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Formulation and In-Vitro Evaluation of Bilayer Tablet of Sumatriptan Succinate

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ABSTRACT:
The goal of the present study was to develop and evaluate bilayer tablet of sumatriptan succinate, an antimigraine drug. The Bilayer tablets (F1-F12) was prepared by direct compression method and formulated using different concentration of polymers. Combination of polymer, HPMCK4M, Xanthan gum, guar gum FT-IR spectroscopy was done to study the compatibility of the drug with various excipients used in formulation. Formulations were subjected for pre-compression and post compression evaluation. The granules of the blend showed excellent flow property & good compressibility index. The compressed tablets were evaluated for post compression parameters and showed compliance with pharmacopoeial limits. Bilayer tablet is one of the great advanced technologies which contain two different layered formulations with one layer of drug provide immediate release and the other as sustained. Sumatriptan succinate is a triptans class of drug used to treat migraine headaches, which acts selectively at 5-HT1B/1D receptors. The objective is to formulate and evaluate the bilayer tablets of sumatriptan succinate of dose 100 mg. In this case immediate release layer is formulated using crospovidone as a super-Disintegrants. Sustained release layer is formulated using hydroxypropyl methylcellulose K4M, xanthan gum and guar gum in various ratios to delay the drug release. FT-IR studies for excipients are tested for compatibility with the drug. Evaluations such as Hardness, Thickness, Friability, Weight variation, Disintegration time and Assay were determined for bilayer tablets. In vitro drug release was performed with USP dissolution apparatus type-II (paddle type) using 0.1 N Hydrochloric acid for two hours and later hours with 6.8 pH phosphate buffer by temperature maintaining at 37˚C ± 0.5 ˚C. Based on results among all formulations F7 formulation containing drug and Guar gum in ratio of 1:1 showed maximum drug release of 91.54%. Thus, drug formulation of F7 has enhanced drug release profile.

KEYWORDS: Sumatriptan succinate, Bilayered tablets, Direct compression method, HPMCK4M, Xanthan gum, Guar gum.

I. INTRODUCTION

For many decades, treatment of acute disease or a chronic illness has been mostly accomplished by delivering drugs using various pharmaceuticals dosage forms, including tablet, capsules, pills, suppositories, creams, ointments, liquids, aerosols, and injectables as carriers. Among various route of drug delivering route is perhaps the most preferred to the patient and the clinician alike. However this route presents some problem for a few drugs. The enzymes in GI-fluids GIT-pH conditions and the enzymes bounds to the enzymes bound to GIT membranes are a few factors responsible for the bioavailability problems. The blood that drains the GIT carries the drug directly to the liver leading to first pass metabolism resulting in poor bioavailability. The inherent problem associated with the drug in some cases can be solved by modifying the formulations or by changing the route of administration parenteral, mucosal and transdermal route circumvent hepatic first-pass metabolism and offer alternative routes for the systemic delivery of drugs.[1]

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Drug may be administered by variety of routes but oral administration is adopted wherever possible. It is safest, easiest and most economical route of drug administration. Among the drugs that are administered orally solid oral dosage forms i.e. tablets and capsules represent the preferred class of products. Solid medicaments may be administered orally as powders, pills, cachets, capsules or tablets. These dosage forms contain a quantity of drug which is given as a single unit and they are known collectively as solid unit dosage forms, even in the case of sustained action preparations which, technically contain the equivalent of several normal doses of drug. The stringent formulation requirements of modern medicaments, the many advantages of tablet and capsule medication, coupled with expanding health services and the commitment need for large-scale economic manufacture, have led to a steady decline in the prescribing of powders and pills. Tablets and capsules on the other hand, currently account for well over two third of the total number and cost of medicines produced all over the world.

Tablet is defined as a compressed solid dosage form containing medicaments with or without excipients. According to the Indian Pharmacopoeia Pharmaceutical tablets are solid, flat or biconvex dishes, unit dosage form, prepared by compressing a drugs or a mixture of drugs, with or without diluents. They vary in shape and differ greatly in size and weight, depending on amount of medicinal substances and the intended mode of administration. It is the most popular dosage form and 70% of the total medicines are dispensed in the form of Tablet. All medicaments are available in the tablet form except where it is difficult to formulate or administer.[2]

ADVANTAGES AND DISADVANTAGES OF TABLETS AS DOSAGE FORMS:[1,2,3]

Tablets are the most popular dosage form used today and therefore there are several advantages associated with their use. However it is also important to highlight the disadvantages associated with their use.

Advantages

❖Tablets are convenient to use and are an elegant dosage form.

❖ Increased convenience for physician and patient,

❖ Improved compliance because fewer daily doses are required compared to traditional systems.

❖ Low cost including production, storage, transport, dispensing and other health system costs.

❖Tested safety and reduction of adverse side effect can be accomplished by targeting the drug release to the absorption site as well as controlling the rate of release, enabling the total drug content to be reduced.

❖ Blood level of a drug can be held at consistent therapeutic level for improved drug delivery, accuracy, safety and reduce side effects.

❖Separate physically or chemically incompatible ingredients.

❖ Tablets are generally an inexpensive dosage form.

❖It is easier to mask the taste of bitter drugs using tablets than for other dosage forms, e.g. liquids.

❖ A wide range of tablet types is available, offering a range of drug release rates and durations of clinical effect. Tablets may be formulated to offer rapid drug release or controlled drug release, the latter reducing the number of daily doses required (and in so doing increasing patient compliance).

❖ Tablets may be formulated to release the therapeutic agent at a particular site within the gastrointestinal tract to reduce side effects, promote absorption at that site and provide a local effect (e.g. ulcerative colitis). This may not be easily achieved by other dosage forms that are administered orally.

❖ Tablets may be formulated to contain more than one therapeutic agent (even if there is a physical or chemical incompatibility between each active agent). Moreover, the release of each

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therapeutic agent may be effectively controlled by the tablet formulation and design.

Disadvantages

❖ Individual layer weight control is difficult to monitor.

❖ Difficult to swallow in case of children and unconscious patient.

❖ Cross-contamination between the layers generally occurs during preparation.

❖ Problems in hardness adjustment.

❖ Overall Reduction in yield.

❖ Complex process and bilayer rotary presses are expensive.

❖ Limitation on flexibility and individualization in dosing.

❖ Exposing patients to risks of additional ingredients.

❖ Insufficient hardness, layer separation, reduced yield.

❖ Inaccurate individual layer weight control.

II. MATERIALS AND METHODS

MATERIALS

Sumatriptan succinate drug got from Yarrow chem. and also gift sample from Mylan laboratories. Superdisintegrants such as Crosspovidone, Polymer such as HPMC K4M, Xanthan gum, Guar gum and Microcrystalline cellulose from Karnataka fine chem, Karnataka.

Formulation of sumatriptan bilayer tablet:

Table No 1 : Formulation development of Sumatriptan Succinate IR layer

Sr.no.	Ingridients	F1	F2	F3
01.	Sumatriptan (1 g eq. to 1.3997 g of sumatriptan succinate.)	30 (42)	30	30
02.	Cross povidone	30(1:1)	45(1:1.5)	60(1:2)
03.	Micro crystalline cellulose	128	113	98
04.	Magnesium stearate	4	4	4
05.	Talc	2	2	2
06.	Ferric oxide red	1	1	1
	Total	207	207	207

Table No 2 : Formulation development of Sumatriptan Succinate SR layer

Sr.no	Ingridients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
01.	Sumatriptan (1g of s = 1.3997g of ss)	70 (98)	70	70	70	70	70	70	70	70	70	70	70
02.	HPMC K4M	70	105	140							35	52.5	70
03.	Xanthan gum				70	105	140				70	35	52.5
04.	Guar gum							70	105	140	52.5	70	35
05.	MCC	116	81	46	116	81	46	116	81	46	28.5	28.5	28.5
06.	Mg. stearate	6	6	6	6	6	6	6	6	6	6	6	6
07.	Talc	3	3	3	3	3	3	3	3	3	3	3	3
	Total	293	293	293	293	293	293	293	293	293	293	293	293

CHARACTERIZATION OF DRUG:

Colour and Appearance:

The sample was observed visually.

Melting Point:

Melting point of drug was determined by Melting point test apparatus.

pH Determination:

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A 2 % saturated solution of Sumatriptan succinate was prepared in distilled water and pH was measured by digital pH meter.

Solubility:

10 mg of Drug dissolve in 10 ml of H_2O and keep that in magnetic stirrer for 24hr continuously stirring on mild heat. Then filter the solution using whatmann filter paper, then take 1ml and dilute it to 10ml and measure the absorbance at 227 nm.

PREFORMULATION STUDY

Preformulation study is the first step in the rational development of dosage forms. It can be defined as an investigation of physical and chemical property of a drug substance alone and when combined with excipients. The main objective is to generate information useful to the formulation in developing most stable and bioavailable dosage form.[4,5]

Objectives Of Preformulation Studies:

- To generate useful information about the drug to the formulator to design an optimum drug delivery system.
- To establish necessary physicochemical parameters of a new drug substance.
- To determine kinetic rate profile.
- To establish physical characteristics of drug.
- To find out compatibility of a drug with commonly used excipients.

DRUG-EXCIPIENTS COMPATIBILITY

- **Differential scanning calorimetry (DSC):-** Sumatriptan succinate powder was mixed with various polymers in the ratio of 1:1.The mixture of drug with polymers to maximize the like hood of obscuring an interaction. Mixture should be examined under Nitrogen to eliminate oxidative and pyrolytic effect at a standard heating rate (2, 5 or 100C/minute) on DSC. Over a temperature range, which will encompass any thermal changes due to the mixture of drug with polymers thermograms of pure drug are used as a reference.

Appearance or disappearance of one or more peaks in thermograms of drug with polymer is considered as an indication of interaction.

- **Fourier transforms Infrared spectroscopy (FTIR):-** The infrared spectrum of Sumatriptan succinate was recorded by using FT-IR (Alfa Bruker) instrument. Sumatriptan succinate powder was mixed with various polymers with equal quantity of potassium bromide in the ratio of 1:1 made in the form of pellet and placed in sample cell to record its IR- spectra List may be presented with each item marked by bullets and numbers.[5]

- **Preparation of Standard Curve of Sumatriptan succinate in 0.1N HCl:**

Weigh accurately about 10 mg of Sumatriptan succinate was dissolved in small quantity of 0.1N HCl and make up to 100ml.From this above 1 ml was pipette out and was made upto100ml with 0.1N HCl in 10ml volumetric flask from this stock, aliquots of 2, 4, 6, 8 and 10 ml was pipette out and transferred to 10 ml volumetric flasks and final volume was made giving concentrations from 2.0 to 10 µg/ml. The absorbance of these solutions was estimated in UV-Visible spectrometer at 227nm utilizing 0.1N HCl as blank.[6]

- **Preparation of Standard Curve of Sumatriptan succinate in 6.8 N phosphate buffer:**

Weigh accurately about 10 mg of Sumatriptan succinate was dissolved in small quantity of 6.8 N phosphate buffer and make up to 100ml.From this above 1 ml was pipette out and was made upto100ml with 6.8 N phosphate buffer in 10ml volumetric flask from this stock, aliquots of 2, 4, 6, 8 and 10 ml was pipette out and transferred to 10 ml volumetric flasks and final volume was made giving concentrations from 2.0 to 10 µg/ml. The absorbance of these solutions was estimated in UV-Visible spectrometer at 227nm utilizing 6.8 N phosphate buffer as blank.[5,6]

EVALUATION OF MICROMERITIC PROPERTIES OF POWDERS:

- **Bulk Density and Tapped Density:**

An accurately weighed quantity of powders and/or granules (W) was carefully poured into the graduated cylinder and the volume (V0) was measured then the graduated cylinder was closed with lid, set into bulk density apparatus which was set for 50 taps. After completion of 50

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taps, the volume (Vf) was measured and continued until the two consecutive readings are equal. The bulk density and tapped density was calculated using the following formula:[6,7]

Bulk Density = W / V_0

Tapped Density = W / V_f

Where, V_0 = Initial volume
V_f = Final Volume

- **Compressibility Index and Hausner's Ratio:**[6,7]

The compressibility index and Hausner's ratio was calculated using measured values for bulk density (ρ bulk) and tapped density (ρ tapped) as follows:

Compressibility index (%) = $\frac{\mathbf{TBD-LBD}}{\mathbf{TBD}}\boldsymbol{X}\mathbf{100}$

Hausner's ratio = $\frac{\mathbf{TBD}}{\mathbf{LB}}$

Where, TBD = Tapped bulk density
LBD = Loose bulk density

Effect of Carr's Index and Hausner's ratio on flow properties

Carr's Index (%)	Flow character	Hausner's ratio
≤10	Excellent	1.0-1.11
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

Angle of Repose:

Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and the horizontal plane. The angle of repose of blended granule was determined by the funnel method. Accurately weighed granules blend was passed through a funnel that is fixed in such a way that it just touches the apex of the blend. The blend was allowed to flow through the funnel freely on to the surface. The diameter of the granule cone was measured and the angle of repose was calculated using the equation:

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

Where,
θ = Angle of repose
h = height of the pile
r = radius of the base of the pile

Effect of Angle of Repose (θ) on Flow property

Angle of Repose (θ)	Type of flow
25-30	Excellent
31-35	Good
36-40	Fair
41-45	Passable
46-55	Poor

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56-65	Very poor
>66	Very very poor

POST-COMPRESSION STUDIES[7,8,9]

Shape and Appearance:

The formulated tablets were visually observed for its shape and color.

Uniformity of thickness:

Thickness and diameter of the tablets were measured using a Vernier Caliper. Three tablets of each formulation were picked randomly and the dimension of each three tablets was measured in mm. This was done in triplicate and standard deviation was calculated. The tablet thickness was controlled within a ± 5% variation of the standard.

Weight Variation Test:

The weight variation test was carried out in order to verify the uniformity of the weight of tablets in each formulation. Twenty tablets were selected randomly and weighed individually to check for the weight variation. The following percentage deviation in weight was allowed as shown in the table

Limits for weight variation (U.S.P)

Average weight of a tablet	Percentage deviation (%)
130 mg or less	10
More than 130 mg and less than 324 mg	7.5
324 mg or more	5

Thickness of Tablets:

The thickness of the tablets was determined using a Vernier Caliper. Ten tablets from each prepared batch of Nifedipine were taken and an average thickness value was calculated. The average thicknesses of all the twelve formulation are given in table no. [10,11]

Friability of Tablets:

The friability of the tablets was determined for ten tablets taken randomly from each formulation. After weighing, the tablets were placed in the plastic chamber of friability test apparatus. The friability was evaluated by the following formula:[10,11,12]

$F = (W_1-W_2)/W_1 \times 100$

Where,

W1 = Weight of the tablets before testing.

W2 = Weight of the tablets after testing.

% friability of the tablets less than 1% is considered acceptable.

Hardness of the Tablets:

The crushing strength of prepared tablets of sumatriptan was determined using Monsanto tablet hardness tester. [12,13]

Disintegration time:

Disintegration apparatus consists of 6 tubes with 3-inch length and the bottom of glass tube have #10 mesh the particles should pass through it; each tablet is placed in each tube and tubes are placed in 1lt of 0.1N HCl. The device is raising and lowering the basket in the immersion fluid at a constant frequency rate of 29 and 32 cycles per minute and is maintained at 37 ±2˚ C. The time taken to disintegrate the tablet is determined when all particles should pass through the #10 mesh in glass tube. [13]

In-vitro Dissolution of Tablets:

Sumatriptan succinate release rate from bilayer tablets was determined using USP Dissolution Testing Apparatus type-II i.e. Paddle apparatus. A sample about 5ml of the solution was regularly withdrawn from the apparatus and the samples were replaced with fresh buffer medium. It is filtered through 0.45µ membrane filter and diluted using respective medium. Absorbance was measured at 227nm using a UV- Visible spectrophotometer.[14,15]

For Sumatriptan Succinate IR Layer:

Medium: 900 ml of 0.1N Hydrochloric acid

RPM: 75 Apparatus: Paddle (USP type-II apparatus)

Time: 15,30,45,60,120 minutes

Wave Length: 227 nm

Temperature: 37˚C ± 0.5˚C

For Sumatriptan Succinate SR Layer:

Medium: 900 ml of 6.8 pH buffer.

RPM: 75 Apparatus: Paddle (USP type-II apparatus)

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Time: 1st, 2nd, 4th, 6th, 8th Hours.
Wave Length: 227 nm
Temperature: 37˚ C ± 0.5˚C

STABILITY STUDIES:

The selected formulation was tested for its stability studies. Short term stability studies were performed at temperature 40±2°C over a period of 3 months. 5 tablets were packed in amber colored screw bottle and kept in stability chamber maintained at 40±2°C .Samples were taken at 1 month interval for their drug content estimation including physical parameters. At the end of 3 months periods, dissolution was performed to determine the drug release profile.[16,17,18]

III. RESULT AND DISCUSSION

Characterization of Drug

Table No. 3: Organoleptic Properties of Sumatriptan succinate

S. No.	Parameters	Reported	Inferences
1	Nature	crystalline powder	crystalline powder
2	Color	white	White
3	Melting point	166-171°C	169±1.081
4	Odor	Odorless	Odorless
5	Taste	Tasteless	Tasteless
6	Solubility	Freely soluble in water , sparingly soluble in methanol, insoluble in methylene chloride.	Freely soluble in water , sparingly soluble in methanol, insoluble in methylene chloride.

Standard calibration plot of Sumatriptan succinate: The λmax of Sumatriptan succinate in 0.1 N HCl was found to be 227 nm. The absorbance values are tabulated in the table no. 3. Sumatriptan succinate obeyed Beer Lamberts law in the concentration range of 0 – 10 µg/ml with good correlation coefficient 0.998 indicating good linearity in the concentration range.

Table No. 4: Data for Calibration Curve of Sumatriptan succinate in 0.1 N HCl at 227

Concentration (µg/ml)	Absorbance
0	0.00
2	0.154
4	0.310
6	0.401
8	0.566
10	0.641

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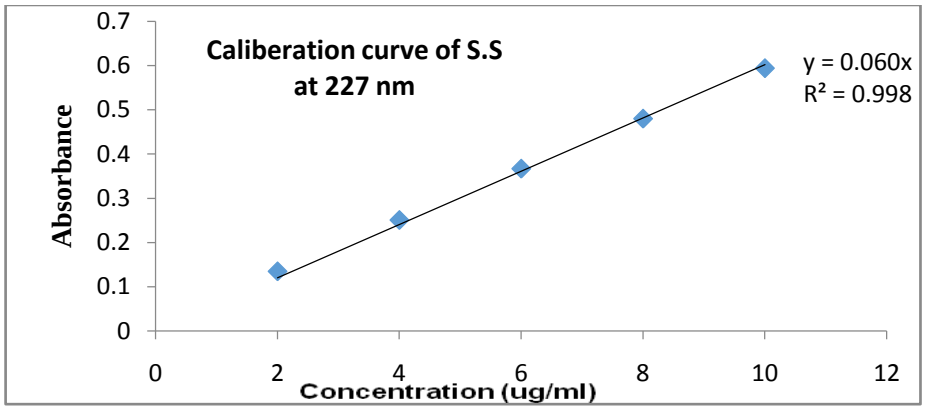

Figure 1: Standard Calibration Curve of Sumatriptan succinate in 0.1 N HCl at 227 nm.

Standard calibration plot of Sumatriptan succinate:

The λmax of Sumatriptan succinate in 6.8 phosphate buffer was found to be 227 nm. The absorbance values are tabulated in the table no. 4 Sumatriptan succinate obeyed Beer Lamberts law in the concentration range of 0 – 10 µg/ml with good correlation coefficient 0.998 indicating good linearity in the concentration range.

Table No. 5: Data for Calibration Curve of Sumatriptan succinate in 6.8 Phosphate buffer at 227 nm

Concentration (µg/ml)	Absorbance
0	0.00
2	0.328
4	0.427
6	0.616
8	0.838
10	0.968

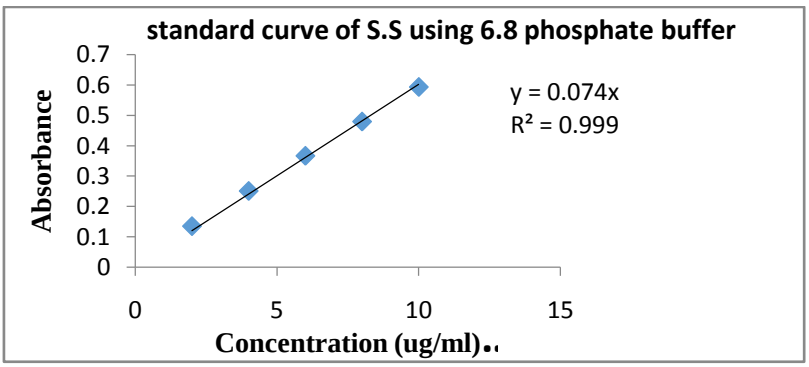

Figure 2: Standard Calibration Curve of Sumatriptan succinate in 6.8 pH phosphate buffer at 227 nm.

DRUG AND POLYMER COMPATIBILITY STUDIES

FTIR Analysis:

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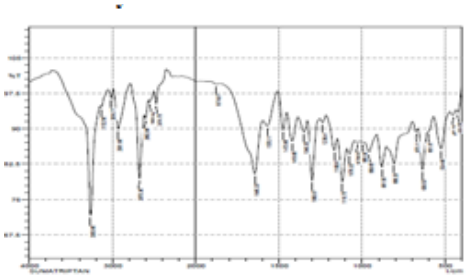


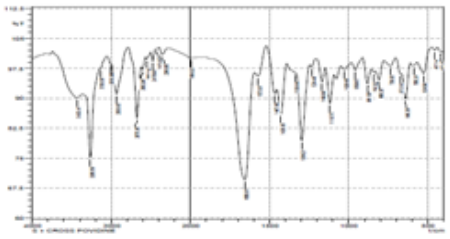
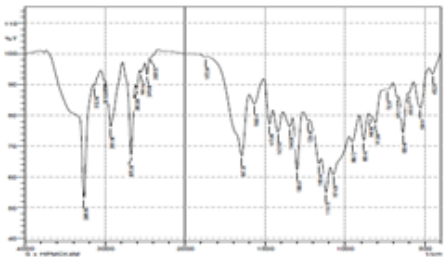


Figure 3: FT-IR Spectrum of Pure Drug (sumatriptan succinate) Figure 4: FT-IR Spectrum of Sumatriptan succinate + crosspovidone



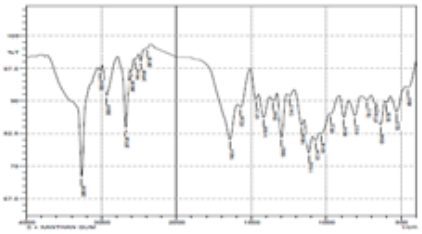


Figure 5: FT-IR Spectrum of Sumatriptan succinate + HPMC K4M Figure 6: FT-IR Spectrum of Sumatriptan succinate + Xanthan gum

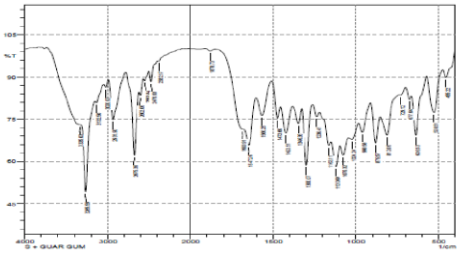


Figure 7: FT-IR Spectrum of Sumatriptan succinate + Guar gum

DRUG CONTENT:

Drug content was found to be uniform among different batches of tablets and ranged from 98.4±0.5 to 101.87±0.1%. These results showed that the all formulations having percentage drug content within the specified limits as per USP.

A. **Pre-compressionEvaluation of Bilayer Tablet Formulations of Sumatriptan succinate.**

Table 6: Preformulation parameters of Sumatriptan Succinate SR blends:

Formulations	Bulk density (gm/ml)	Tapped density (gm/ml)	Angle of repose (θ) (°)	Carr's index (%)	Hausner's Ratio
F1	0.351±0.002	0.413±0.006	30.44°±3.40	14.98±1.7	1.17±1.2
F2	0.429±0.004	0.459±0.009	33.39°±1.20	6.53±0.8	1.06±0.7
F3	0.343±0.005	0.386±0.007	30.37°±0.77	11.13±1.1	1.12±1.0
F4	0.373±0.001	0.423±0.004	36.07°±1.30	11.82±0.9	1.13±1.3
F5	0.415±0.006	0.478±0.005	30.80°±1.56	11.82±1.8	1.15±1.3
F6	0.392±0.007	0.449±0.004	31.83°±0.48	12.69±1.3	1.14±0.9
F7	0.447±0.002	0.521±0.006	25.26°±1.76	14.20±0.9	1.16±0.7

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F8	0.450±0.009	0.485±0.003	25.17°±1.64	7.21±1.2	1.07±1.2
F9	0.420±0.005	0.477±0.007	30.96°±1.76	11.94±1.7	1.13±0.4
F10	0.411±0.001	0.458±0.003	28.80°±0.28	10.26±1.2	1.11±1.1
F11	0.421±0.08	0.478±0.004	32.58°±1.88	11.92±1.4	1.13±1.5
F12	0.342±0.005	0.385±0.008	30.56°±0.84	11.16±0.4	1.12±1.2

Table 7: Preformulation parameters of Sumatriptan Succinate IR layer:

Preformulation parameters	**F1**	**F2**	**F3**
Bulk density (g/ml)	0.384±0.004	0.344±0.008	0.319±0.005
Tapped density (g/ml)	0.465±0.001	0.386±0.006	0.361±0.006
Angle of repose(θ)°	26.90±1.4	29.83±1.79	26±2.96
Carr's index (%)	17.24±1.4	10.93±0.9	11.63±1.3
Hausner's ratio	1.20±1.1	1.12±1.3	1.13±0.4

A. Post-compression evaluation of Formulated Sumatriptan succinate Bilayer tablets.

Formulation Code	Thickness** (mm)	Hardness** (Kg/cm^2)	Friability* (%w/w)	Weight Variation (mg)	Drug Content* (%)
F1	6.9±0.9	5.5±0.7	0.40	495.7±1.25	99.49±0.17
F2	6.8±0.2	6.0±0.9	0.30	489.6±1.30	100.16±0.16
F3	5.5±0.6	6.5±0.2	0.10	498.2±1.95	99.88±0.25
F4	7.0±0.6	7.3±0.7	0.51	496.6±1.75	100.5±0.17
F5	7.1±0.4	7.6±0.4	0.435	496.8±1.58	98.36±0.25
F6	6.9±0.2	6.7±0.8	0.878	495.1±1.41	98.98±0.16
F7	6.8±0.8	6.8±1.2	0.502	498.4±1.01	99.60±0.25
F8	7.0±0.5	8.4±1.8	0.306	492.3±1.12	99.09±0.25
F9	7.2±0.2	6.4±0.9	0.407	498.1±1.10	100.72±0.19
F10	6.8±0.6	6.3±0.42	0.670	493.8±1.05	101.87±0.1
F11	5.9±0.3	6.1±0.51	0.602	495.6±1.68	98.45±0.12
F12	5.8±0.8	6.4±0.34	0.434	482.5±1.65	99.01±0.12

*All the values are expressed as a mean ± SD., n = 3

** All the values are expressed as a mean ± SD., n = 6

DRUG RELEASE KINETICS:

The data obtained from invitro dissolution studies were fitted to zero order, first order, Higuchi, korsmeyers-peppas equation. To confirm the exact mechanism of the drug release korsmeyer and peppas equation superposes two apparently independent mechanism of drug transport, Fickian diffusion and a case-II transport, for the description of drug release from a swelling polymer.

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Table No. 8: Different Kinetic Models for Bilayer Tablets of Sumatriptan succinate

Formulation Code	Zero Order	First Order	Higuchi	Korsmeyer-Peppas		Best Fit Model
	R^2	R^2	R^2	R^2	N	
F1	0.987	0.944	0.967	0.956	0.956	Zero order
F2	0.991	0.967	0.973	0.982	0.627	Zero order
F3	0.986	0.968	0.980	0.987	0.649	Peppas Model
F4	0.978	0.975	0.983	0.988	0.643	Peppas Model
F5	0.988	0.976	0.982	0.985	0.611	Zero order
F6	0.974	0.923	0.987	0.989	0.669	Peppas Model
F7	0.961	0.976	0985	0.980	0.691	Higuchi Model
F8	0.995	0.969	0.979	0.986	0.614	Zero oder
F9	0.991	0.970	0.980	0.993	0.609	Peppas model
F10	0.975	0.968	0.959	0.956	0.612	Zero order
F11	0.988	0.969	0.986	0.993	0.614	Peppas model
F12	0.980	0.966	0.977	0.979	0.575	Zero order

STABILITY STUDY

From the results it was found that formulation F7 is the best formulation amongst the 12 formulations. Thus formulation F7 was selected for stability studies. From the stability studies, it was clear that the formulations were physically and chemically stable for 90 days and there was no significant change in the physical parameters, drug content and in-vitro dissolution release profiles.

Table 9: Stability studies of F7 formulation at 40±2°C

S. No.	Parameters	Observation						
		Initial	1 month		2 month		3 month	
			RT	40°C	RT	40°C	RT	40°C
1	Nature	Compact solid	Compact solid	Compact solid	Compact solid	Compact solid	Compact solid	Compact solid
2	Colour	Pink/white	Pink/white	Pink/white	Pink/white	Pink/white	Pink/white	Pink/white
3	Hardness (kg/cm^2)	6.8	6.7	6.8	6.7	6.8	6.8	6.8
4	Friability (%)	0.502	0.502	0.493	0.491	0.500	0.511	0.501
5	Content uniformity (%)	99.60	99.17	98.83	98.86	98.81	99.53	98.70

*RT – Room Temperature (25±2°C)

Table 10: In-vitro drug release study for stability testing of formulation F7 at 40±2°C

S. No.	Time (hrs)	90^{th} day cumulative % drug release
1	0	0.00
2	1	22.03
3	2	22.92

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4	3	33.78
5	4	49.50
6	5	57.16
7	6	62.94
8	7	75.18
9	8	84.60

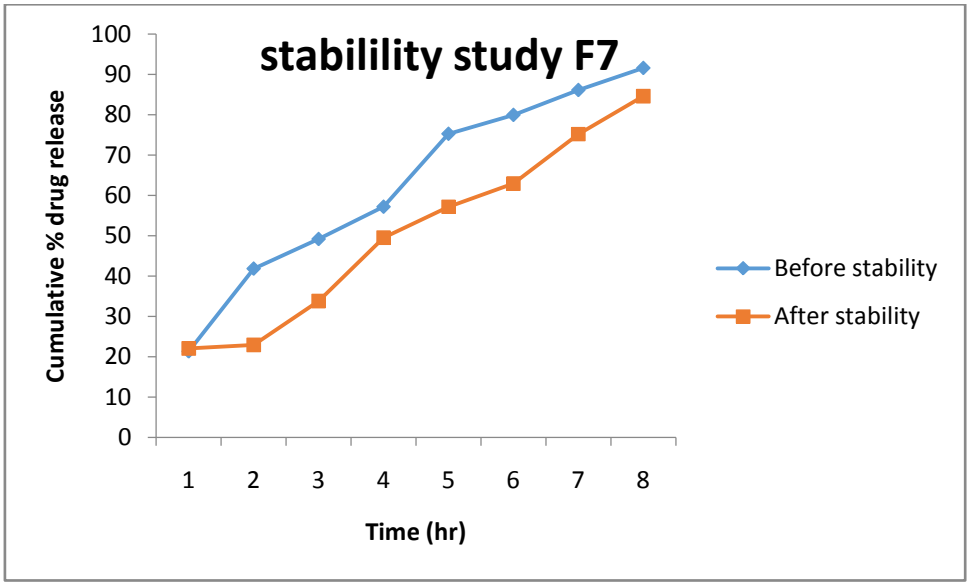

Fig no. 8 : In-vitro drug release of F7 Before stability and after stability at 40±2°C

IV. CONCLUSION AND SUMMARY

The formulation development and in-vitro evaluation of bilayer drug delivery system of Sumatriptan succinate tablets was performed in the present study. The bilayer tablets of sumatriptan succinate were prepared by using polymers like guar gum, xanthan gum, HPMCK4M, guar gum for the treatment of migraine. The dissolution study of F7 bilayer tablets containing guar gum and drug was concluded the best formulation among other formulations, which showing the most desired drug release. It will be considered as optimized formulation. The optimized formulation F7 was subjected for stability studies, the formulation was found to be stable in short term stability study. Preformulation study was carried out for powder blends, it was evaluated to determine the flow characteristics by angle of repose, bulk density, tapped density, carr's index and Hausner's ratio. The data obtained from these studies indicated that the powder blends had good flow properties.

The tablets were prepared with different ratios of polymers by direct compression technique. The formulated tablets were evaluated for physical characterization like thickness, hardness, friability, weight variation and drug content. All the physical parameters of prepared tablets comply with IP specifications. Evaluation studies of all formulations showed that the drug content, weight variation and friability as per the standards given in IP. The hardness of all formulations was within the limits. The in-vitro dissolution studies closely indicate that among nine formulations the formulation F7 was found to be the best with good retard of drug release.

The regression correlation co-efficient value was concluded in kinetics modeling of drug dissolution profile for all formulations. The formulation F7 having R^2 value lies between 0.5 to 1.0. Hence it is concluded that formulation F7 following Higuchi drug release. From the stability data, it can be concluded that there was no

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significant changes in any parameters. Hence the formulation F7 is considered to be highly stable formulation.

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