein Digest Agar Medium and second, 1ml of test sample and 20ml of molten and tempered Soyabeen Casein Digest Agar Medium with antibiotic.These plates were incubated at 30-35°C (Bacterial Growth) for 3-5 days.

Total Mould Count: Two petri plates were prepared. first, 1ml of test sample and 20ml of molten and tempered Sabroud Dextrose agar Medium and second, 1ml of test sample and 20ml of molten and tempered Sabroud Dextrose agar Medium with

antibiotic. These prepared plates were kept inverted and incubate at 20-25°C for 5-7 days. Test dilution were mixed by rotating or tilting the plates, kept for solidification. The microbial colony (CFU) was counted by following formula 2.12.

$$\text{CFU} = \frac{\text{Total number of colony on Agar plates} \times \text{Dilution}}{\text{Weight of sample taken}} \qquad 2.12$$

The total microbial contamination results were found with in specified limits and results are mentioned in table-7.

Table- 7; Microbiological Evaluation Test Report of Sumatriptan Succinate

Batch / Test	F1 (Cfu/g)	F2 (Cfu/g)	F3 (Cfu/g)	F4 (Cfu/g)	F5 (Cfu/g)	F6 (Cfu/g)	F7 (Cfu/g)	F8 (Cfu/g)
TABC	<85	<94	<82	<98	<81	<90	<78	<93
TFC	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent
E. Coli, F. Salmonella Sp. G. P. Aeruginosa, Staphylococcus	Absent	Absent	Absent	Absent	Absent	Absent	Absent	Absent

XI. STABILITY STUDIES

The stability study is to provide evidence how the quality of a drug substance/product stable with time on influence of various factors like temperature, humidity and light, enabling recommended storage conditions, retest periods and shelf-lives.

As per evaluation study, formulation batch F3 had been displayed the better results in comparison to other formulations. based on results Formulation F3 was selected for accelerated stability study for six months. These tablets were packed suitably and kept in humidity chamber at accelerated conditions (40±2°C/75±5% RH). The stability study test were conducted at 0, 3, 6 months intervals.

All subjected tablets of batch F3 did not showed any significant changes in physical i.e. appearance, weight, percentage drug content, disintegration time, chemical stability i.e. in-vitro drug release profile and microbial purity. It was conclude that the prepared fast dissolving tablets of sumatriptan succinate found stable and may stored in moisture proof packaging for long period of time without any changes.

Refer table-8 for results of Stability Study.

Table 8: Accelerated stability studies of formulation F3

PARAMETERS	TIME INTERVAL		
	Initial	3 months	6 months
Appearance	No change	No change	No change
Average weight (mg)	201.1±1.49	201.1±1.3	201±1.3
Hardness (KP)	3.8±0.17	3.7±0.13	3.9±0.15
Drug content (%)	101.41	99.60	99.42
Disintegration time (sec.)	19.35	19.65	20.01
Wetting time (sec.)	31	39	37
Water absorbtion ratio (%)	83.2	84.6	83.8
Drug release (%)	99.82	99.35	98.91
TABC (cfu)	<100	<100	<100
TMC (cfu)	Nil	Nil	Nil
Specified micro-organism	Absent	Absent	Absent

XII. RESULT AND DISCUSSION

In this study, the fast dissolving tablets of sumatriptan succinate were prepared by dry granulation method with crospovidone (Kollidon CL), croscarmellose sodium (Ac-di-sol) and pregelatinized starch (Starch 1500) used as superdisintegrants with different-2 concentrations. Avicel PH-102 was used as binder/diluents, Aspartame as sweetening agent which mask bitter taste of drug. Pineapple (dry) use as flavoring agent and Tartrazine yellow lake were used as coloring agent which makes to elegant product quality.

Bulk granules were prepared by dry granulation methods contained sumatriptan succinate, superdisintegrants and excipients. These prepared granules were evaluated for physicochemical parameters like bulk density, tapped density, angle of repose, carr's index and housners ratio. All pre-compression parameters were found within specified limit which provides good flow properties to bulk granules. The prepared granules of sumatriptan succinate containing mixture of superdisintegrants and excipients, evaluated for physicochemical parameters like bulk density, tapped density, angle of repose, carr's index and housner's ratio. These parameters were found within specified a limit, which indicates the good flow properties to the bulk granules. The bulk lubricated granules were used to compress the tablets.

All compressed tablets batches (F1-F8) were subjected to evaluate the physical appearance, thickness, weight variation, hardness, disintegration time, wetting time, drug content uniformity and *in-vitro* drug release. Post compression parameters result all formulations were complies with specified limits. Based on evaluation studies, formulation batch F3 containing the combination of crospovidone (Kollidon CL, 4%), croscarmellose (Ac-di-sol, 1.5%) was found rapid disintegration within 19±1.35sec. and almost 99.78% drug was released within 15 minutes due to highly porous structure and water wicking mechanism of Ac-di-sol and Kollidon CL. The stability studies was performed as per I.C.H guidelines and found no significant variations in physical appearance, weight variation, hardness, disintegration time, wetting time, drug content uniformity and *in-vitro* drug release and microbial contaminants also.

XIII. CONCLUSION

In the present study, it is concluded that the fast dissolving tablets of sumatriptan succinate can be prepared with combination of Kollidon CL and Ac-di-sol as superdisintegrants in 4% and 1.5% concentrations with Avicel PH102 showing enhanced dissolution rate which will lead to improved bioavailability and effective therapy by using dry granulation method. The above mentioned promising results of batch F3 with respect to *in-vitro* dissolution, disintegration time, wetting time which provides the stable and patient compliance dosage form. This research objective was to develop a stable dosage form with better patient's compliance which provides quick onset of action. Sumatriptan succinate is an antimigraine agent which have bitter taste and hygroscopic nature.

XIV. REFERENCES

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