ISSN: 0976-7126
Yadav *et al.*, 12(10):24-30, 2021

International Journal of Pharmacy & Life Sciences
Open Access to Researcher

Formulation and Evaluation of Orodispersible Tablets of Sumatriptan Succinate

Vinita Yadav*, Anjana Bhardwaj and Alok Pal Jain

RKDF College of Pharmacy, Sarvepalli Radhakrishnan University, Bhopal (M.P.) - India

Article info

Received: 03/09/2021

Revised: 21/09/2021

Accepted: 21/10/2021

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Abstract

In the present study an attempt has been made to prepare fast dissolving tablets of Sumatriptan Succinate to improve dissolution rate of the drug in oral cavity & hence better patient's compliance & effective therapy. Sumatriptan Succinate is a 5-HT1D (5-hydroxy tryptamine 1D) receptor agonist, used in the treatment of migraine and cluster headache. It has low bioavailability due to its first pass metabolism. Hence the main objective of the study was to formulate fast dissolving tablets of Sumatriptan succinate to achieve a better dissolution rate and further improving the bioavailability of the drug. Fast dissolving Sumatriptan succinate was prepared using superdisintegrants Crospovidone, Croscarmellose Sodium, and Preglatinised Starch using the direct compression method. The tablets prepared were evaluated for Thickness, Uniformity of weight, Drug content, Hardness, Friability, Wetting time, in vitro and in vivo disintegration time, in vitro drug release. The formulation F8 containing Crospovidone (8%) was found to give the best result since it showed enhanced dissolution, which leads to improved bioavailability, improved effectiveness and hence better patient compliance.

Keywords: Sumatriptan Succinate. Fast Dissolving tablet, Direct compression, in vitro and in vivo disintegration time

Introduction

Fast-dissolving drug delivery systems have rapidly gained acceptance as an important new way of administering drugs. Improved patient compliance is a primary benefit of the fast dissolving drug delivery systems. This fast dissolving action is primarily due to the large surface area of the film, which wets quickly when exposed to the moist oral environment. These additional, superior benefits allow patients to take their medication anytime and anyplace under all circumstances. The fast dissolving drug delivery system offers a giant leap forward in drug administration by providing a new and easy way of taking medication [1].

Sumatriptan succinate (STS) is an agonist 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. It is a white to off line white powder bitter in taste and is readily soluble in water and in saline. The oral bioavailability of Sumatriptan Succinate is 14 ± 5 % owing to an important first pass metabolism. It has an elimination half-life of 2.5 hours and absorption zone from the upper intestinal tract. Plasma protein binding is low 14% to 21% [2].

***Corresponding Author**
E.mail: vyb1997@gmail.com

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 [2-3].

Material and Methods

Preformulation testing is first step in the rational development of dosage forms of a drug substance. It can be defined as – "as investigation of physical and chemical properties of a drug substance alone and when combined with excipients". The overall objective of preformulation testing is to generate information useful to the formulation in developing stable and bioavailable dosage forms that can be mass produced. The preformulation should start at the point after biological screening, when a decision is made for further development of compound in clinical trials. The following preformulation studies were performed for the obtained sample of drug.

Organoleptic properties

Color and nature

Transferred small quantity of the sample on a white piece of paper, spreaded the powder and examined visually. White fine powder

Taste and odour

Very less quantity of Escitalopram was used to get taste with the help of tongue as well as smelled to get the odor

Particle Size , Shape and Surface Area

Various physical and chemical properties of drug substances are affected by their particle size distribution and shapes. Size also plays role in the homogeneity of final tablet. When large differences in size exist between the API and excipients mutual sieving (demixing) effects can occur making through mixing difficult on, it a) attained, difficult to maintain during the subsequent processing steps.

If the material become too fine, then undesirable properties such as electrostatic force effects and other surface active properties causing undue stickiness and lack of flowability manifest. It is probably safest to grind most drugs having particles that are approx 100µm in diameter.

Table 1: General Techniques for Determining Particle Size

Techniques	Particle size(µm)
Microscopic	1-100
Sieve	>50
Sedimentation	>1
Eutriation	1-50
Centrifugal	<50
Permeability	>1
Light Scattering	0.5-50

Physical characteristics:

Flow properties:

The flow properties of powders are critical for an efficient tableting operation. A good flow of powder or granulation to be compressed is necessary to assure efficient missing and acceptable weight uniformity for the compressed tablets. If a drug is identified at the pre formulation stage to be "poorly flowable", the problem can be solved by selecting appropriate excipients. In some cases, drug powders may have to be pre-compressed or granulated to improve their flow properties. During pre formulation evaluation of drug substance, therefore, its flowability characteristic should be studied, especially when the anticipated dose of the drug is large.

Melting point:

It is one of the parameters to judge the purity of crude drugs. In case of pure chemicals, melting points are very sharp and constant. A small quantity of powder was placed into a fusion tube. That tube is placed in the melting point apparatus containing castor oil. The temperature of the castor oil was gradual increased automatically and read the temperature at which powder started to melt and the temperature when all the powder gets melted.

Solution properties:

pH of the solution

Weighed and transferred accurately about 1.0 g of sample in a 200 ml clean and dried beaker, dissolved in carbon dioxide free water and made up the volume to 100 ml with same solvent, mixed. Read the pH of freshly prepared solution by using precalibrated pH meter. The results are shown in table.8.

Solubility:
A semi quantitative determination of the solubility was made by adding solvent in small incremental amount to a test tube containing fixed quantity of solute or vice versa. After each addition, the system is vigorously shaken and examined visually for any undissolved solute particles. The solubility are expressed in terms of ratio of solute and solvent.

Identification of drug and compatibility study:
By Physical observation
It was determined as per procedure given in method section. The following table illustrated the result.

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Table 5: Physical Compatibility Studies

Test	Observations	Inference
Physical compatibility	No change of color	These materials are compatible for formulations

Uv spectroscopic method for analysis of Sumatriptan Succinate

Calibration curve of Sumatriptan Succinate:
Measured the absorbance of the above prepared standard solutions at 226 nm
Plotted a graph of concentration (in □g/ml) on X axis and absorbance (in nm) on Y axis.

Table 6: Calibration curve for Sumatriptan Succinate

S. No.	Concentration (□g/ml)	Absorbance (nm)
1	0	0
2	2	0.226
3	4	0.386
4	6	0.581
5	8	0.768
6	10	0.958
Slope	**0.0247**	
R^2	**0.9992**	

Results and Discussion

Pre formulation Studies:

Organoleptic properties:
These tests were performed as per procedure. The results are illustrated in following table.

Table 7: Organoleptic Properties

Test	Specification / limits	Observations
Color	White color	white powder
Odour	Odourless	Odourless

Angle of repose:
It was determined as per procedure given in material and method part. The results are,

Table 8: Flow properties

Material	Angle of repose
Sumatriptan Succinate	36º.17”

Bulk density and tapped density:
It was determined as per procedure given in material and method part. The results are,

Table 9: Density

Material	Bulk Density (gm/ml)	Tapped density (gm/ml)
Sumatriptan Succinate	0.26	0.22

Powder compressibility:
It was determined as per procedure given in material and method part. The results are,

Table 10: Powder Compressibility

Materials	Compressibility index	Hausner ratio
Sumatriptan Succinate	31.45%	1.24

Melting point:
It was determined as per procedure given in material and method part. The results are

Table 11: Melting point

Material	Melting point range	Result
Sumatriptan Succinate	169-171 °C	Complies

Solution Properties:

pH of the solutions

pH of the solution was determined as per procedure given in material and method part.

Table 12: pH

Material	Test	Specification	Observation
Sumatriptan Succinate	pH	8.90	8.85

Solubility:

It was determined as per procedure given in 9.4.2 in material and method part. The following table illustrated the result.

Table 13: Solubility

Test	Specification	Result
Solubility	Freely soluble in Water, DMSO, insoluble in Ethanol	Complies

The result complies as per specification

Drug - Excipient Compatibility Studies

A) Physical Observation:

There are no such changes in the physical observation after mixing of ingredients.

Precompression Parameters:

Table 14: Evaluations of Granules

Batch. N0.	Angle of Repose(0)	Bulk Density (g/ml)	Tapped bulk density(g/ml)	Carr's index (%)	Hausner's Ratio
F1	27°46'	0.453	0.512	11.40	1.24
F2	26°27'	0.489	0.532	11.81	1.29
F3	27°32'	0.412	0.554	13.63	1.21
F4	24°17'	0.409	0.512	14.96	1.26
F5	24°.52'	0.467	0.568	12.13	1.19
F6	24°.26'	0.449	0.587	11.12	1.11
F7	25°.33'	0.456	0.501	11.33	1.23
F8	27°.68'	0.467	0.569	12.28	1.22

The angle of repose for the formulated blend F1-F8 was found to be in the range 24^0.17' to 27^0.68' shows good flow property. Compressibility index for the formulations F1-F8 found between 11.12%-14.96% indicating the powder blend has the required flow property for compression. Hausner's Ratio for the formulations F1-F8 found between 1.11-1.29 indicating the powder blend has the required flow property for compression.

Evaluation of Sumatriptan Succinate Tablets

Table 15: Weight Variation and Friability

Batch. No	Weight Variation (%)	Friability (%)
F1	350±1.52	0.41
F2	350±2.37	0.34
F3	348±1.44	0.30
F4	351±1.88	0.48
F5	351±2.59	0.48
F6	351±2.13	0.48
F7	350±1.52	0.39
F8	351±1.49	0.40

The weight variation of the tablet in the range of 1.49 % to ± 2.56 % (below 5%) complying with pharmacopoeial specification. The friability of the tablet in the range of 0.30 % to 0.48% **(**below 1%) complying with pharmacopoeial specifications.

Table 16: Thickness, Hardness and Disintegration Time

Batch. No	Thickness (mm)	Hardness (Kg/cm^2)
F1	2.12±0.2	2.13
F2	2.02±0.2	2.61
F3	2.23±0.1	2.12
F4	2.12±0.1	2.34
F5	2.23±0.1	2.69
F6	2.10±0.1	2.79
F7	2.05±0.2	2.51
F8	2.08±0.3	2.59

The thickness of the formulations from F1- F8 was found to be in the range of 2.02±0.2 to 2.23±0.2 and hardness of the formulated tablets was found to 2.13 to 2.79 indicating a satisfactory mechanical strength.

Table 17: Wetting Time and Disintegration Time

Batch. No	Wetting Time (Sec)	Disintegration Time (Sec)
F1	130	135
F2	104	108
F3	76	80
F4	63	66
F5	118	122
F6	81	84
F7	53	56
F8	45	48

ISSN: 0976-7126
Yadav *et al.*, 12(10):24-30, 2021

The Wetting time of the formulations from F1-F12 was found to be in the range of 45- 130 seconds. Lower wetting time implies a quicker disintegration of the tablet. F6 shows very lower wetting time it reflects in faster DT. Water absorption ration is around 63% shows for the formulation F8.

Table 18: Cumulative % Release of Sumatriptan Succinate Mouth Dissolving F1-F4

Time (mts)	% Drug Release of Formulations			
	F1	F2	F3	F4
0	0	0	0	0
1	24.21	28.21	31.47	34.71
2	40.39	46.45	50.39	54.07
4	53.91	59.62	61.22	64.73
6	66.26	68.71	71.46	78.38
8	75.54	76.63	81.92	86.42
10	89.19	85.22	89.75	92.53
12	93.65	91.38	93.71	97.34
15	96.78	98.76	99.27	99.81
17	98.37	---	---	---

From the *in-vitro* dissolution study of all formulations (F1-F8), formulation F8 release around 98% of drug at the end of 8 min's for a immediate release tablets of Sumatriptan Succinate. Therefore the F8 formulation chosen as the best formulation from all 12 batches.

Table 19: Cumulative % Release of Sumatriptan Succinate Mouth Dissolving F5-F8

Time (mts)	% Drug Release of Formulations			
	F5	F6	F7	F8
0	0	0	0	0
1	22.13	30.12	34.23	40.41
2	38.39	46.43	51.17	56.43
4	53.12	64.64	69.17	76.73
6	69.46	77.31	82.45	89.27
8	82.31	89.37	90.90	98.14
10	97.18	99.33	98.92	---
12	97.25	---	---	---
15	---	---	---	---
17	---	---	---	---

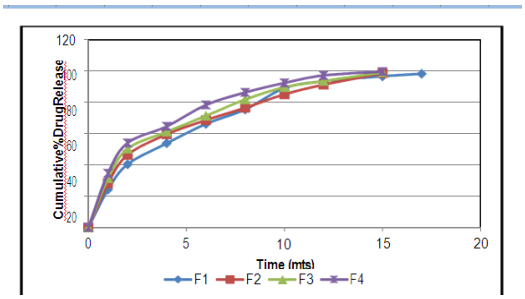

Figure 1: Graph of Cumulative % Release of Sumatriptan Succinate Mouth Dissolving Tablets F1-F4

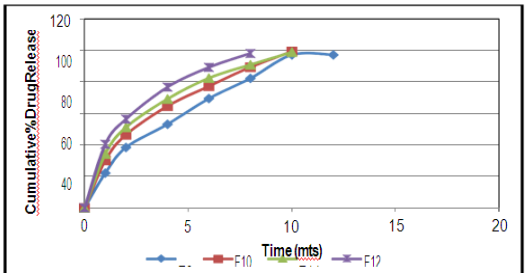

Figure 2: Graph of Cumulative % Release of Sumatriptan Succinate Mouth Dissolving Tablets F5-F8

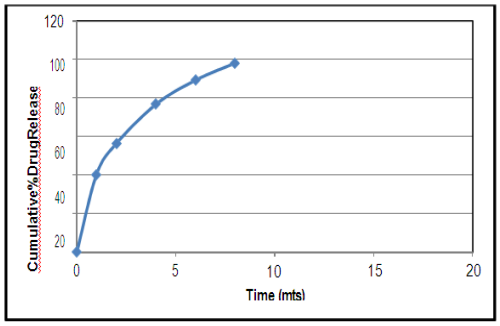

Figure 3: Graph: Cumulative % Release of Sumatriptan Succinate Mouth Dissolving Tablets F8

Conclusion

Fast dissolving tablets of Sumatriptan Succinate were prepared by direct compression method using Croscarmellose sodium, crospovidone and Preglatinised Starch 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 in direct compression method, crospovidone was best superdisintegrant with MCC as binding agent. Hence, it could be concluded that the superdisintegrant based fast dissolving tablets of Sumatriptan Succinate would providing quick onset of action without need of water for swallowing or administration.

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Cite this article as:
Yadav V., Bhardwaj A. and Jain A.P. (2021). Formulation and Evaluation of Orodispersible Tablets of Sumatriptan Succinate, *Int. J. of Pharm. & Life Sci.*, 12(10):24-30.

Source of Support: Nil
Conflict of Interest: Not declared
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