Research Article

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FORMULATION AND EVALUATION OF ORAL DISINTEGRATING FILMS OF SUMATRIPTAN SUCCINATE

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Abstract

The aim of the present investigation was to develop oral disintegrating film of sumatriptan succinate, anti migraine agent and investigate the effect of the formulation variables like concentration of film forming polymer, emulsifying agent and plasticizer on the physico chemical properties and in vitro diffusion studies. Hydroxyl propyl methyl cellulose was used as a film former, tween 80 as an emulsifying agent and glycerin as plasticizer. The three variables were studied at two level thus, a 2^3 full factorial design was applied and eight different formulations were developed by solvent casting method and evaluated. The role of HPMC in deciding the film properties was significant. It affected folding endurance, tensile strength, percentage elongation, disintegration time and invitro diffusion rate significantly. The in low level and tween 80 (5mg / film ie. 2x3 cm^2) and PEG 4000 (8mg/fil ie. 2x3 cm^2) in high level was found to be suitable for film formation with desirable physiochemical properties, faster disintegration and optimum invitro release. Here tween 80 and glycerin at high level which acted as solubility enhancers.

Keywords: Oral disintegrating film, Sumatriptan succinate, Anti migraine agent.

Introduction

The pharmaceutical dosages are administered in the form of pills, granules, powders and liquids. Generally, a pill is designed for swallowing intact or chewing to deliver a precise dose of medication to patients. The pills, which include tablets and capsules, are able to retain their shapes under moderate pressure. However some patients, particularly pediatric and geriatric patients, have difficulty in swallowing or chewing solid dosage forms. Many pediatric and geriatric patients are unwilling to take these solid preparations due to fear of throat choking. In order to assist these patients, several fast dissolving drug delivery have been developed. Fast dissolving drug delivery systems can be manufactured by a variety of technologies, including direct compression, wet granulation and freeze drying. Some make use of different disintegrating mechanisms, such as high level of disintegrating or effervescent agents, which cause the dosages to disintegrate rapidly in the mouth. Most of the existing fast dissolving drug delivery systems are in the form of tablets and are

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designed to dissolve or disintegrate in the patient's mouth within a few seconds or minutes without the need of water or chew.

The oral route of administration still continues to be widely used accepted route, contributing to 50 - 60% of total drug formulations because of ease of administration, self-medication, and pain avoidance as compared to parenterals. Mainly elderly patients may experience problems in swallowing solid dosage forms. Oral administration of conventional tablets poses problems, when patient is mentally ill, developmentally disabled and in nausea. In some cases motion sickness, sudden episode of allergic attack or coughing and unavailability of water, poses problem in swallowing. To fulfill these medical needs pharmaceutical technologists developed several mouth dissolving drug delivery systems.

Following are the characteristics of the mouth dissolving film:

1. Require no water for the administration (to swallow).
2. Dissolve or disintegrate in the mouth in few seconds.
3. Posses pleasant taste, high stability and transportability.
4. Leave minimal or no residue in the mouth after administration.
5. Need no special packaging materials or processing requirements.

Advantages of mouth dissolving films:

1. The film alleviates fear of throat choking.
2. The film is easy to handle and administer.
3. The film maintains a simple and convenient packaging.
4. The film alleviates unpleasant taste and is easy to manufacturer.
5. This system allows children, elderly and the general population to take their medication directly wherever and whenever needed.
6. The fast dissolving action is primarily due to the large surface area of the film.
7. The films are tough, solid, soft, flexible and do not require special packaging.
8. The films are thin and can be carried in a patients pocket, wallet.

Materials and methods

Table No. 01: List of chemicals

S.No	Drug / Excipients	Source
01.	Sumatriptan Succinate	Gift sample from KAPL
02.	HPMC (15 cps)	Gift sample from Remidex
03.	Glycerin	Ranbaxy fine chemicals ltd
04.	Ethanol	Ranbaxy fine chemicals ltd
05.	Polysorbate – 80	Rea chem
06.	Menthol	Thomas Baker Chemicals ltd

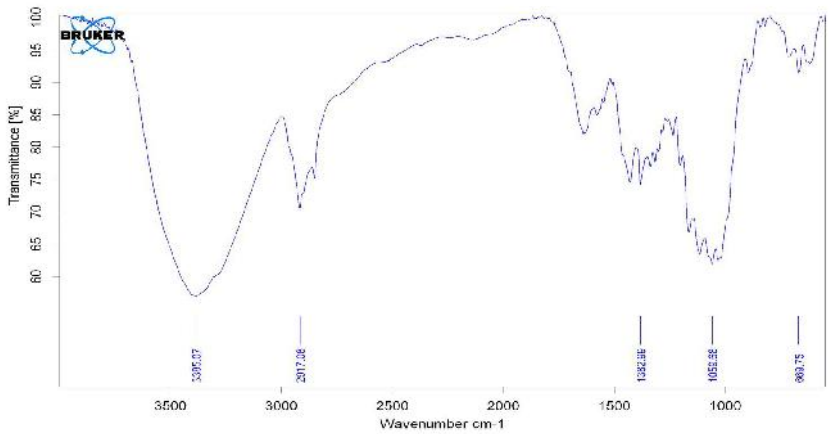

Fig. No. 01: Sumatriptan Optimized formula

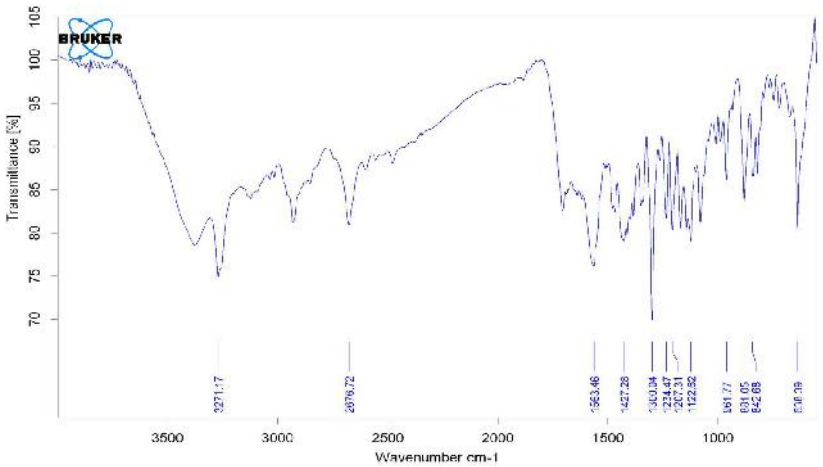

Fig. No. 02: Sumatriptan Succinate Solid

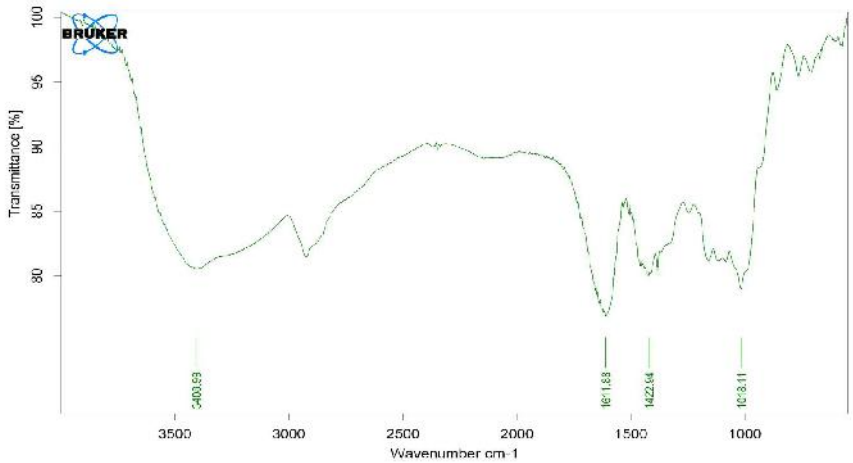

Fig. No. 03: Sumatriptan + HPMC K 100 Solid

Formulation of mouth dissolving films

Mouth dissolving films containing Sumatriptan Succinate were prepared by casting method. The films of HPMC (low viscosity) were prepared with an objective to dissolve the film in the mouth. 3 and 4 % w/v each of HPMC films were exhibited desired mouth dissolving time and other film parameters, compared to 1 and 2 % w/v of HPMC films which were difficult to remove from the mould. 5 and 6 % w/v of HPMC films exhibited unacceptable mouth dissolving time. Hence 3 and 4 % w/v of HPMC films were used for the study.

Table No. 02: Formulae of oral thin films of Sumatriptan Succinate

Formulation Code	HPMC	Tween 80	Glycerol	Citric Acid	Methnol
F1	400mg	30mg	45mg	70mg	30ml
F2	300mg	30 mg	45mg	70mg	30ml
F3	400mg	40 mg	45mg	70mg	30ml
F4	300mg	40 mg	45mg	70mg	30ml
F5	400mg	30 mg	60mg	70mg	30ml
F6	300mg	30 mg	60mg	70mg	30ml
F7	400mg	40 mg	60mg	70mg	30ml
F8	300mg	40 mg	60mg	70mg	30ml

Results

Table No. 03: FT-IR Spectra data of Sumatriptan and polymers

Group in cm^{-1}	Standard Frequency in cm^{-1}	Frequency of Sumatriptan Optimized formula in cm^{-1}	Frequency of Sumatriptan Succinate Solid in cm^{-1}	Frequency of Sumatriptan + HPMC K 100 Solid in cm^{-1}
1740 – 1795	C=O stretching (Lactones)	1382.99	1563.46	1422.94
2840 – 3000	C– H stretching (Alkanes)	2917.08	2676.72	–
3000 – 3100	C– H stretching (Aromatic)	3385.07	3271.17	3408.99
1120 - 1160	S=O Sulfones	1059.68	1122.62	1018.11
700 – 750	Monosubstituted Benzene	669.75	638.39	

Thickness of the film

The thickness of the drug loaded films were measured with the help of screw gauge by combining of eight films of film, as it was difficult to measure the thickness of the single film, thickness varies from 0.323 ± 0.0208 to 0.3633 ± 0.0153 mm.

Table No. 04: Comparative evaluation of Thickness of the mouth dissolving films

SL.No	Formulation Code	Average thickness in mm			Mean ± S.D*
		Trial 01	Trial 02	Trial 03	
01	F1	0.31	0.34	0.33	0.326 ± 0.015
02	F2	0.35	0.38	0.36	0.363 ± 0.015
03	F3	0.25	0.28	0.27	0.266 ± 0.447
04	F4	0.28	0.32	0.31	0.303 ± 0.547
05	F5	0.24	0.28	0.27	0.263 ± 0.526
06	F6	0.25	0.27	0.26	0.266 ±0.538
07	F7	0.21	0.25	0.24	0.233 ± 0.753
08	F8	0.26	0.29	0.28	0.276 ±0.634

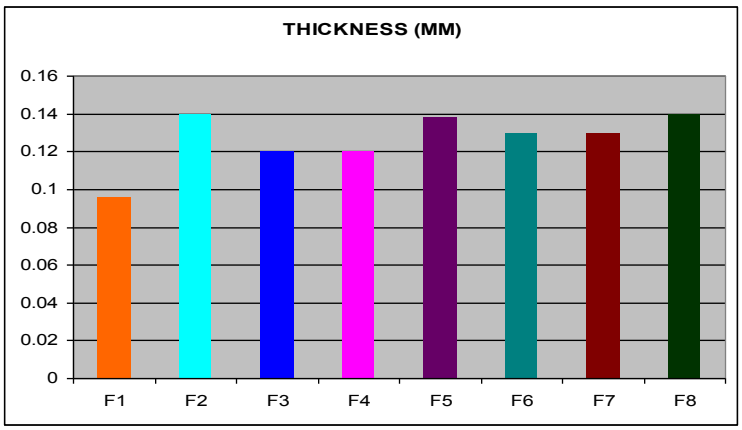

Fig. No. 04: Comparison of Thickness of the film

Tensile strength of the films

The film of 3 inch X 10 mm was taken for the studies. From the results it is clear that when the concentration of the polymer increases, the tensile strength of the film also increases. The formulation F II shows the maximum tensile strength, percentage elongation and folding endurance. Presence of glycerin as a plasticizer imparts the flexibility to the polymers. Tensile strength measures the ability of the film to withstand rupture. The formulation F II shows the maximum value of tensile strength 1.526 ± 0.0745,percentage elongation 31.74 ± 0.8442 and folding endurance was 183 (no of folds) as shown in the table 5.

Table No. 05: Tensile strength of mouth dissolving films

SL.NO	Formulation Code	Tensile Strength in kgs			Mean
		Trial 01	Trial 02	Trial 03	
01	F1	2.849	2.965	2.645	2.819
02	F2	3.143	3.294	3.046	3.161
03	F3	2.267	2.345	2.142	2.251
04	F4	2.486	2.621	2.216	2.441
05	F5	2.142	2.326	2.012	2.160
06	F6	1.621	1.781	1.221	1.541
07	F7	1.159	1.205	1.105	1.156
08	F8	1.346	1.374	1.290	1.336

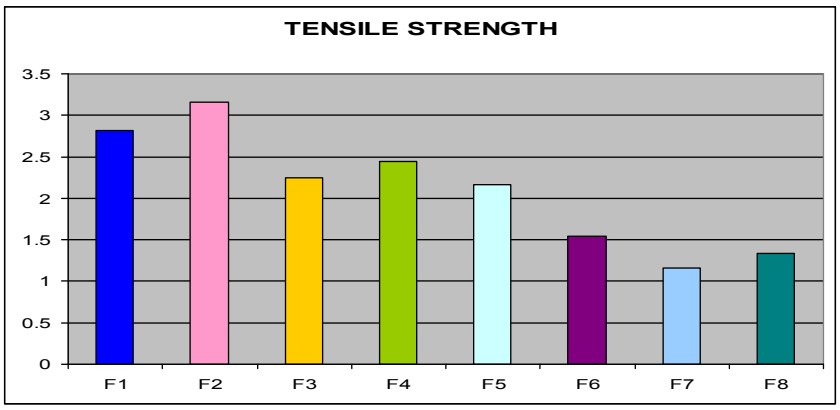

Fig. No. 05: Comparison of Tensile Strength of the films

Folding endurance of the films

A strip of film 4squre cm was cut and subjected for the folding endurance studies until it broke at the same place. Folding endurance increases with increase in polymer concentration.

Table No. 06: Comparative evaluation of folding endurance of mouth dissolving films

SL.NO	Formulation Code	Folding endurance (no of folds)			Mean
		Trial 01	Trial 02	Trial 03	
01	F1	92	85	97	91.3
02	F2	108	115	95	10.6
03	F3	90	115	95	88.3
04	F4	105	112	93	103.3
05	F5	88	80	90	86
06	F6	102	108	91	100.3
07	F7	84	77	88	83
08	F8	98	102	86	95.3

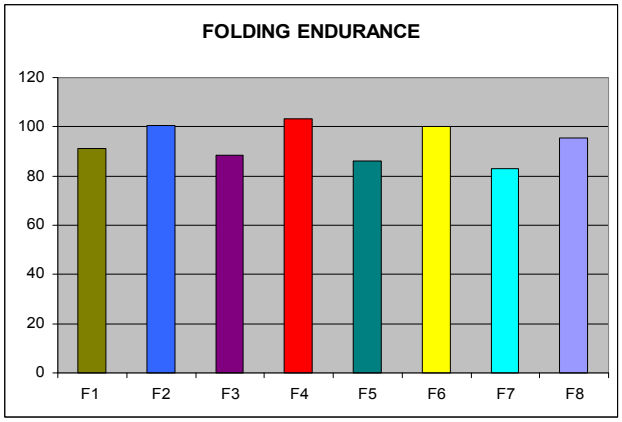

Fig. No. 06: Comparison of Folding Endurance

Disintegration time

The disintegration time of the film was done by using tablet disintegration test apparatus. A size of one square inch film was subjected for this study. Disintegration times of the films were found to be increased with increase in the concentration of the polymer. The formulation F2 shows 62.6Sec (disintegration time) and F7 fastest disintegration (32Sec). Being emulsifier it facilitates the dissolution of fluid into the film resulting in faster disintegration of the film. Hence the films formulated with high Tween 80 content dissolution faster as compared to the films prepared with low Tween 80 content.

Table No. 07: Comparative evaluation of Disintegration time of mouth dissolving films

SL.NO	Formulation Code	Disintegration time in Sec			Mean
		Trial 01	Trial 02	Trial 03	
01	F1	58	54	60	57.3
02	F2	60	58	70	62.6
03	F3	42	41	45	42.6
04	F4	45	42	38	41.6
05	F5	38	36	43	39
06	F6	40	36	41	39
07	F7	32	31	34	32
08	F8	34	32	36	34

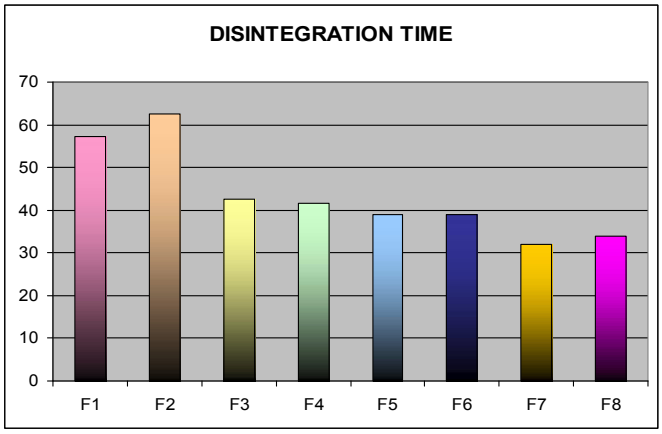

Fig. No. 07: Comparison of Disintegration Time

***In vitro* dissolution studies**

Dissolution profiles of the mouth dissolving films containing Sumatriptan Succinate formulations were compared with pure drug. Comparative dissolution profile of all batches is given in Fig.8. Formulation F7 released drug completely in about 30 min. this may be due to low level of HPMC and high level of Tween 80 and glycerol. Whereas release rates of formulation F2 is slowest. This indicates when HPMC is present in high concentration and emulsifier and plasticizer are present in low concentration drug release is retarded. Here the role of plasticizer and emulsifier must be to act as dissolution facilitating agent.

Table No. 08: Comparative evaluation of *Invitro* dissolution profiles of Mouth Dissolving Films

SL.No.	Formulation Code	Time in minutes					
		3	6	9	12	15	18
01	F1	30	36	44.6	52.4	64.5	75.2
02	F2	28	33	41	47.2	61	73
03	F3	35	40	48	55	68	78
04	F4	32.4	38.2	45	53.5	65	74
05	F5	38.8	45	54	58	75	87
06	F6	36.2	43	51.6	64	76	84
07	F7	45	49.6	58.2	65	86	93.8
08	F8	42	46.3	55.7	64	82	91.4

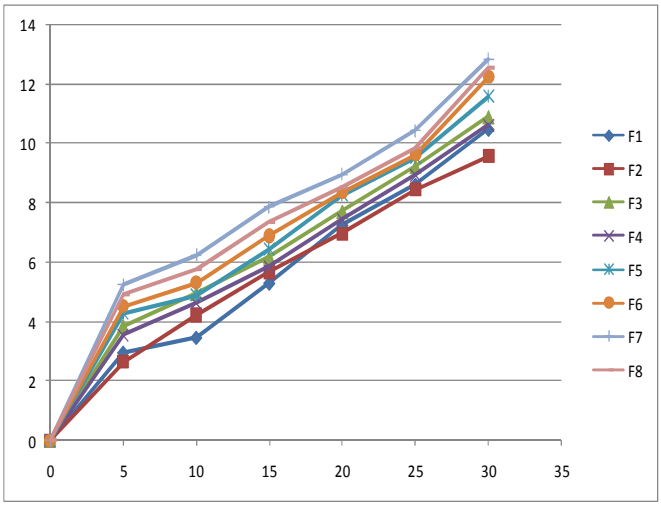

Fig. No. 08 : Comparison of dissolution of Mouth Dissolving Films

Conclusion

Oral fast disintegrating thin films of sumatriptan succinate with fast disintegration time and suitable mechanical strength for treatment of migraine disease were prepared. Average daily dose of sumatripton 10mg 2 to 3 divided doses.The film can be formulated using HPMC K15 hydrophillic polymer bases of the film, while glycerine were used as plasticizer and Polysorbate 80 as emulsifying agent, additionally citric acid as a taste stimulating agent.

The uniformity invitro disintegration time, drug release, folding endurance, tensile strength, thickness and percentage elongation were examined. The invitro result showed that 94%. Sumatriptan was released Within 30min with mean disintegration time of 32sec. Result of the stability studies indicated that film containing high percentage of polymer and percentage of plasticizer and emulsifier become brittle after storing at high temperature. Physical changes were not observed in the formulation F7 and F8.These films (F7 & F8) that contain HPMC (300mg) in low level and tween 80 (40mg) in high level was found to be suitable for film with desirable physiochemical properties, faster disintegration and optimum invitro release. Therefore, sumatriptan can be conveniently administered orally in the form of films with lesser occurrence of its side effects and with improved bio availability.

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