Research Article **CODEN: IJRPJK** **ISSN: 2319 – 9563**

International Journal of Research in Pharmaceutical and Nano Sciences

Journal homepage: **www.ijrpns.com**

FORMULATION AND EVALUATION OF ORAL FAST DISINTEGRATING TABLETS OF SUMATRIPTAN SUCCINATE

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ABSTRACT

The present research work was to formulate and evaluate the oral fast disintegrating tablets of sumatriptan succinate of dose 25 mg an anti-migraine drug. The tablets are prepared by direct compression method. The formulations was optimized by incorporating varying composition of Carboxy methyl cellulose (Avicel PH 102) mannitol as diluent, crospovidone as superdisintegrants magnesium stearate as lubricant, Micro crystaline cellulose as a glidant. All the excipients are tested for compatability with model drug, which revealed that there was no physical and chemical interaction occurred. The preformulation parameters analyzed for prepared tablet blend before compression. The thickness, hardness, friability, weight variation, disintegration time and drug content uniformity was evaluated for tablets. The effect of these variables on drug release also studied. The In-Vitro drug release studied were Performed in Schimadzu dissolution apparatus using phosphate buffer of pH 6.8 as dissolution media at 50 rpm speed and temperature of 37±5°C the sampling was done at periodic time intervals of 2, 4, 6, 8 and 10 minutes and was replaced by equal volume of dissolution media after each withdrawal and the amount of drug released was estimated by using UV-Spectrophotometer at 228nm. All the formulations showed low weight variation with disintegration and wetting time less than three minutes and rapid in vitro dissolution. The present study demonstrated potentials for rapid absorption, improved bioavailability, effective therapy and patient compliance.

KEYWORDS

Fast disintegrating tablet, Sumatriptan succinate, Carboxy methyl cellulose, Crospovidone, Pre gelatinized strach, Microcrystalline cellulose, Magnesium Sterate and Direct Compression.

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INTRODUCTION

Oral fast disintegrating drug delivery systems improved patient compliance is a primary benefit. This Oral fast disintegration action is primarily due to the large surface area of the film, which wets quickly when exposed to the moist oral environment.

Oral fast drug delivery system offers a giant leap forward in drug administration by providing a new and easy way of taking medication.

Sumatriptan succinate is an aganist for 5-Hydroxytryptamine receptors and it is widely prescribed for the treatment of migraine and cluster headaches. Sumatriptan undergoes an extensive biotransformation, mainly through Mono Amino Oxidase-A. The oral bioavailability of Sumatriptan Succinate is 14 ± 5% owing to an important first pass metabolism.

Sumatriptan stimulates 5-HT receptors (1D subtype) resulting in selective vasoconstriction of inflamed and dilated cranial blood vessels in the carotid circulation. It also blocks the release of vasoactive neuropeptides from perivascular trigeminal axons in the dura mater during migraine and may inhibit the release of inflammatory mediators from the trigeminal nerve.

MATERIAL AND METHODS

Sumatrptan Succinate was a gift sample from Signet Chemical Corporation, Mumbai. Crospovdone, Pregelatinized Syarch were gift samples from Elder Pharmaceuticals Dehradun. Compressible microcrystalline cellulose (MCC), aspartame and mannitol were obtained from S. D Fine Chem. Ltd. Mumbai. All the ingredients were of analytical grade.

METHODOLOGY

Preparation of standard curve stock I: 100mg of the drug was accurately weighed and transferred into the 100 ml volumetric flask. It was dissolved in sufficient quantity of phosphate buffer and volume was made up to the mark with phosphate buffer to get a 1000 µg/ml solution. This was the standard stock solution containing 1 mg/ml of model drug. (Stock I). UV Absorption Maxima (λ max) of drug sample in 6.8 pH Phosphate Buffer Stock II: One ml of the above solution was then further diluted to 100 ml with phosphate buffer to get a stock solution of 10µg/ml. UV scanning was done for 10 µg/ml drug solution from 200-400 nm using 6.8 pH phosphate buffer as a blank in schimadzu, UV spectrophotometer. The wavelength maximum was found to be at 228 nm. Preparation of the calibration curve from the stock II solution 2, 4, 6, 8 and 10ml were transferred to 10 ml volumetric flasks and were diluted with the phosphate buffer, up to the mark to obtain concentration of 2, 4, 6, 8 and 10 respectively. Absorbance of each solution was measured at 228 nm. The Standard curve preparation was performed. The absorbances were plotted against the concentrations and the graph with the straight line equation and r2 value were obtained 0.998 obeys Beer's Lamberts law.

Compatability study of drug and excipients

Selection of excipients depends upon compact ability of the drug which should prevent drug degradation by various factors these are added facilitate administration, promote the consistent release and bioavability of the drug important. Compatibility of the drug with the excipients is determined by subjecting.

Preparation of Oral Fast disintegrating Tablets

Sumatriptan Succinate Oral fast disintegrating were prepared by Direct Compression .In which all the Ingredients were passed through sieve no: 60. Required quantity of each ingredient was taken for each specified formulation and all the ingredients were co-grinded in mortar and pestle.

EVALUATION

Hardness and Friability

Hardness of prepared tablets was 3.16±3.84 K.g/cm^2. The friability of a sample of twenty tablets was measured using a USP type Roche friabilator (Pharma lab, Ahmedabad, India). Pre-weighed tablets were placed in a plastic chambered friabilator attached to a motor revolving at a speed of 25 rpm for 4 min. The tablets were then dusted, reweighed and percentage weight loss (friability) was calculated and found to be >1.0%.

Weight Variation

Twenty tablets were selected randomly from each formulation and weighed individually using a Shimadzu digital balance (BL-220H) for F1 to F9 Formulations was found to be within limits as mentioned in below table.

Thickness

Ten tablets from each formulation were taken randomly and their thickness was measured with a micrometer screw gauge.

Drug Content Uniformity

Ten tablets were weighed and pulverized to a fine powder, a quantity of powder equivalent to 50 mg of Sumatriptan Succinate was extracted into distilled water and liquid was filtered (0.22 mm membrane filter disc (Millipore Corporation). The Sumatriptan Succinate content was determined by measuring the absorbance at 228 nm (using UV-vis spectrophotometer, Shimadzu 1700) after appropriate dilution with distilled water. The drug content was determined using standard calibration curve as shown in Figure No.1. The mean percent drug content was calculated as an average of three determinations.

***In vitro* Dispersion Time**

One tablet was placed in a beaker containing 10 ml of pH 6.8 phosphate buffer at 37±0.5ºC and the time required for complete dispersion was determined.

***In-vitro* Disintegration Time**

One tablet was placed in each of the six tubes of the Disintegrating apparatus and one disc was added to each tube and Disintegrating time of all the formulations from F1 to F9 > 3minutes.

Water Absorption and Wetting Time

A piece of tissue paper folded twice was placed in a small Petridis containing 6 ml of water and wetting time of tablets was observed. The wetted tablet was then weighed, water absorption ratio R was determined.

***In-vitro* Drug Release Study**

Dissolution rate was studied by using schimadzu 900 ml of phosphate buffer pH 6.8 as dissolution medium. Temperature of the dissolution medium was maintained at 37±0.5ºC; aliquot of dissolution medium was withdrawn at every 5 minute interval and filtered. The absorbance of filtered solution was checked by UV spectrophotometric method at 228 nm and concentration of the drug was determined from standard calibration curve. Dissolution rate was studied for all designed formulations and the results are showed in the graph is shown in Figure No.2.

Stability Studies

The stability studies of formulated tablets was carried out at 40°C ± 2°C/ 75%±5% RH using a stability chamber for one month. Dissolution study of selected formulation F7 was carried out after subjecting the formulation for stability study and found to be stable.

RESULTS AND DISCUSSION

The present study was undertaken to formulate and evaluate Oral fast disintegrating tablets of Sumatriptan Succinate by direct compression method using crospovidone and Caeboxy methyl cellulose as a super disintegrants. The amount of Superdisintegrants was optimized total 9 formulations were (F1-F9) prepared using different concentration either crospovidone or Carboxy Methyl Celulose in different formulations to study its effect on disintegration time.

Percent weight variation was observed between 99.1±0.70 and 101.5±0.37 which were well within the acceptable limit for uncoated tablets as per Indian Pharmacopoeia. It is well known that the tablets with more hardness show longer disintegration time. Since mechanical integrity is of paramount importance in successful formulations hence the hardness of tablets was determined and was found to be in the range of 3.5 to 3.8 Kg/cm2. Friability was observed which is below 1% indicating sufficient mechanical integrity and strength of prepared tablets. The disintegration time for all formulations was found to be 28 to 48 seconds and wetting time was 18-98 seconds.

The *in vitro* dissolution study was performed for all formulations in vitro dissolution studies showed that more than 90% of the drug was released from the all formulations within 10 minutes. The F7 formulation containing crospovidone in concentration of 5% showed minimum disintegration time of 28 seconds, wetting time of 18 seconds and drug content of 99.26% and percentage drug released was 96.04% within 10min.

S.No	Concentration(µg/ ml)	Absorbance
1	0	0
2	2	0.207
3	4	0.396
4	6	0.698
5	8	0.838
6	10	1.046

S.No	Parameters	Initial month	1st month	2nd month	3rd month
1	Appearance	White Coloured	White coloured	White coloured	White coloured
2	Thickness (mm)	2.93±0.04	2.93±0.04	2.93±0.03	2.93±0.04
3	Hardness(kg/cm^2)	3.16±0.76	3.16±0.76	3.16±0.76	3.16±0.76
4	Friability	0.656	0.656	0.656	0.656
5	Assay				
6	Sumatriptan Succinate	100.4%	99.4%	98.9%	98.2%

Table No.1: Composition of Sumatriptan Succinaate fast disintegrating tablet

S.No	Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	Sumatriptan	25	25	25	25	25	25	25	25	25
2	Mannitol	60	60	60	60	60	60	60	60	60
3	Starch	5	5	5	5	5	5	-	5	-
4	Primogel	-	3	-	3	3	2	5	2	5
5	Aspartame	3	1	2	2	1	3	2	-	1
6	Talc	1	2	3	2	-	3	2	3	3
7	Mg. Sterate	5	3	3	-	3	2	3	2	3
8	Crosprovidone	2	1	2	3	3	-	3	3	3
9	Total	100mg	100mg	100mg	100mg	100mg	100mg	100mg	100mg	100mg

Table No.2: Pre compression blend characterization of sumatriptan succinate

S.No	Formulation code	Angle of repose (degrees)	Bulk density	Tapped density	Carr's index	Hausner's ratio	Total porosity %
1	F1	27.50±0.182	0.3913±0.007	0.4615±0.011	15.20±0.011	1.17±0.023	15.19±1.61
2	F2	27.42±0.075	0.3913±0.007	0.4615±0.010	15.20±1.62	1.17±0.023	15.19±1.61
3	F3	27.54±0.137	0.4186±0.008	0.4866±0.011	13.97±0.282	1.16±0.003	13.95±0.282
4	F4	28.32±0.219	0.3750±0.008	0.4391±0.009	14.56±1.80	1.16±0.023	14.58±1.80
5	F5	27.73±0.344	0.4140±0.014	0.4933±0.011	14.92±1.52	1.17±0.023	14.91±1.53
6	F6	28.33±0.225	0.3833±0.014	0.4395±0.019	13.7±1.89	1.15±0.028	13.68±1.91
7	F7	25.36±0.05	0.4235±0.008	0.4933±0.011	14.13±0.282	1.16±0.003	14.11±0.282
8	F8	25.52±0.275	0.3956±0.007	0.4615±0.014	14.26±1.62	1.16±0.023	14.26±1.61
9	F9	27.43±0.273	0.4000±0.012	0.4676±0.014	14.43±1.92	1.16±0.23	14.44±1.92

Table No.3: Post compression parameters of sumatriptan

S.No	Formulation Code	Hardness (kg/cm^2)	Thick-ness (mm)	Weight variation	Friability %	Wetting Time	Drug content%
1	F1	3.83±0.28	2.92±0.05	101.1±1.21	0.396	98±1.21	100.8±0.8
2	F2	3.16±0.28	2.91±0.05	101±1.21	0.524	60±1.21	98.72±0.44
3	F3	3.66±0.28	2.95±0.04	100.3±1.02	0.402	54±1.64	98.52±1.17
4	F4	3.83±0.28	2.91±0.06	101.5±1.01	0.530	38±1.10	98.82±1.83
5	F5	3.33±0.28	2.86±0.05	101.25±0.37	0.658	30±0.64	99.41±1.63
6	F6	3.16±0.28	2.88±0.03	100.9±1.65	0.663	28±0.64	92.98±1.7
7	F7	3.96±0.76	2.93±0.04	100.5±1.85	0.796	18±0.64	99.26±0.7
8	F8	3.16±0.28	2.85±0.07	99.1±0.70	0.656	27.66±0.5	97±1.95
9	F9	3.83±1.85	2.83±0.04	102±1.85	0.656	18±0.64	99.26±0.7

Table No.4: *In-vitro* disintegrating time, drug content and % drug release of formulation f1to f9

S.No	Formulation	Disintegration time (sec)	% Drug release	Drug content uniformity
1	F1	35±0.65	92	100.8±0.8
2	F2	33±0.78	92	98.72±0.44
3	F3	48±0.67	93	98.52±1.17
4	F4	37±0.78	96	98.82±1.83
5	F5	36±0.12	95	99.41±1.63
6	F6	38±0.54	96	92.98±1.7
7	F7	28±0.69	98.45	99.26±0.7
8	F8	30±0.46	97	97±1.95
9	F9	31±0.89	97	99.26±0.7

Dissolution profile of a batch f1 to f9

S.No	Time	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	0	0	0	0	0	0	0	0	0	0
2	5	47.2	69.78	73.06	70.84	73.23	75.78	85.5	74.6	71.7
3	10	69.66	86.74	88.68	84.14	78.02	82.85	92.04	82.67	80.87
4	15	74.42	85.72	89.58	83.48	82.79	90.1	96.14	80.74	76.54
5	30	93.54	94.09	92.01	97.04	96.5	94.46	100	94.54	95.23

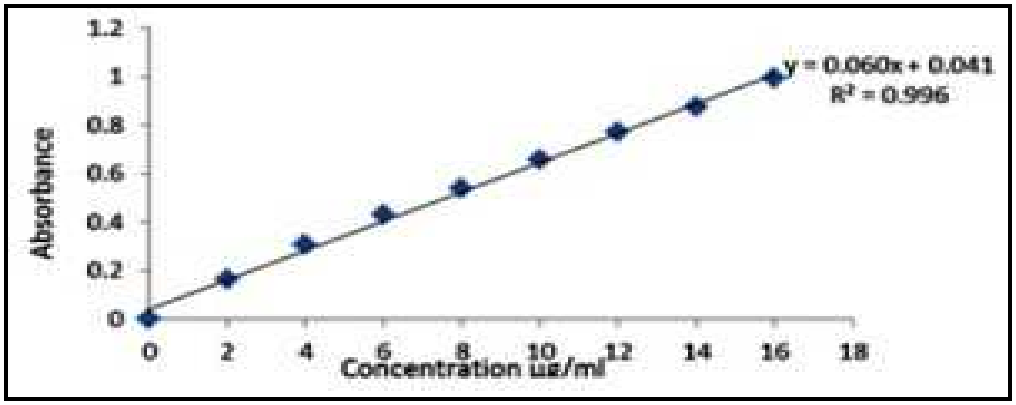


Figure No.1: Standard curve of sumatriptan succinate in phosphate buffer ph 6.8

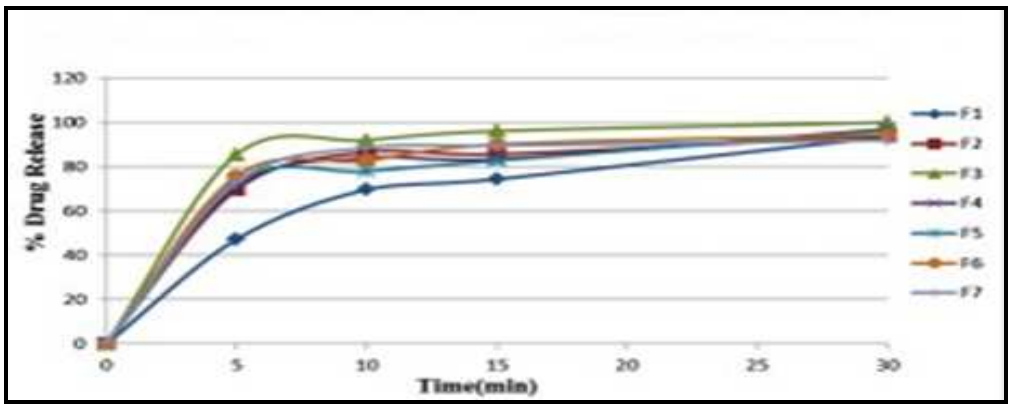
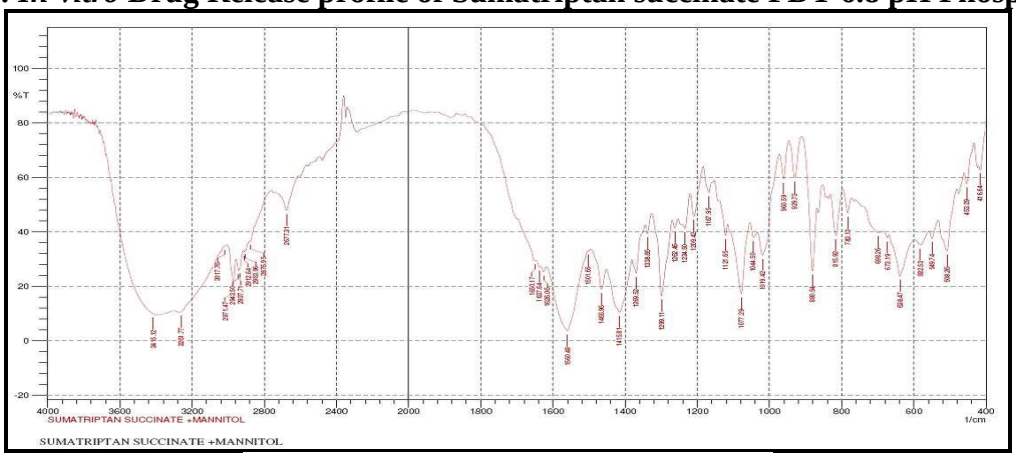


Figure No.2: *In-vitro* Drug Release profile of Sumatriptan succinate FDT 6.8 pH Phosphate Buffer



FTIR spectra of sumatriptan succinate

CONCLUSION

Fast disintegrating tablets of Sumatriptan Succinate were prepared by direct compression method using crospovidone and carboxy methyl cellulose as a superdisintegrants. The tablets disintegrated rapidly in oral cavity and had acceptable hardness and friability. *In vitro* drug release from the tablets shows significantly improved drug dissolution. It was concluded that fast disintegration tablets of Sumatriptan Succinate would providing quick onset of action with good patient compliance.

ACKNOWLEDGEMENT

The authors wish to express their sincere gratitude to Department of Pharmaceutics, Safa College of Pharmacy, B. Thandrapadu, Kurnool, Andhra Pradesh, India for providing necessary facilities to carry out this research work.

CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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Please cite this article in press as: Nazemoon R *et al.* Formulation and evaluation of oral fast disintegrating tablets of sumatriptan succinate, *International Journal* of *Research in Pharmaceutical and Nano Sciences,* 6(3), 2017, 111-117.