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Formulation And Evalution Of Oral-Dispersible Tablet Of Sumatriptan.

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ABSTRACT

Sumatriptan malate is a triptan class selective serotonin receptar agonist drug with rapid action, highest bioavailability and low side effects. Fast dissolving tablets of Sumatriptan malate were prepared by wet granulation technique using sodium starch glycolate, Crosscarmellose sodium and Crosspovidone (2%, 4%, and 6%), respectively, FT-IR spectroscopy and differential Scanned calorimetry was used to examine the physical properties of the drug. Granules were examined at mild, bulk density, density, index, and Hausner's relationship angle. The developed tablets were evaluated for hardness, drug content, spring time, wetting time, wetting absorption ratio, -vitro drug release and deposition time. Formulation with 4% crosspovidone showed disintegration time of 21.5 sec. In vitro dissolution studies showed drug release of 94.66% after 12 minutes.

Keywords: Sumatriptan, selective serotonin receptar agonist , Fast dissolving tablet.

INTRODUCTION:

Mouth Dissolving tablets:

Mouth dissolving Tablet are those that get solubilized within less time in saliva i.e; (15s to 3min) without requirement of water and chewing /swallowing. Disintegrants are added for rapid disintegration and sweeteners or masking agents are used for good mouth feel. They are termed by various names such as:

- Mouth dissolving tablets
- Fast dissolving tablets
- Mouth dissolving Tablet
- Rapid dissolving tablets

- Quick disintegrating tablets
- Porous tablets
- Fast disintegrating tablets
- Rapid melts.

ADVANTAGES

These drugs or doage forms doesn't leave any residuein mouth and gives a pleasant mouth feel.

- Taste masking agents such as sweetening agents, masks bitter taste of drug.
- They are highly stable and are unaffected by environmental conditions.
- High amount of drug can be loaded.
- It immediately gets dissolved and has advantages of rapid absorption.
- Stable and easily adopted to manufacture and packaging techniques.

DISADVANTAGES

- MDTs absorb moisture easily and so should be maintained dry.
- Special packaging methods are required to maintain stability and safety of the product during storage.

MIGRAINE

Migraine is neurological disease which is characterized by mild to severe headaches that lasts from 1 hour to several hours with symptoms effecting autonomic nervous system.It is a greek word meaning pain on one side of the head. Pain is caused in pulsating nature on one side of the head lasting from 2 to 72 hours.Several other symptoms are associated with it like nausea, vomiting and sensitivity to sound, light. Generally migraine headache is followed by aura which is a visual, sensory or motor disturbance. Hence the migraine headache might be with or without aura. Physical activity worsens the headache

EXPERIMENTAL METHODS:

Construction of calibration curve in pH 6.8 phosphate buffer

Procedure: Scanning of Drug: Different concentrations of drug solution were scanned in U.V spectrophotometer in the wavelength range of 200 – 400nm. Then the wavelength at which the drugs show the highest peak for most of the concentrations was taken as maximum wavelength of drugs.

Preparation of Standard Stock Solution:

Accurately 100 mg of pure drug was weighed and transferred into 100 ml volumetric flask. 2-3ml of methanol was added to dissolve it and the volume was made upto 100ml with buffer solution. This is stock solution A. From this solution 1ml was withdrawn and diluted to 100ml in 100 ml volumetric flask to get a solution of concentration 10µg/ml. This is labeled stock solution B.

Preparation of working standard Solutions

From stock solution B 2,4,6,8 ml of solutions

was pipette out and transferred into 10ml volumetric flasks and the volume was made upto 10ml with phosphate buffer pH 6.8 to get the solutions of concentrations 2, 4, 6&8µg/ml. Their absorbance was measured by U.V.spectrophotometer at their aximum wavelength analytically & calibration curve was plotted.

DRUG-EXCIPIENT COMPATIBILITY STUDIES :

Drug excipient compatibility studies were conducted to monitor or determine the interactions among the active pharmaceutical ingredients and all the excipients that were employed in various formulations. The study was carried out individually and also in combination of compounds which has shown the efficacy of drug upon combining with other compounds and also the functional groups that are present in the drug were represented by peaks that were interpreted to know in detail the bonds present in the structure of drug.

DSC study : Differential scanning calorimetry of pure drugs and excipients were studied to investigate any changes in melting points of the drug after combining with excipients. Differential scanning calorimetry curves were obtained by a differential scanning calorimeter(Schimadzu DSC- 50) at a heating rate of 10^{o}c/min from 25^{o}– 250^{o}c in nitrogen atmosphere (20mL/min) with a sample weight of 5mg – 25mg.

FORMULATION OF ORO-DISPERSIBLE TABLETS OF ANTI MIGRAINE DRUGS:

Mouth Dissolving tablets were formulated by direct compression method. All the ingredients were weighed according to the formula given in the tables below and were mixed well by physical mixing in a poly bag and passed through 44 mesh coarse sieve and then were compressed into tablets by uniformly weighing each ingredient and transferring it into die cavity. The hardness was adjusted to 3 – 4kg/cm2 and they were compressed using 6mm punch by cadmach for all batches.

Table : Composition of Sumatriptan Mouth DissolvingTablets

F Formulation Code	F1	F2	F3	F4	F5
Sumatriptan	12.5	12.5	12.5	12.5	12.5
SSG	10	10	10	10	10
Starch	100	120	140	160	-
MCC	-	-	-	-	100
Aspartame	10	10	10	10	10
Aerosil	2	2	2	2	2
Mg stearate	3	3	3	3	3
Talc	5	5	5	5	5
Total weight (mg)	142.5	162.5	182.5	202.5	142.5

EVALUATON PARAMETERS

The formulation blend and compressed tablets were tested for the following properties.

Precompression Parameters

Method Preparation of Mixed Blend of Drug and Excipients

All ingredients were weighed in required quantities and are sieved to get uniform particle size and were mixed by physical mixing finally magnesium stearate and talc were added.

Angle of repose

The powder blend was flown from the funnel onto a sheet of paper to form a heap and the radius of the heap and height of the pile were noted. The angle of repose was calculated by formula**Bulk density**

Bulk density is the density possessed by total mass of the powder. The weighed powder blend was taken ina graduated cylinder and the volume of the powder covered was noted. The bulk density was determined by the formula.

Tapped density

Tapped density was determined by subjecting the cylinder containing bulk mass of powder to 100 tapings placing it on bulk density apparatus. The tapping was done from a height of 10cm every 2 seconds interval. Then the volume of

Compressibility index:

Compressibility/ Carr‟s index is a measure of the range of free flow of powder. Based on the compressibility index the powders can be categorized based on their flow property. It was calculated from the formula

Hausner's Ratio

Hausener‟s ratio also gives information regarding the flow properties of powders. It serves as an index.

POSTCOMPRESSION PARAMETER

Thickness : Randomly 10 tablets were taken from each formulation and their thickness was measured using a digital micrometer (Mitutoyo Corp, Kawasaki, Japan). Average thickness and standard deviation values were calculated. The tablet thickness should be controlled within a ± 5% variation of standard value.

Tablet hardness: The compression force of the punch with which the tablet is compressed imparts hardness to the tablet. It was tested by Monsanto or Pfizer hardness tester and expressed in kg/cm2. Hardness influences the disintegration time of tablet. Generally, a minimum hardness of 2.5 kg / cm^2 is considered acceptable for uncoated tablets. The hardness for FDTs should be preferably 2.5 to 3 kg / cm^2.

Tablet friability: A tablet with unit mass equal to or less than 650mg requires a sample of tablets equivalent to 6.5g to conduct the test. Tablets are carefully dedusted prior to testing and accurately weighed before placing in the drum. This weight was takn as W1. The drum was rotated 100times and the tablets were removed. Any loose dust from the tablets was removed and was weighed again accurately. This was taken as final weight W2. The %friability of the tablets can be caluculated from the formula

Wetting time

Wetting time is the time taken for the tablet to completely absorb water to disintegrate rapidly. A petri plate was taken and filled with certain volume of buffer solution. Filter paper or tissue paper was placed in the petri plate in thebuffer solution and the tablet was placed on it. The time taken for the buffer solution to completely wet the tablet was noted. More the wetting timeresults more disintegration time taken by the tablet and vice versa.

Water absorption ratio:

The tablets were initially weighed and the weight was noted as W1. Then they were evaluated for wetting time and the tablet weight after complete wetting was noted as

***In-vitro* Disintegration studies:**

Disintegration time is the time in which complete tablet breaks down into finer particles and goes into the fluid. This is specific test for ODT‟s as they ought to show very less disintegration time. Electrolab disintegration test apparatus was employed containing 6 tubes 3 inches long, held by 10mesh screen and open at top. 1 tablet was placed in each tube & the basket was moved up and down in a beaker containing 1 liter pH 6.8 phosphate buffer at a height of 2.5cm and the temperature of 37 ±0.5^{o}c. Then the disintegration time of tablets was noted and the average was calculated.

Drug content uniformity

The tablets formulated were tested for uniformity in drug content. The percentage of drug actually present in them compared to the incorporated drug. 20 tablets were weighed accurately and powdered, the powder equivalent to the dose of thedrugwas transferred to 100 ml of buffer solution and was dissolved thoroughly by shaking and was allowed to stand for 24 – 48 hrs. Then a sample was withdrawn, filtered through wattman filter paper and diluted suitably. The absorbance was measured from which the amount of drug was calculated. The % drug content was then calculated practically.

Dissolution studies

The dissolution/ drug release studies were carried out using paddle type USP-II dissolution apparatus. pH 6.8 phosphate buffer was employed as dissolution fluid in volume of 900ml, the rpm was maintained 50rpm, temperature was maintainedat 37±0.5^{o}c. Aliquotes of 5ml were collected at regular intervals and replaced with equal

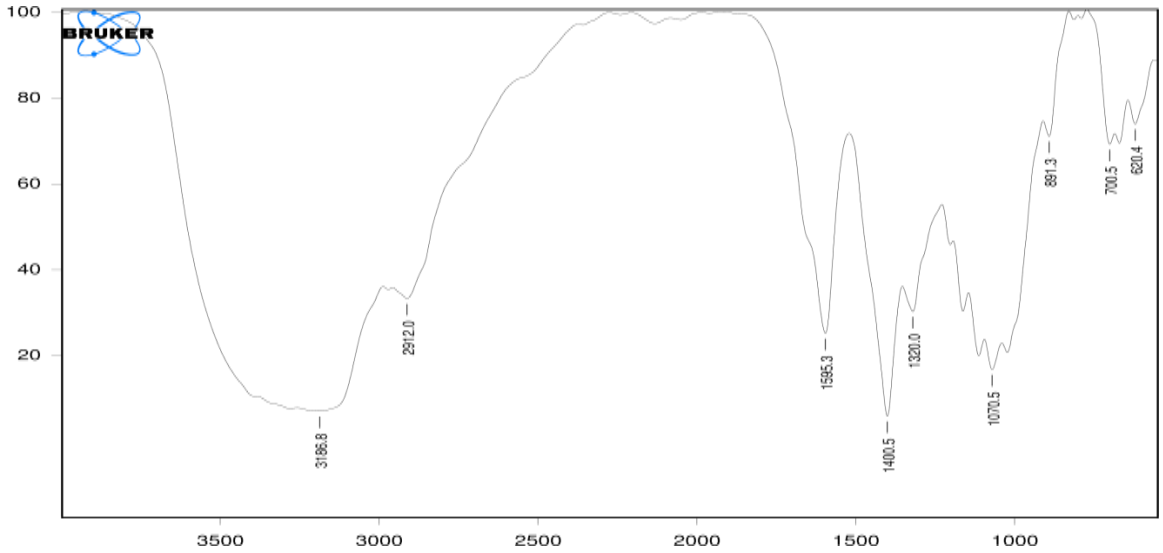
volume of fresh buffer to maintain sink conditions. The samples were filtered, suitably diluted and analysed by U.V-spectrophotometer at maximum wavelength of the drugs

Table: Composition of optimised formulation of Sumatriptan Mouth Dissolving tablets:

S.NO	INGREDIENT	WEIGHT (mg)
1	Sumatriptan	12.5
2	SSG	10
3	Mannitol	130
4	Aspartame	10
5	Aerosil	2
6	Mg stearate	4
7	Talc	4
Total weight		172.5

Formulation Code	Derived properties		Flow properties		
	Bulk density	Tappeddensity	Angle ofrepose	Carr'sndex	Hausner'sratio
	(mean±SD)	(mean±SD)	(mean±SD)	(mean±SD)	(mean±SD)
F1	0.436±0.01	0.492±0.015	26.48±0.30	11.47±1.97	1.128±0.02
F2	0.449±0.015	0.505±0.02	22.24±0.39	11.21±1.96	1.129±0.03
F3	0.491±0.015	0.58±0.01	24.98±0.68	11.88±3.97	1.137±0.05
F4	0.478±0.015	0.527±0.015	23.23±0.96	9.46±1.81	1.108±0.02
F5	0.432±0.02	0.499±0.03	25.97±0.73	12.68±2.25	1.148±0.03

Fig: IR spectrum of pure drug of Sumatriptan



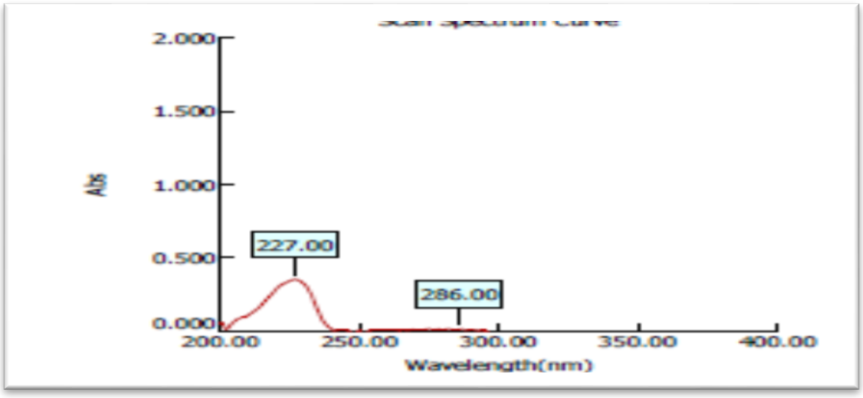
Result and Discussion

Precompression parameters of Powder blend of Sumatriptan

Table: Solubility data of four drugs in four different solvents

S.N O	Medium	Sumatriptan (mg/ml)
1	0.1N HCL	28
3	water	95
4	Phosphate buffer pH(6.8)	92

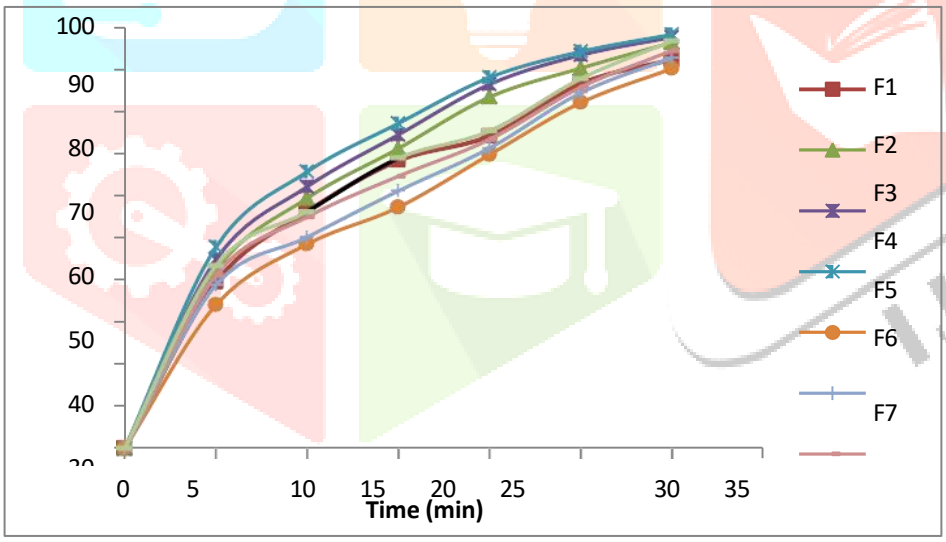
Fig: UV scan spectrum of Sumatriptan pure drug



Data of Post-compression parameters of Sumatriptan Table

F code	Average Weight	Thickness (mm)	Hardness (kp)	Friability (%)	Disintegration time(sec)	% of drug Content	Wetting time (sec)	Water absorption ratio
F1	144.03±0.015	3.91±0.016	3.52±0.036	0.17±0.051	30±0.035	97.57±0.025	28±0.022	0.19±0.022
F2	164.5±0.017	4.02±0.054	3.74±0.054	0.14±0.025	29±0.033	98.52±0.055	29±0.054	0.195±0.031
F3	182.9±0.02	4.4±0.084	3.88±0.043	0.15±0.031	30±0.084	98.48±0.093	23±0.011	0.2±0.082
F4	203.2±0.035	4.6±0.012	3.95±0.063	0.31±0.046	33±0.065	99.17±0.054	25±0.063	0.25±0.054
F5	143.7±0.064	3.94±0.054	3.53±0.022	0.13±0.084	29±0.022	99.73±0.077	20±0.038	0.18±0.093

Fig : Cumulative drug release curves of Almotripta formulati



CONCLUSION

1. The solubility of the drugs was determined in various solvents.
2. The drugs and excipients were found to be compatible with each other as found by IR spectroscopy studies.
3. The purity interactions and nature of the drugs was determined by DSC and and was found to be satisfactory.
4. The physical mixtures of the formulations were found to have good flow properties when tested for precompression parameters. Hence these were subjected to direct compression.
5. The evaluation parameters such as thickness, weight variation, hardness, friability, and drug content were found to be in satisfactory limits.
6. The wetting time and water absorption ratio were found to be relevant to give a rapid dispersion or disintegration of the drug formulation.
7. The drug release from all the formulations was found to be rapid

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