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Research Article

FORMULATION DEVELOPMENT AND EVALUATION OF QUICK DISSOLVING ORAL STRIPs CONTAINING SUMATRIPTAN SUCCINATE

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ABSTRACT

The present study was aimed to formulate and evaluate quick dissolving oral strips (QDOS) of Sumatriptan succinate for the treatment of migraine headaches. Sumatriptan succinate is 5-HT_{1D} agonist which is antimigraine. Hydroxyl propyl methyl cellulose is used as film forming agent. Quick dissolving oral strips are meant to be dissolved in saliva and remain in oral cavity until swallowed. Hence, taste masking becomes critically important. The strips were prepared by solvent casting method and characterized by UV, FTIR studies. Suitable plasticizer and its concentration were selected on the basis of flexibility, tensile strength and sticking of strip. In the present study glycerol was used as plasticizer. Strips were evaluated for drug content, the dissolution profile, disintegration time, stability studies and mechanical properties like folding endurance, percent elongation and tensile strength were found to be satisfactory. Hence, Sumatriptan succinate HPMC Quick dissolving oral strips are developed and evaluated successfully.

Keywords: Quick dissolving oral strips, Hydroxyl propyl methyl cellulose, Sumatriptan succinate

INTRODUCTION

Quick dissolving oral strip technology evolved over past few years from the confection and oral care markets in the form of breath strips and became a novel and widely accepted form by consumers[3].

Salient features of quick dissolving oral strips[6]

1. The strip alleviates fear of throat choking.
2. The strip alleviates unpleasant taste and is easy to manufacturer.
3. The strip allows children, elderly, and the general population to take their medication directly and whenever and wherever they needed.
4. Ability to provide advantage of liquid medication in the form of solid preparation.
5. Require no water.
6. Cost effective.

Advantages

- Convenient dosing.
- Fast disintegration or dissolution followed by quick effect which is desirable in some cases such as pain.

Disadvantages

- The disadvantage of QDOS is that high dose cannot be incorporated into the strip.
- Expensive packaging of oral strip.

It is estimated that migraine affects more than 10 percent people globally [1]. Disability due to migraine headache associated symptoms has been estimated to cost American employers $ US 13 billion per year, due to missed work days and impaired work performance. Epidemiological studies in migraine reveal that the vast majority of patients (>90 %) have experienced nausea during a migraine attack. Similarly, most (almost 70 %) have vomited at some time during an attack. So, they avoid intake of liquid. The vascular theory holds that initial vasoconstriction or shunting of blood through carotid arterio-venous anastomoses produces cerebral ischemia and starts the attack. The neurogenic theory considers it to be a spreading depression of cortical electrical activity followed by vascular phenomena[2].

Sumatriptan succinate is a potent and selective 5-hydroxytryptamine agonist chemically it is 3-[2-(dimethyl amino) ethyl]-N-methyl-1H-indol-5-methanesulfonamide butane -1,4-dioate it is an effective agent in the treatment of acute migraine attack. It provides rapid symptoms relief up to 85-90% of migraine patient within two hours of treatment. Sumatriptan succinate is rapidly but incompletely absorbed following oral administration and undergoes first pass metabolism resulting in a low absolute bioavailability of 15%. The biological half-life of Sumatriptan succinate is about 2.5 h[1].

The objective of the present investigation is to develop quick dissolving oral strips taking sumatriptan succinate as a model drug to reduce the lag time and providing faster onset of action to relieve immediately acute migraine attack. At present sumatriptan succinate is available in the form of tablets and injections, in the market. Patients are non co-operative with these dosage forms. Hence oral strips become important tool to improve the patient compliance.

MATERIALS AND METHODS

Sumatriptan succinate, hydroxyl propyl methyl cellulose E 15, sucralose, glycerol, anhydrous citric acid, sodium starch glycolate, xanthan gum and strawberry flavor were arranged by Nu Life pharmaceuticals-pune.

UV spectrum analysis of sumatriptan succinate

The solution was scanned using UV-visible double beam spectrophotometer (Shimadzu) in the range of 200 to 400 nm to fix the maximum wave length and UV spectrum was obtained[4].

Standard plot of sumatriptan succinate in pH 6.8 phosphate buffer

The standard plot of sumatriptan succinate was prepared in pH 6.8 phosphate buffer. 50 mg of drug was weighed accurately and dissolved in 50 ml of phosphate buffer. Appropriate dilutions were made with buffer to obtain test solution ranging from 2µg/ml to 8µg/ml. The absorbance of the drug in the buffer was then measured on a double beam UV-visible spectrophotometer at λ_{max} of 226.2 nm against the respective blank.

Formulation of drug strips[4, 5]

The formulation of oral strip was prepared by using solvent casting method. Drug was dissolved separately in one third of

the total water. The polymer and the plasticizer were dissolved separately in half of the total water. Other excipients were dissolved in remaining of the water. All solutions were sonicated to remove air bubbles. Then, all three solutions were mixed by using mixing device for 45 minutes with rotating speed 80-90 rpm. The resulting solution was sonicated and was casted slowly and with continuous flow in petriplates. The plates were kept in hot air oven at 50°C for 24 hours. The plates were then kept in refrigerator for 30 minutes. Then, the dried strip was gently separated from glass plate and cut into desired size. (Figure-1)

Drug polymer compatibility studies

Study was carried out using IR affinity 1 (Shimadzu). FT-IR spectra of pure drug and drug with polymer were obtained.

Weight variation[8]

One square inch film was cut at five different places in the casted strip. The weight of each strip was taken and the weight variation was calculated.

Thickness

The thickness of the strip was measured using IR affinity 1 (Shimadzu) at different points of the strip and average thickness was calculated.

Tensile strength[7]

Tensile strength of the strip was determined using QTS texture analyzer (Brookfield). The test strip of specific size 3 cm× 1 cm was taken and force was gradually applied till the film breaks.

Percentage Elongation

Percentage Elongation of the strip was determined using QTS texture analyzer. The test strip of specific size 3 cm× 1 cm was taken and force was gradually applied till the film breaks. The readings were taken from the instrument.

Folding endurance[7]

The folding endurance is expressed as the number of folds required to break the specimen or develop visible cracks. A small strip of 4 square cm was subjected to this test by folding the strip at the same plane repeatedly.

In vitro disintegration time

A small strip was placed in phosphate buffer pH 6.8. The time required for the strip to break was noted as In vitro disintegration time.

Content uniformity

The strips were tested for content uniformity. Strip of size (4 × 5 cm^2) was cut, placed in 100 ml phosphate buffer pH 6.8 and dissolved and kept on magnetic stirrer for 1 hr. solution was suitably diluted. The absorbance of the solution was measured at 226.2 nm. The drug content was determined by plotting a standard calibration curve of drug in Phosphate buffer pH 6.8.

In vitro dissolution studies[8]

Dissolution study was carried out using USP type II (paddle apparatus) (Electrolab, model no.TDT-06) with 900 ml phosphate buffer pH 6.8, as a dissolution medium maintained at 37±0.5°C. Medium was stirred at100 rpm for a period of 30 minutes. Samples were withdrawn and replacing the same amount with the fresh medium. Samples were suitable diluted and analyzed for drug content at 226.2 nm.

Table 1: Composition of all formulations

Ingredients	M1	M2	M3	M4
Drugs	210	210	210	210
HPMC E 15	250	300	400	500
Glycerol	100	100	100	100
Citric acid	10	10	10	10
Xanthan gum	30	30	30	30
Sodium lauryl sulphate	1	1	1	1
Sodium methyl paraben	1	1	1	1
Sucralose	5	10	15	20
Sodium starch glycolate	2	2	2	2
Flavor	5	5	5	5
Water (ml)	20	20	20	20

*All weights except water are in milligrams (mg)

Table 2: Physiochemical evaluation data of strips

Formulation	Weight variation (mg)	Thickness (mm)	Folding endurance	Tensile strength (N/cm^2)	% Elongation	In vitro disintegration time (sec)	% Drug content
M1	43.11±0.11	0.101±0.008	135±4.147	3.235	9.873	15.66	91.32
M2	52.24±0.241	0.109±0.005	142±6.340	3.761	11.530	20.33	93.70
M3	62.47±0.407	0.116±0.006	147.7±5.507	4.311	15.44	23.33	98.15
M4	74.18±0.262	0.126±0.0017	183.3±10.263	6.812	19.55	26.66	99.27

Table 3: In vitro dissolution studies of all formulations

Time (minutes)	M1	M2	M3	M4
0.25	6.35	8.30	9	10.23
1	15.04	20.04	27.2	34.56
2	25.27	29.7	32	58.12
3	35.56	46.64	55.71	78.43
4	49.78	61.23	72.28	85
5	62.6	74.35	83.15	99.58
6	73	86.1	96.28	
7	85.51	91.21		
8	91.1	95.5		

Table 4: Stability studies for M4

Parameters	Stability studies	
	Initial	3 months (40°C±75% RH)
Thickness (mm)	0.126±0.017	0.125±0.008
Folding endurance	183.3±10.263	181.9±8.91
Tensile strength (N/cm²)	6.812	6.618
In vitro disintegration (sec)	26.66	28
In vitro dissolution	99.58 %	99.23 %

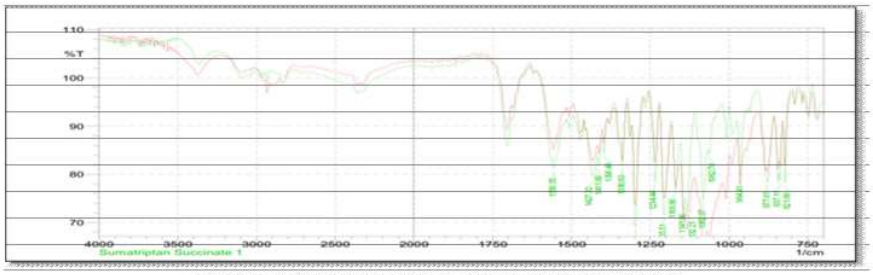


Figure 1: FTIR Spectra of Pure drug and Drug+ Polymer

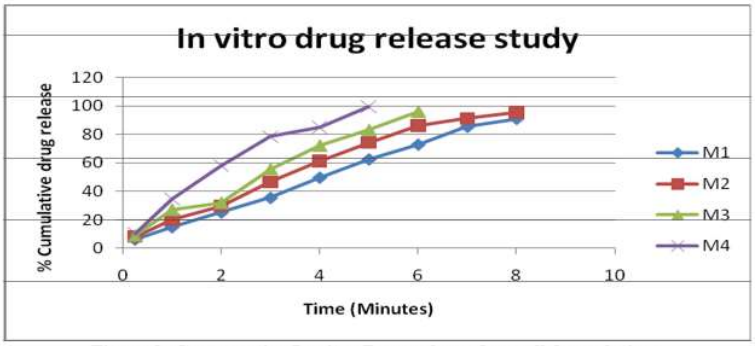


Figure 2: Comparative In vitro Drug release from all formulations



Figure 3: Quick dissolving oral strip (M4)

RESULTS AND DISCUSSION

Drug polymer compatibility study

Both the spectra are reported in figure-1. There is no interaction between drug and polymer. Hence, it can be concluded that the drug was in the Free State and can release easily from the formulation.

Weight variation

The results of weight variations were shown in the Table-2. As polymer concentration was increases, weight of strip also increases.

Thickness

The results were reported in the Table-2. Thickness varied from 0.101±0.008 to 0.126±0.0017 mm.

Tensile strength

The results were reported in the Table-2. The tensile strength was found to be in the range of 3.245 to 6.812 N/ cm². The formulation M4 showed the best tensile strength.

% elongation

The results were reported in the Table-2. Percentage elongation was found to increase in increase concentration of polymer in the strip. The formulation M4 showed desirable result.

Folding endurance

The results were reported in the Table-2. The folding endurance was found to be in the range of 135±4.147 to 183±10.263. The formulation M4 showed good flexibility.

In vitro disintegration time[8]

The results were reported in the Table-2. The disintegration time of the strips were found to be increased with increase in the concentration of the polymer.

Drug content

All values were tabulated in the Table-2. It was observed that the drug content in M4 was found to be 99.27%.

In vitro dissolution studies

The results obtained from all formulations were tabulated in Table-3 and figure-2. Formulation M4 gave 99.58% within 5 minutes.

Stability studies

The accelerated stability studies of M4 were carried according to ICH to assess the drug formulation study. Optimized formulation was sealed in aluminum packaging laminated with polyethylene. The results were tabulated in the Table-4.

CONCLUSION

The Sumatriptan succinate is a 5-HT_1 agonist used for treatment of migraine. The half-life of drug is 2.5-3 hrs and its oral absolute bioavailability is 17-25%. So, in order to improve bioavailability and efficacy, we have prepared Quick dissolving oral strips of Sumatriptan succinate using HPMC E 15 polymer. FTIR study showed no interaction between drug and polymer. Formulation M4 showed good mechanical properties and good drug release. Stability studies indicating that there was no degradation of the formulation at high temperature and high humidity. The formulation was stable (Figure-3).

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