International Journal of Medicine and Nanotechnology e ISSN: 2394-4269
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An International Peer Review Journal

Original Article

Formulation and Development of Fast Dissolving Tablets (FDTS) of Sumatriptan Succinate Using Simple and Cost Effective Technique

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Article Info - Received: 30-12-2015 Accepted: 07-01-2016

Abstract:
The basic need of this study is to develop an fast dissolving tablet of sumatriptan succinate used in the treatment of migrain ,with an aim of reduces the lag time and providing faster onset of action. Present investigation is to formulate fast dissolving tablets (FDTs) of sumatriptan using simple and cost effective technique. The tablets were prepared by direct compression method using superdisintegrants such as poly plasdone XL, polacrilin potassium, primogel,L-HPC and pregelatinized starch, with pearlitol SD 200 and Spraydried lactose as diluent. Improve the palatability of the drug with sweetening agent and flavor. Find out the suitable diluent and disintegrant combination, to formulate the fast dissolving tablets of sumatriptan succinate. Formulation (F14) with polyplasdone 5% was considered as the optimized fast dissolving tablets. It shows drug release of 92.00% of drug in 5 min and 98.17% in 10min. These results were comparable with the marketed product suminat-25. Based on the optimization results it is concluded that the objective of formulating fast dissolving tablets containing sumatriptan succinate was achieved by simple and cost effective technique.

Key words:
Sumatriptan succinate, Primogel,L-HPC, Pearlitol SD 200 and Polacrilin potassium

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1. INTRODUCTION

For delivery of pharmaceutical dosage form, the oral route of administration still continues to be the most preferred route due to its manifold advantages including ease of ingestion, non invasiveness, versatility and most important patient compliance. But, still, many patients find it difficult to swallow tablets and hard gelatin capsules and do not take their medication as prescribed. It is estimated that about 50% of the population is affected by this problem which result in a high incidence of non-compliance and ineffective therapy. [1-3]

The difficulty is not only experienced in particular, by pediatrics and geriatric patients, but this also apply to patients who are ill in bed and who are active working patients, who are busy or traveling, especially those who have no access to water. The elderly people eventually will experience difficulties in taking conventional oral dosage forms (viz., solution, suspension, tablets and capsules) because of hand tremors and dysphagia. Swallowing problem also is common in young individuals because of their under developed muscular and nervous system. Other groups that may experience problem using conventional oral dosage forms include the mentally ill, the developmentally disable, and patients who are non-cooperative or are nauseated. [4]

2. MATERIALS AND METHOD

Prepartion of standard graph of Sumatriptan succinate in pH 6.8 phosphate buffer

Accurately weighed amount (100 mg) of the drug was dissolved in pH 6.8 phosphate buffer in 100 ml volumetric flask and the volume was made up to 100ml. from this stock solution 10ml is withdrawn in to volumetric flask, made the volume up to 100ml with pH 6.8 buffer. From this second stock solution (100µg/ml), concentrations of 10, 20, 30, 40, 50, 60 µg/ml solutions were prepared and the corresponding absorbance was measured at wave length (λmax) 282 nm in a UV Visible spectrophotometer. [5, 6]

Preparation of standard graph of Sumatriptan succinate in distilled water

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

Preparation of Fast Dissolving Tablets of Sumatriptan Succinate By Direct Compression Method

Each tablet (weight 100mg) consisted of sumatriptan succinate, superdisintegrants such as pregelatinized starch,polyplasdone XL, primogel, kyron 314,low subsituated hydroxyl propyl cellulose (L-HPC), pearlitol SD200,spray dried lactose, saccharin sodium,flavor, talc and magnesium stearate ,prepared by direct compression method.The drug, diluent, superdisintegrant, sweetners, are passed through the sieve no. 60. All the ingredients are mixed well in the motor. Then mixed with lubricant for 3 min in a motor. The mixer was compressed by using 6mm flat punches on twele station rotary tablet compression machiene.

Table 1: Composition of different formulations with pearlitol SD200.

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Sumatriptan	25	25	25	25	25	25	25	25	25	25
Pearlitol	65	60	68	65	68	62	68	60	65	45
Spray Dried Lactose										
PG Starch	5	10								
Polyplasdone XL			2	5						
Primogel					2	8				
Kyron 314							2	10		
L-HPC									5	25
Saccharin Na	1	1	1	1	1	1	1	1	1	1
Flavor	1	1	1	1	1	1	1	1	1	1
Talc	2	2	2	2	2	2	2	2	2	2
Magnessim Sterate	1	1	1	1	1	1	1	1	1	1
Total weight	100	100	100	100	100	100	100	100	100	100

Evaluation of Powder Blend

Angle of repose

The flow characteristics are measured by angle of repose. Improper flow of powder is due to frictional forces between the particles. These frictional forces are quantified by 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. [7, 8]

By definition

$\tan \theta = h/r$

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

where h is the height of pile.

r is radius of the base of the pile.

θ is the angle of repose.

Table 2: Angle of repose limits.

Angle of repose	Type of flow
<20	Excellent
20-30	Good
30 – 34	Passable
>34	Very poor

Bulk density

When particles are packed loosely, lots of gaps between particles are observed. Hence bulk volume increases making the powder light. Based on bulk volume, powders are classified as ‘‘light’’ and ‘‘heavy’’. Light powders have high bulk volume. On the other hand, smaller particles may sift between the larger particles, the powder assume low bulk volume or high bulk density. Such powders are called heavy powders. The bulk density depends on particle size distribution, shape and cohesiveness of particles.It is defined mathematically as

$$\text{Bulk density } (\rho) = \frac{\text{Mass of powder (w)}}{\text{---------------------------}}$$

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Bulk volume (V_b)

A powder (about 60 g) is passed through a standard sieve No. 20. A weighed amount (approximately 50 g) is introduced into a 100 ml graduated cylinder. The cylinder is fixed on the Bulk density. Apparatus and the timer knob is set (regulator) for 100 tappings. The volume occupied the powder is noted. Further, another 50 taps may be continued and the final volume is noted. For reproducible results, the process of tapings may be continued until concurrent volume is achieved. This final volume is the bulk volume. Then bulk density is calculated using equation. [9, 10]

Bulk volume is also measured by dropping the cylinder (containing powder) onto a hard wooden surface 3 times from a height of 1 inch at 2 s intervals. Sometimes, to get an appropriate volume, the container has to be dropped or tapped 500 times.

Tapped density

Tapped density was determined by USP method II. The powder sample under test was screened through sieve No. 18 and 10 g of tablet bend was filled in 100 ml graduated cylinder of tap density tester (Electrolab,ETD 1020). The mechanical tapping of the cylinder was carried out using tapped density tester at a nominal rate of 250 drops per minute for 500 times initially and the initial tapped volume (Va) was noted. Tapping was proceeded further for additional 750 times and volume was noted. The difference between two tapping volumes was calculated. Tapping was continued for additional 1250 times if the difference is more than 2%. This was continued in increments of 1250 taps until difference between volumes of subsequent tapings was less than 2%. This volume was noted as, the final tapped volume (Vb). The tapped density (Dt) was calculated in g/ml by the formula,

$$Dt = M/Vb$$

where M is the weight of sample powder taken.

Vb is tapped volume.

Determinations were carried out in 3 replicates. The mean value of three determinations are considered.

Evaluation of Tablets

Thickness and diameter

Tablet thickness is an important characteristic in reproducing appearance and also in counting by using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Ten tablets were taken and their thickness was recorded using micrometer.

Weight variation

Weight variation. With a tablet designed to contain a specific amount of drug in a specific amount of tablet formula, the weight of the tablet being made is routinely measured to help ensure that a tablet contains the proper amount of drug. In practice, composite samples of tablets (usually 10) are taken and weighed throughout the compression process.

The composite weight divided by 10, however, provides an average weight but contains the usual problems of averaged values.Within the composite sample that has an acceptable average weight, there could be tablets excessively overweight or underweight.To help alleviate this problem the United States Pharmacopoeia(USP)/National Formulary (NF) provides limits for the permissible variations in the weights of individual tablets expressed as a percentage of the average weight of the sample. The USP weight variation test is run by weighing 20 tablets individually, calculating the average weight, and comparing the individual tablet weights to the average. The tablets meet the USP test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit. The weight variation tolerances for uncoated tablets differ depending on average tablet weight. [11, 12]

1. RESULTS AND DISCUSSON

The present study was carried out to develop fast dissolving tablets of sumatriptan succinate by direct compression method.hence it was necessary to find suitable excipients with their compatability and the disintegrating ability.

Preformulation

In the preformulation study it was found that the estimation of sumatriptan succinte by UV spectrophotometric method at λ_{max} 282nm in 6.8pH phosphate buffer and have a good reproducibility.The correlation coefficient for the standard curve was found to be 0.999 at the concentration range 0 – 60mcg/ml the regression equation generated was y = 0.016x (Figure 2)

Drug excipients compatibility

Fourier trans form infra red spectroscopy (FTIR) was carried out to check for the possible drug excipients

interaction. Drug Excipient compatability was determine through FTIR spectroscopy(bruker alfa).FTIR spectra of pure drug show principle bands at wave number of 3372.73$cm^{-1}$for amino group (N-H),3098.19$cm^{-1}$for (C-H)group in aromatic ring,1565.39$cm^{-1}$for (C=C)group in aromatic ring,1708.16$cm^{-1}$for (C=O)group in carboxylic acid group,1235.06cm^{-1} for sulphate (S=O) group,which indicates that selected drug is identified as sumatriptan succinate.

FTIR spectra of drug with all excipients shows different bands at specific wave number region with respective functional groups as identified in pure drug which indicates that there is no interaction between drug and excipients.

FTIR spectra of optimized formulation show different bands at specific wave number region which represents specific functional groups. in formulation importantly bands were obtained for drug at wave number 3425.92cm^{-1},2676.58cm^{-1},1631.41cm^{-1},955.21$cm^{-1}$and 1383.61cm^{-1}which represents functional groups N-H,O-H,C=C,C-H and S=O. Bands were obtained for polyplasdone XL 1744cm^{-1},1360.93cm^{-1} and 2852.90cm^{-1} which represents the functional groups C=O,C-N and C-H respectively. Bands were obtained for spray dried lactose is 1156.23cm^{-1} and 2926.58cm^{-1} which represents the functional groups –O–,C-H respectively.

This established that the drug and all the excipients used in the study showed no interaction between them and indicated that they were compatable with each other.

Formulation of fast dissolving tablets

Pearlitol SD200 and spray dried lactose were selected as directly compressible diluents.pregelatinized starch, polyplasdoneXL,primogel,kyron-314,L-HPC were as disintegrants,saccharin sodium as sweetening agent,orange flavor as flavoring agent,magnesium sterate and talc as lubricant and glidant respectively.All the formulations were prepared by direct compression (Table 7 & 8).

Pre compression parmeters

Precompression parmeters bulk density,tapped density,hansnr's ratio,angle of repose and compressibility index of all formulations had acceptable flow properties

Table 3*: In-Vitro* disintegration time.

Formulation	Time(Sec)
F11	50 ± 0.58
F12	31 ± 0.58
F13	41 ± 0.58
F14	10 ± 0.58
F15	31 ± 1.15
F16	37 ± 0.58
F17	38 ± 0.58
F18	25 ± 0.58
F19	31 ± 0.58
F20	20 ± 0.58

For all formulations (mean ±SD. ,n=3)

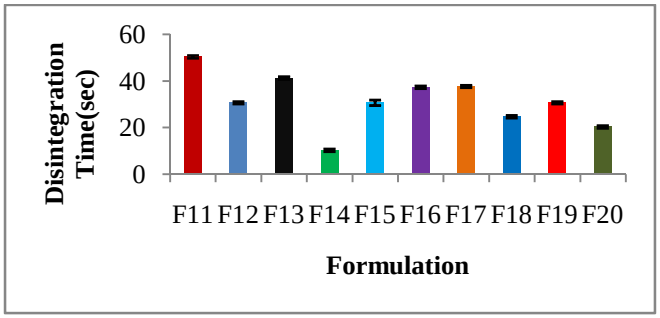

Fig 1: Comparison of disintegration time.

Post compression parameters

Weight variation

Formulations are have weight variation is found within limits.96.64mg – 99.68mg.which indicates the average weight of tablets with in standard limits.

Hardness

Hardness of all the formulations kept at the 3.5kg/cm^2 .the obtained results were found to be within the range of 3.0 to 4.0 kg/cm^2.

Friability

Friability of the formulations found to be 0.34%.and it was noted that friability of all formulations below the limt. That all the formulated tablets are mechanically stable.

Disintegration time

Formulations with polyplasdone XL and L-HPC was exhibits faster disintegration of tablets than compare to other disintegrants pregelatinized starch,primogel,kyron 314.Among these polyplasdone XL and L-HPC were better disitegrants to formulate fast dissolving tablets of sumatriptan succinate by direct compression method.This can be attributed to the extent of water uptake and the swelling power of disintegrants .

Wetting time

Formulations with polyplasdone XL and L-HPC was exhibited faster disintegration and wetting time of tablets than compare to other disintegrants pregelatinized starch,primogel,kyron 314

Wettability

All formulations was found to from 40.52% to 93.68%. Formulations with polyplasdone XL and L-HPC was exhibited good wettability of tablets than compare to other disintegrants pregelatinized starch,primogel,kyron 314

Drug content

In the evaluation of tablets all the formulations drug content was found to be 96.6% to 100.2%.All formulated fast dissolving tablets of sumtriptan succinate had with in limits.The better optmised formulation(F14)was 100.2% obtained with sprayed dried lactose contain polyplasdone XL.

***Invitro* drug release**

Dissolution study was performed by apparatus USP II paddle method. All the formulations complete the drug release within 15 min. Drug release from the formulations containing spray dried lactose was found to be more when compare to formulations with perlitol. Formulation F14 (Figure 11) with poly plasdone XL (5 %) having disintegration time of 10 sec releases 92.00 ± 1.04 of drug in 5 min and almost complet drug release was observed in 10min, where as formulations having pregelatinized starch (10%) release only 77.64 ± 1.52 % drug, where as kyron in 10% concentration release

80.68 ± 0.88% of drug. L-HPC at the concentration of 25% releases 86.50 ± 1.18 of drug. Primogel (8%) release 84.35 ± 0.77 of drug by the end of 5 min. when comparing drug release from formulations with different superdisintegrants, polyplasdone XL at 5% concentration a rapid drug release was observed due to both swelling and wicking mechanisms. F14 formulation was considered as better optimized formula and was selected to compare with marketed product of Suminat-25.

***Invitro* drug release comparison**

The drug release of formulated tablets(F14) was compared with marketed product rapid release tablets of sumatriptan succinate (suminat-25), formulated tablets releases 92.00% in 5 min, and marketed product suminat-25 was showed 93.32%. Both the formulations complete the drug release with in 15 min, which indicates that the formulated product shows similar drug release profile, when compared with suminat-25 rapid release tablets.

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Conflict of Interest: None
Source of Funding: Nil