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Fast Dissolving Sublingual Film of Rizatriptan Benzoate for Management of Migraine

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ABSTRACT

The present article explores the study about formulation and evaluation of fast dissolving sublingual film using natural polymer. Fast dissolving sublingual film of Rizatriptan Benzoate was prepared by the solvent casting method using different concentrations of polymers including Gum Carrageenan and pectin. The batches containing various concentration of drug and polymer were made. The study showed a significant rapid dissolution of fast dissolving sublingual film which disintegrates in 45 seconds where the optimized formulation A4 showed a disintegration time of 26 ± 0.20 seconds and % drug content of 98.01 ± 0.06. The study demonstrated that Gum Carrageenan can be used as a very good film-forming agent and used for fast dissolving film formulation.

INTRODUCTION

Among the delivery routes, oral drug administration has been one of the most convenient and widely accepted routes of delivery for most therapeutic agents. There some known oral dosage forms such as tablets, capsules, and liquid preparations that are taken orally, swallowed, and they transit the gastrointestinal tract (GIT) for post buccal absorption. The target sites for local drug delivery in the oral cavity include the following: buccal, sublingual, periodontal, periodontal pocket, peribuccal, prelingual, tongue (i.e., lingual), and gum (i.e., gingival). (1,2)

Systemic drug delivery through the sublingual route had emerged from the desire to provide immediate onset of pharmacological effect. Dysphagia (difficulty in swallowing) is a common problem of all age groups, especially elderly, children, and patients who are mentally retarded, uncooperative, nauseated, or on reduced liquid intake/diets have difficulties in swallowing these dosage forms. Sublingual administration of the drug means the placement of the drug under the tongue and drug reaches directly into the bloodstream through the ventral surface of the tongue and floor of the mouth.

The orally fast-dissolving film is a new drug delivery system for the oral delivery of the drugs, in which the film when laced in the oral cavity rapidly disintegrates and dissolves to release the medication for oromucosal and intragastric absorption, without chewing or intake of water. (3) The sublingual mucosa is relatively permeable due to thin membrane and large veins. It gives rapid absorption and instant bioavailability of drugs due to high blood flow. (4,5) As the fast-dissolving film is taken through the sublingual route, rapid absorption of the drug is possible, which finally leads to the quick onset of action and prevent the first-pass metabolism of the drug.

Migraine is one of the ten most disabling disorders worldwide, and despite recent developments in the management of migraine, it remains underdiagnosed and undertreated. (6) The migraine sufferers have marked a reduction in their functional abilities so they would be benefited from the acute treatment that helps them to resume their functional abilities as quickly as possible. The new generation anti-migraine drug, Rizatriptan Benzoate is an orally active serotonin 5- HT1receptor agonist that potently and selectively binds to 5-HT1B/1D subtypes. Chemically it is N, N-dimethyl- 5-(1H-1, 2, 4-triazol-1-ylmethyl)-1H-indole- 3-ethanamine monobenzoate. The initial gut absorption of Rizatriptan is high (90%); however,

the compound undergoes moderate first-pass metabolism, which limits the bioavailability to 47%. (7) The migraine sufferers have marked a reduction in their functional abilities so they would be benefited from the acute treatment that helps them to resume their functional abilities as quickly as possible. So orally fast dissolving sublingual films of Rizatriptan prevents its first-pass metabolism and eliminates the need for intake of water by the patient during the migraine attack and provide fast onset of action which would be beneficial to migraine sufferers in resuming their functional abilities as soon as possible.

MATERIALS AND METHOD

MATERIALS

Rizatriptan Benzoate was obtained as a gift sample from Torrent laboratories, Ahmedabad. Pure Pectin and Gum Carrageenan was obtained from Gangwal Chemicals, Mumbai. Propylene Glycol, Glycerin, Mannitol, Cross Carmellose, Citric Acid were of Loba Chemicals.

METHODS

Characterization of Gum Carrageenan & Pectin:

Both the gums were subjected to identification tests and studied concerning their organoleptic properties, solubility, pH, and swelling index. They were characterized by determination of % Ash value, Acid Insoluble Ash, Loss on drying.

Drug Excipient Compatibility Study:

Drug compatibility studies were performed to determine the compatibility of drugs with polymers i.e. Gum Carrageenan and Pectin using Fourier Transform Infrared (FTIR) and Differential Scanning Calorimetry (DSC).

Calibration Curve of Rizatriptan Benzoate:

The absorbance of the drug in a salivary fluid having pH 6.8 was noted at various concentrations. The standard calibration curve for Rizatriptan Benzoate is shown in figure 9. The relation between concentration and absorbance is linear and curve obeys Beer-Lambert's law within the concentration of 2-10µg/ml for salivary fluid pH 6.8 as depicted in figure 9. The correlation coefficient value for the calibration curve is 0.996. The calculation of drug

content, *in-vitro*, and *ex-vivo* drug release was based on the calibration curve.

Formulation of Fast Dissolving sublingual film:

The sublingual films were formulated using the solvent casting method. (8,9) In this method, the polymers were soaked in water. The drug and other excipients were dissolved separately in water. All the solutions were mixed on a magnetic stirrer to which propylene glycol was added. The solution was then sonicated and cast into a film in a Petri plate and allowed to dry.

Evaluation of Fast Dissolving sublingual film:

Weight variation:

For weight variation three films of every formulation were taken weighed individually on digital balance (Wensar, PGB200 Mumbai) then the average weight was calculated with ± standard deviation.

Film thickness:

The thickness of each film was measured using a digital Vernier caliper (Mitutoyo, Japan) at different positions of the film and the average was calculated with ± standard deviation.

Surface pH:

The film is slightly wet with the help of water. The pH is measured by bringing the electrode in contact with the surface of the oral film. This study is performed on three films of each formulation and means ± standard deviation calculated.

Folding Endurance:

The folding endurance was determined by repeatedly folding one film at the same place till it broke. The number of times the film could be folded at the same place without breaking gives the value of the folding endurance.

Disintegration Test:

The disintegration time is the time when a film breaks or disintegrates. The film (2×2 cm) was placed in a glass Petri dish containing 10ml simulated salivary fluid. Slight agitation at

every 10 seconds interval was given. The time required for breaking of the film was noted as in vitro disintegration time.

Drug Content:

The percent drug content of Rizatriptan Benzoate in fast-dissolving films was estimated by a dissolving film of 2×2 cm and put in a volumetric flask containing 100 ml of simulated salivary fluid at pH 6.8. The samples were sonicated using ultrasonicator (Remi Equipments, Mumbai) for 15 min and the sample was filtered through Whatman filter paper (No. 41) analyzed using a UV spectrophotometer (1601, Shimadzu Corporation, Japan) and absorbances were taken. Experiments were carried out in triplicate for each sample and the results are presented as an average ± standard deviation.

***In-vitro* Dissolution Test:**

The in vitro dissolution test was performed using the USP II paddle-type apparatus. The dissolution studies carried out at 37 ± 0.50C; with stirring speed 50 rpm in 250ml simulated salivary fluid. The film size required for dose delivery was 2×2 cm. 5 ml aliquots of dissolution media collected at a specific time interval of 30, 60, 90, 120, 150, 180, 210, 240 seconds, up to 4 min, an equal volume of fresh dissolution medium was added. After each withdrawal sample was filtered through Whatman filter paper (No. 41) and analyzed for drug content using a UV spectrophotometer for cumulative percent drug release determined at 227 nm wavelength. Experiments were carried out in triplicate for each sample, and the results are presented as an average ± standard deviation.

Accelerated Stability Study of Optimized Batch:

In any rational design and evaluation of the dosage form for drugs, the stability of the active component must be major criteria in determining their acceptance or rejection. During the stability studies the product to expose to normal conditions of temperature and humidity however the studies will take a longer time and hence it would be convenient to carry out the accelerated stability studies where the product is stored under extreme conditions of temperature.

The optimized formulation was subjected to stability studies as per ICH guidelines. The sample was packed in aluminum foil. Then stored in stability chamber at 40ºC/75% RH for 1

month and evaluated for their disintegration time, drug content, drug release, mechanical properties at 15 days intervals of time and results were reported.(10–13)

RESULTS AND DISCUSSION

Characterization of Gum Pectin and Gum Carrageenan:

Identification and Standardization of Gum Carrageenan Polymer and Pectin:

Identification Test:

Identification tests for Gum Carrageenan were performed as per IP 1996 and results are reported in Tables 1 and 2.

Table No. 1: Identification of Gum Carrageenan

Sr. No.	Parameter	Gum Carrageenan	Standard as per IP 1996
1	Dissolving 100 mg in 20 water with heating, add 3 ml of barium chloride and 5 ml of HCl acid, dilute, filter and boil for 5 min	white crystalline precipitate form	white crystalline precipitate form

Table No. 2: Identification of Pectin

Sr. No.	Parameter	Pectin	Observation as per IP 1996
1	Heat the 1g of pectin with 9 ml water on a water bath	The stiff gel is formed	The stiff gel is formed
2	To a 1% solution of pectin add an equal volume of ethanol	Translucent gelatinous precipitate form	Translucent gelatinous precipitate form
3	5ml of 1% pectin solution + add 1 ml of 2% w/v sol of KOH + set at room temperature For 15 min acidify gel with dilute HCl & boil	Transparent gel or semi gel form	Transparent gel or semi gel form

Standardization of Gum Carrageenan and Pectin as per 1996:

The standardization of polymer was carried out by determining % Ash value, Acid Insoluble Ash, Loss on drying. The results are shown in Table 3.

Table No. 3: Standardization of Gum Carrageenan & Pectin

Sr. No.	Parameter	Gum Carrageenan	Standard value	Pectin	Standard value
1	% Ash value	14.35±0.1	NMT 15%	3.4±0.2	NMT < 4%
2	Acid insoluble ash	0.67±0.033	NMT 1%	0.26±0.05	NMT 0.4 %
3	Loss on drying	8.39±0.046	NMT 12%	6.33±1.52	NMT 10%

Data represented as ± Standard Deviation (n=3)

Percent Ash Value:

The Ash value of Gum Carrageenan and pectin was found to be 14.35 ± 0.1 and 3.4 ± 0.2 respectively.

Acid Insoluble Ash:

The Acid insoluble ash of Gum Carrageenan and pectin was found to be 0.67 ± 0.033 and 0.26 ± 0.05 respectively.

Loss on Drying:

Loss on drying was found to be of Gum Carrageenan and pectin was found to be 8.39 ± 0.046 and 6.33 ± 1.52 respectively.

Physical Evaluation of Gum Carrageenan and Pectin:

Organoleptic Properties:

The organoleptic properties of Gum Carrageenan and pectin were analyzed. Results were reported in table 4.

Table No. 4: Organoleptic Properties of Gum Carrageenan and Pectin

Sr. No.	Parameter	Gum Carrageenan	Pectin
1	Color	Yellowish white	Yellowish white
2	Odor	Odorless	Odorless
3	Texture	Coarse	Coarse
4	Shape	Amorphous	Amorphous
5	Touch	Hard	Hard

Solubility:

Solubility studies of Gum Carrageenan and pectin were carried out in various solvents and results are as follows in table 5.

Table No. 5: Solubility of Gum Carrageenan and Pectin in various solvents

Sr. No.	Solvents	Gum Carrageenan	Pectin
1	Hot and cold water	Colloidal solution	Colloidal solution
2	The organic solvent (methanol, ethanol, chloroform, benzene)	Insoluble	Insoluble

Both polymers having a solubility in hot and cold water forming a colloidal solution while it is insoluble in organic solvents such as ethanol, methanol, acetone, isopropyl alcohol, benzene, chloroform, and ether.

Determination of Swelling Index:

The swelling index of Gum Carrageenan was found to be and that of pectin was found to be 6.76 ± 0.25. The results are shown in Table 6.

Determination of pH:

The pH of Gum Carrageenan (1%w/v) was found to be 7.3 ± 0.12. The pH of pectin (1%w/v) was found to be 3.7 ± 0.25 showing that it is slightly acidic as shown in table 6.

Table No. 6: Characterization Parameters of Gum Carrageenan and Pectin

Sr. No.	Parameter	Gum Carrageenan	Pectin
1	Swelling Index	3.2±0.13	6.76±0.25
2	pH	7.3±0.12	3.7±0.25

Data represented as ± Standard Deviation (n=3)

Micromeretic Evaluation:

The preformulation studies *Gum Carrageenan* and pectin were carried out and results were reported in table 7.

Table No. 7: Micromeretic Evaluation of Gum Carrageenan and Pectin

Sr. No.	Parameter	Gum Carrageenan	Pectin
1	The angle of Repose (◦)	23.33±0.46	28.56±1.42
2	Bulk Density (g/cm^3)	0.62±0.02	0.53±0.015
3	Tapped Density (g/cm^3)	0.80±0.013	0.75±0.025
4	% Compressibility	22.45±0.045	19.16±1.04
5	Hausner's Ratio	1.28±0.2	0.75±0.025

Data represented as ± Standard Deviation (n=3)

Drug Excipient Compatibility Study:

Fourier Transform Infrared (FT-IR):

The FT-IR spectrum was measured in the solid-state as potassium bromide dispersion.

FTIR of Rizatriptan Benzoate:

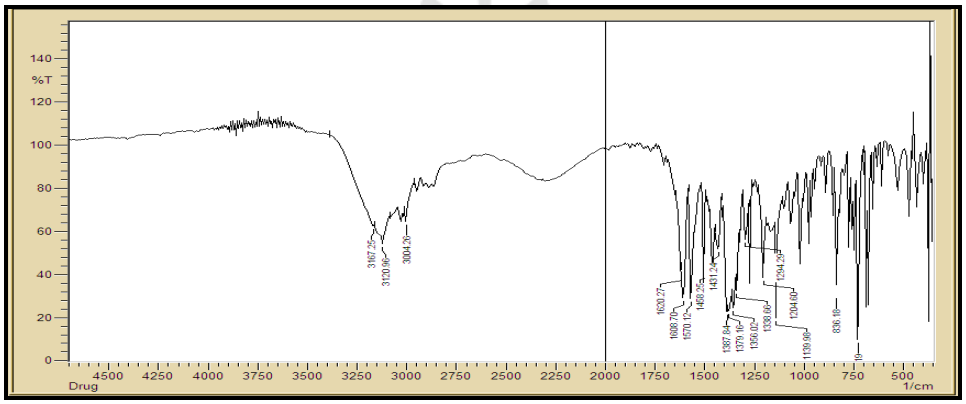

Figure No. 1: FTIR of Rizatriptan Benzoate

FTIR of Gum Carrageenan:

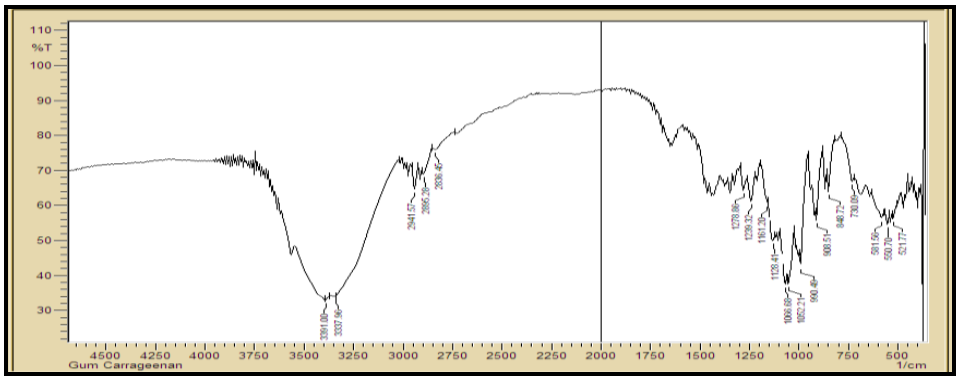

Figure No. 2: FTIR of Gum Carrageenan

FTIR of Pectin:

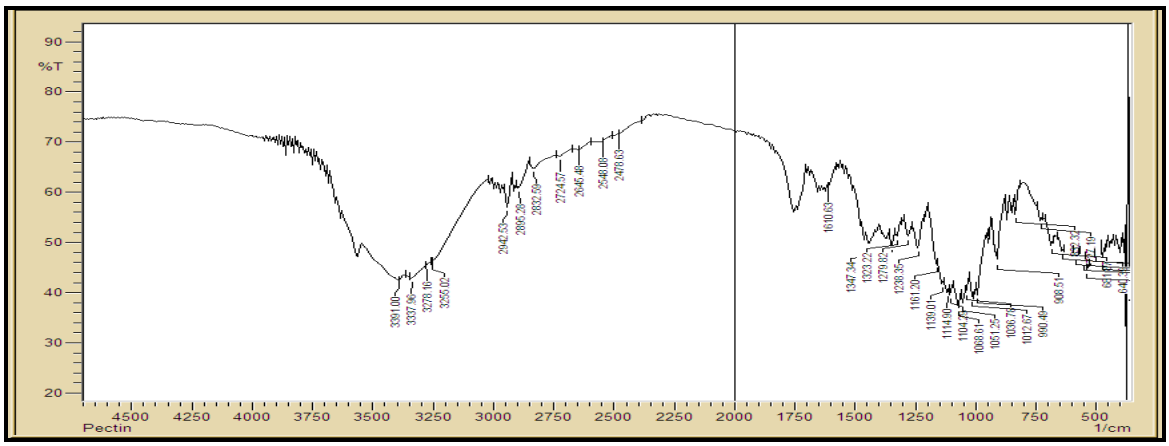

Figure No. 3: FTIR of Pectin

FTIR of Rizatriptan Benzoate, Gum Carrageenan, and Pectin:

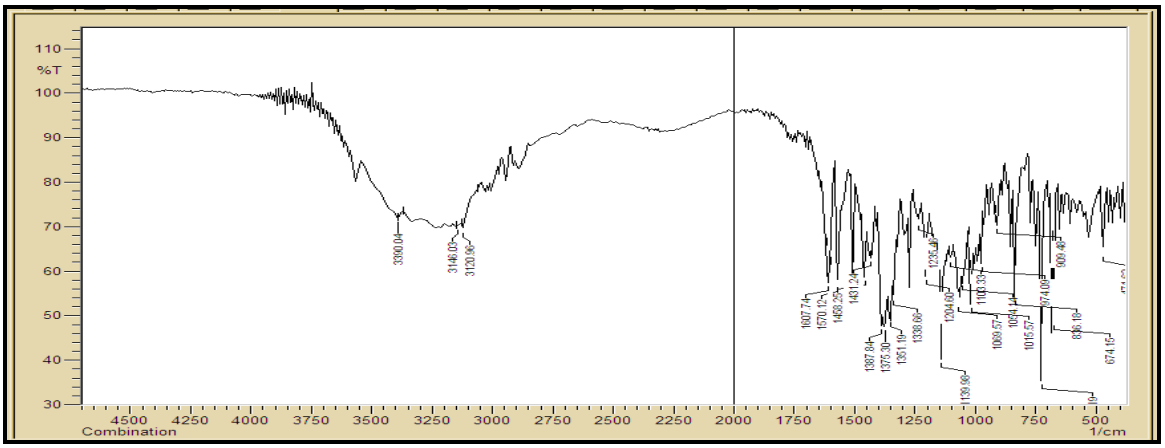

Figure No. 4: FTIR of Rizatriptan Benzoate, Gum Carrageenan, and pectin

FTIR spectroscopy was employed to ascertain the compatibility of Rizatriptan Benzoate with polymers. The individual drug, polymer, and combination of drugs and polymers were separately scanned. From the above FTIR graphs, it can be depicted that FTIR of Rizatriptan shows a peak at 3120.78 indicating C-H stretching (aromatic). The peak at 3058.27 indicates =C-H stretching (alkenes). Peaks at 827.50-633.64 indicated C-Cl stretch (alkyl halide). The peak at 1324-1260 indicates C-N stretching (aromatic amine). FTIR of Gum Carrageenan shows a peak at 3391.97 indicating the presence of OH (alcohols and phenols) i.e. OH stretch. The peak at 3326.39-3326.99 indicates the acetylene group, while the peak at 3031.26-2843.20 indicates OH stretch in a carboxylic acid. FTIR of pectin shows a peak at 3565.57-3243.44 indicating OH stretching (H-bonded alcohols, phenols). Also, it indicates OH stretching (carboxylic acid). Peaks at 909.48-681.47 indicate C-H (aromatic) group. FTIR of a combination of Rizatriptan Benzoate and polymers i.e. Gum Carrageenan and pectin shows no significant variation in height, intensity, and position of peaks, suggesting that the drug and polymers were compatible. There is no interaction between drug and polymer.

Differential Scanning Calorimetry (DSC):

Differential Scanning Calorimetry was performed for the compatibility study of drug and polymer at different temperatures.

DSC of Rizatriptan Benzoate:

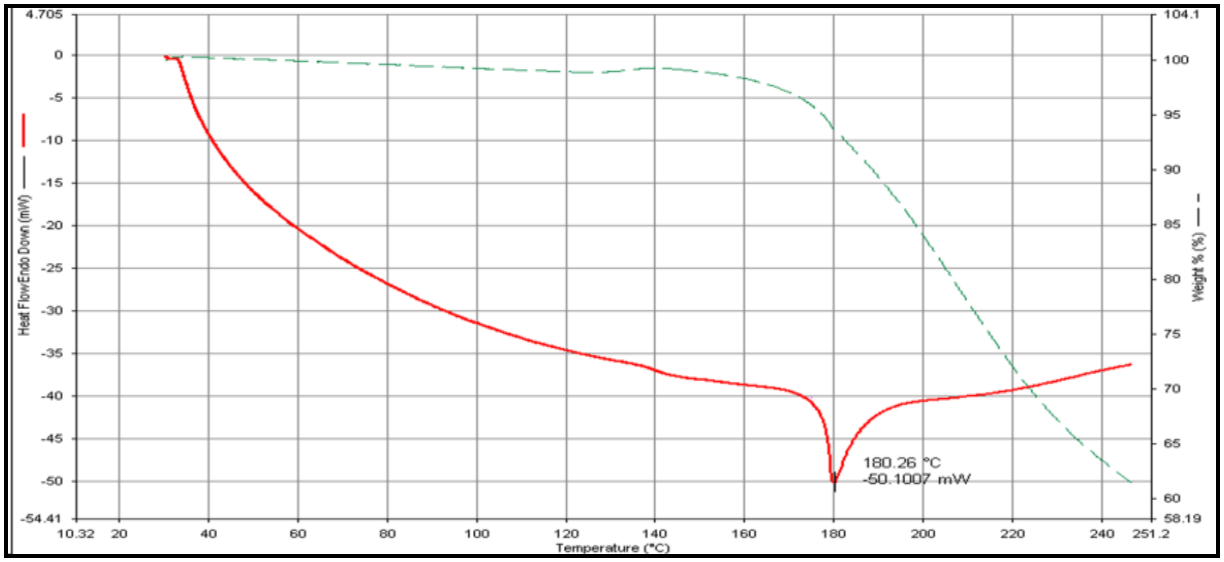

Figure No. 5: DSC of Rizatriptan Benzoate

DSC of Gum Carrageenan:

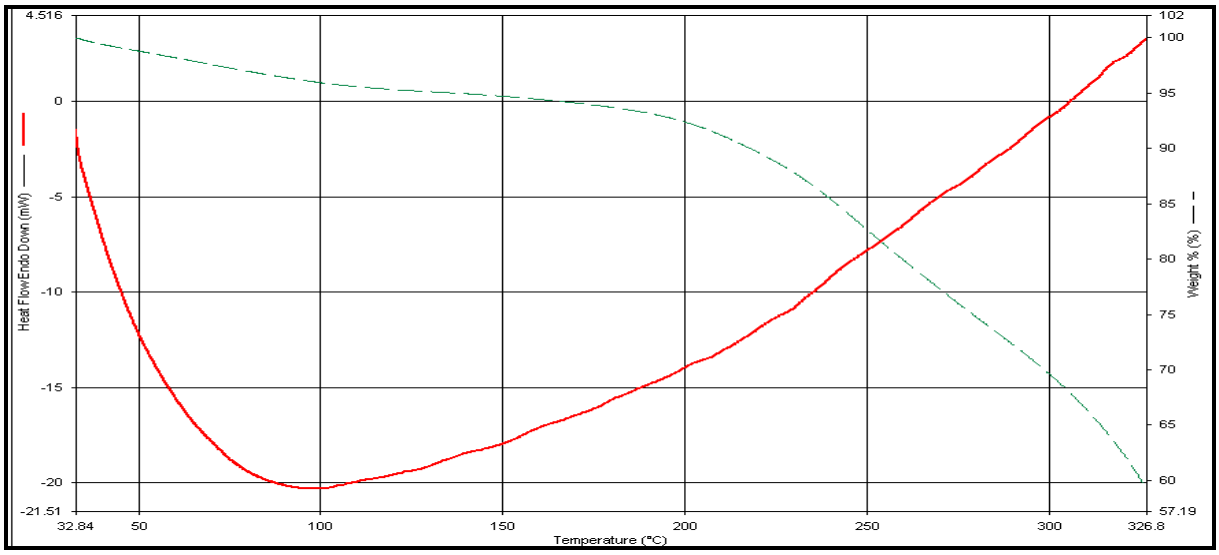

Figure No. 6: DSC of Gum Carrageenan

DSC of Pectin:

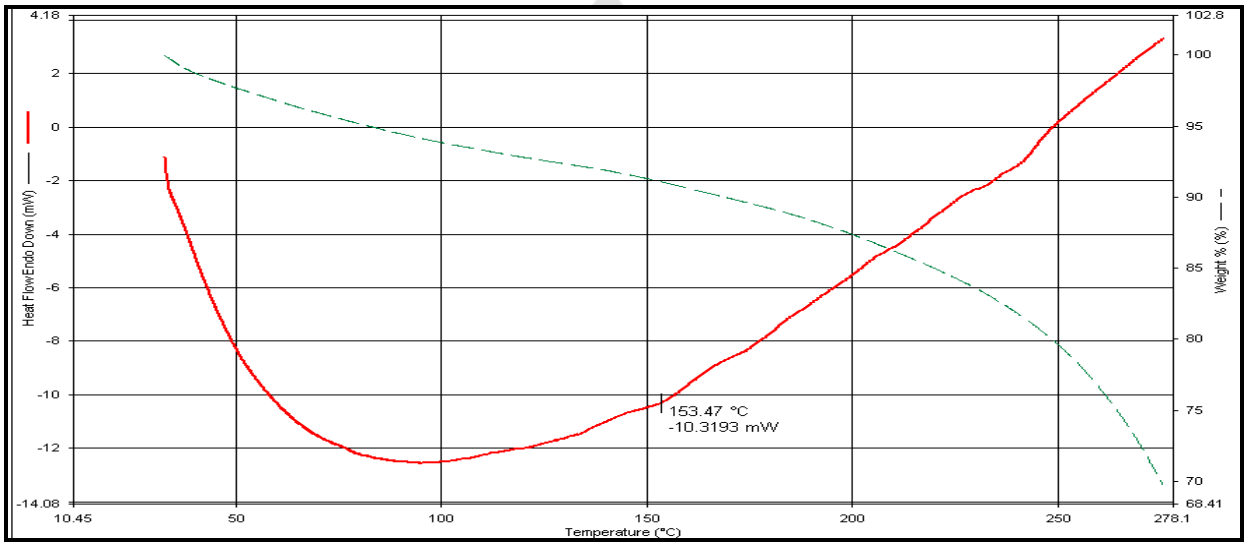

Figure No. 7: DSC of Pectin

DSC of Rizatriptan Benzoate, Gum Carrageenan and Pectin:

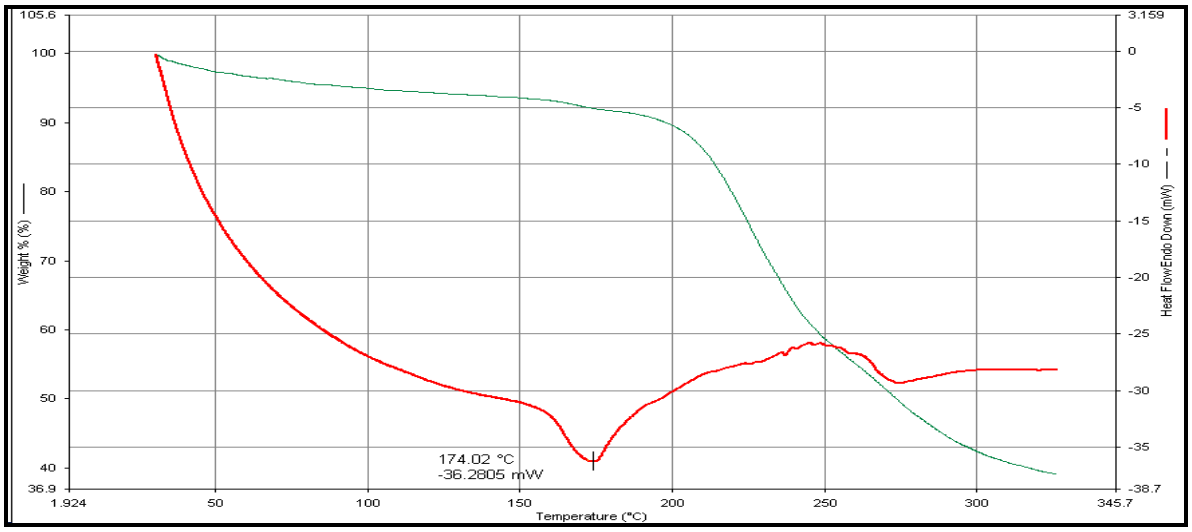

Figure No. 8: DSC of Rizatriptan Benzoate, Gum Carrageenan, and Pectin

DSC thermogram of Rizatriptan Benzoate shows a sharp endothermic peak at 180.26°C, indicating the melting point of the stable crystalline drug. However, the DSC thermograms of a combination of Rizatriptan Benzoate, Gum Carrageenan, and pectin show a sharp endothermic peak at 174.02°C. The thermogram shows no significant change in the peak shape, area, and no shift of peak was found. Therefore, this study revealed that there was no interaction between the drug and the pectin.

Calibration Curve of Rizatriptan Benzoate:

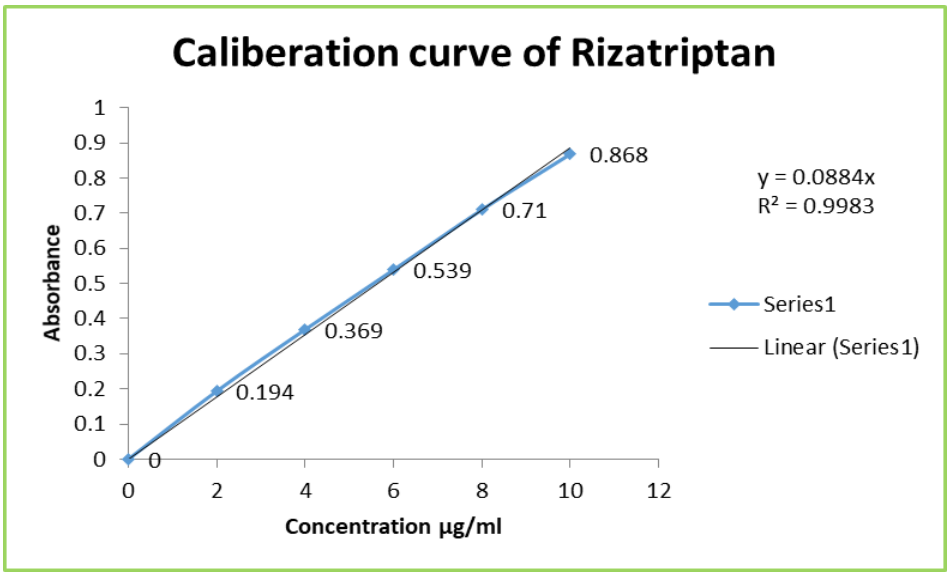

Figure No. 9: Standard calibration curve of Rizatriptan Benzoate in salivary fluid

Formulation of Fast Dissolving sublingual film:

Various formulations of the film were prepared with different ratios of Gum Carrageenan and pectin as given in table 8.

Table No. 8: Formulation of film

Code	Rizatriptan Benzoate (mg)	Gum Carrageenan (mg)	Pectin	Cross Carmallose (mg)	Mannitol (mg)	Citric acid (mg)	M.Para (mg)	PEG (ml)	Water
A_1	5	100	100	20	80	25	10	0.2	10
A_2	5	100	100	50	80	25	10	0.2	10
A_3	5	100	100	70	80	25	10	0.2	10
A_4	5	100	200	20	80	25	10	0.2	10
A_5	5	100	200	50	80	25	10	0.2	10
A_6	5	100	200	70	80	25	10	0.2	10
A_7	5	100	300	20	80	25	10	0.2	10
A_8	5	100	300	50	80	25	10	0.2	10
A_9	5	100	300	70	80	25	10	0.2	10

EVALUATION OF FAST DISSOLVING SUBLINGUAL FILM:

Formulation A

The fast-dissolving film formulated using gum carrageenan and pectin were evaluated for thickness (mm), weight variation (g), disintegration time (sec), drug content (%), surface pH, and folding endurance.

Table No. 9: Evaluation of Formulation

Code	Thickness (mm)	Weight variation (g)	Disintegration time (sec)	Drug content	Surface pH	Folding endurance
A_1	0.11±0.01	0.071±0.01	32±0.85	94.93±1.45	6.66±0.10	308±17
A_2	0.13±0.02	0.065±0.56	38±0.75	95.72±0.81	6.63±0.05	302±75
A_3	0.13 ± 0.02	0.063±0.25	40±0.89	96.06±0.37	6.66±0.10	272±9.2
A_4	0.10±0.01	0.066±0.02	26±0.20	98.01±0.06	6.63±0.15	412±20.3
A_5	0.15±0.02	0.061±0.03	50±0.52	97.5±0.03	6.67±0.06	252±15.5
A_6	0.14±0.03	0.062±0.04	58±0.05	96.01±0.08	6.67±0.05	368±9.25
A_7	0.16±0.04	0.059±0.02	45±0.06	96.06±0.08	6.60±0.06	345±14
A_8	0.12±0.08	0.050±0.31	93±0.07	93.6±0.08	6.66±0.061	282±19
A_9	0.14±0.05	0.052±0.25	89±0.07	94.8±0.07	6.64±0.061	278±10

Data represented as ± Standard Deviation (n=3)

***In-vitro* Drug Release of formulation batches:**

In-vitro drug release study for batches A_1, A_2, A_3, A_4, A_5, A_6, A_7, A_8 have been performed and results are shown in figure 10.

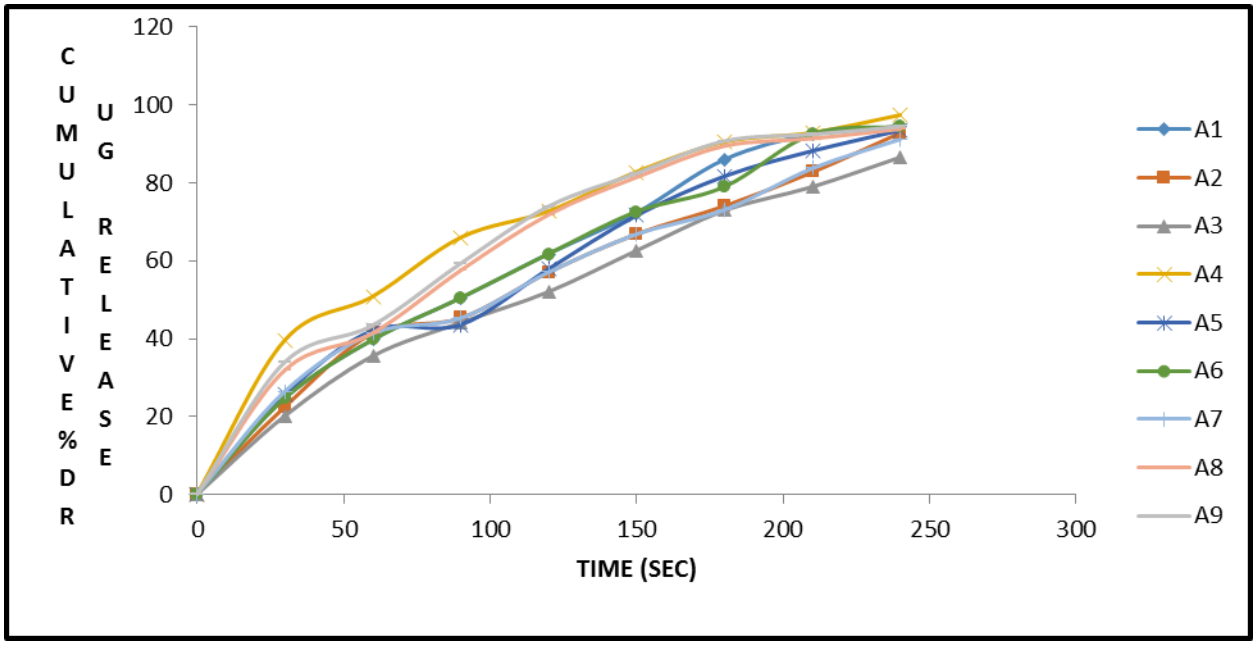

Figure No. 10: *In-vitro* Drug Release of Formulation A Batches

From the above data it can be indicated that, amongst all these batches, A_4 batch with Gum Carrageenan and pectin was found to have weight variation (0.066±0.02), thickness (0.10±0.01mm), swelling index (42.52±0.17%), folding endurance (412±20.3), surface pH (6.63±0.15), drug content (98.01±0.06), disintegration time (26±0.20 sec), *in-vitro* dissolution % drug release (97.3±0.28).

On this basis, formulation A_4 is optimized and compared with the marketed formulation and the results are given in figure no. Also, the accelerated stability studies of the same formulation were carried out and the results are shown in Table 10.

Comparative Dissolution Study of Optimized Fast Dissolving Film and Marketed Tablet:

Comparative study of % drug release in optimized batch A_4 and marketed sublingual tablet of Rizatriptan. Rizact 5 SL is been performed at salivary pH 6.8.

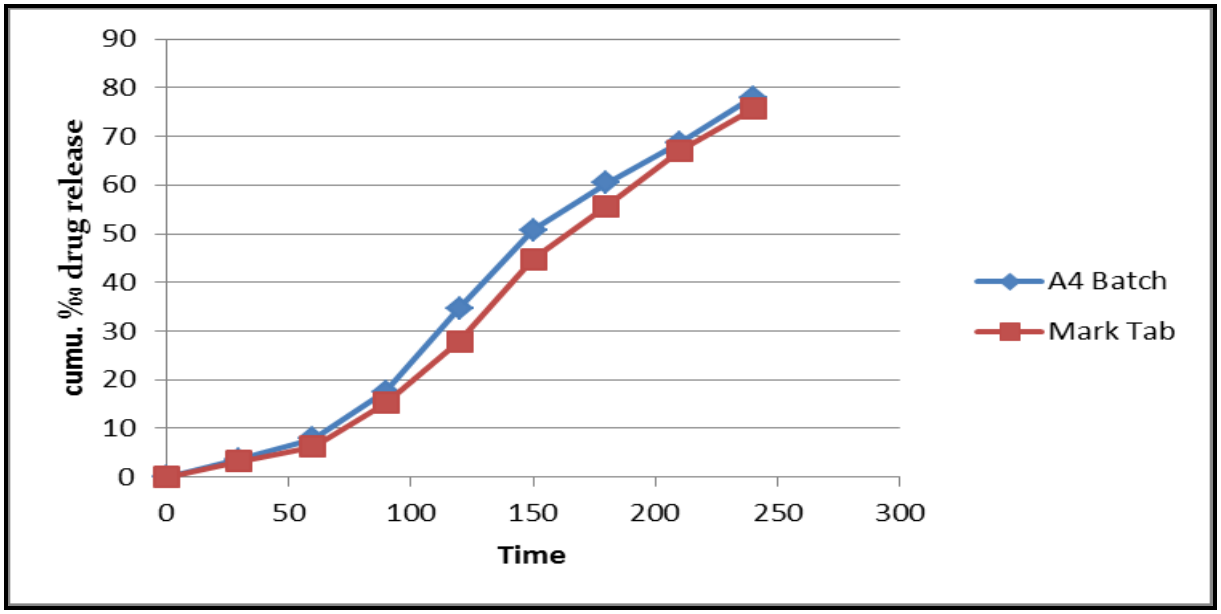

Figure No. 11: Comparative Dissolution Study of Optimized A_4 batch and Marketed Tablet

Accelerated Stability Studies of Optimized Formulation:

The accelerated stability studies of the optimized formulation A_4 was carried out and the results are shown in Table 10.

Table No. 10: Accelerated Stability Testing of Optimized Formulation A_4 (40ºC/75% RH)

Parameters	0 day	15 days	30 Days
Weight variation	0.066±0.02	0.067± 0.85	0.067±0.85
Thickness	0.10±0.010mm	0.10±0.01mm	0.11±0.05mm
Disintegration time	26±0.2sec	26.±0.2 sec	27.0±0.75
Drug content	98.01±0.06	98.01±0.01	97±0.075
% drug release	97.3±0.28	98. 06±0.015	97.3± 0.06
Folding endurance	412±20.3	410±0.02	410±0.02
pH	6.63±0.15	6.64± 0.02	6.64±0.02

Data represented ± Standard Deviation (n=3)

CONCLUSION

Rizatriptan Benzoate a BCS class III drug with metallic taste could be successfully incorporated into the fast-dissolving sublingual film. Optimized formulation passed all evaluation tests with faster disintegration time and subsequent % drug release and scored better compliance and convenience with the marketed sublingual tablets of Rizatriptan Benzoate. It could be concluded that suitable packaging and storage conditions would be essential for the fast dissolving film of Rizatriptan Benzoate. The in-vitro of films confirmed their potential as innovative dosage forms to improve the delivery of Rizatriptan Benzoate.

ACKNOWLEDGMENTS

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REFERENCES

1. Galgatte U, Khanchandan S, Jadhav Y, Chaudhari P. Investigation of different polymers, plasticizers, and super disintegrating agents alone and in combination for use in the formulation of fast dissolving oral films. Int J

PharmTech Res. 2013;5(4):1465–72.
2. Asija R, Sharma M, Gupta A, Bhatt S. Orodispersible Film: A novel approach for patient compliance. Int J Med Pharm Res. 2013;1:386–92.
3. Jani R, Patel D. Hot melt extrusion: An industrially feasible approach for casting orodispersible film. Asian J Pharm Sci. 2015;10(4):292–305.
4. Siddiqui N, Garg G, Sharma PK. Fast dissolving tablets: Preparation, characterization and evaluation: An overview. Int J Pharm Sci Rev Res. 2010;4(2):87–96.
5. Patel R, Naik S, Patel J, Baria A. Formulation development and evaluation of mouth melting film of ondansetron. Arch Pharm Sci Res. 2009;1(2):212–7.
6. Vidyadhara S, Balakrishna T, Sasidhar RLC, Babu CS, Harika DL. Formulation and evaluation of zolmitriptan fast dissolving buccal films. Sch Res Libr. 2013;5(4):145–52.
7. Pandey P, Chauhan S. Fast dissolving sublingual films of Zolmitriptan: A novel treatment approach for migraine attacks. Indian J Pharm Educ Res. 2014;48:67–72.
8. Necas J, Bartosikova L. Carrageenan: a review. Vet Med (Praha). 2013;58(4).
9. Kianfar F, Antonijevic MD, Chowdhry BZ, Boateng JS. Formulation development of a carrageenan based delivery system for buccal drug delivery using ibuprofen as a model drug. J Biomater Nanobiotechnol. 2011;2(05A):582–95.
10. Upadhye K, Senpal D, Nimbalwar M, Dixit G, Bhoyar V. Formulation and Evaluation of Fish Oil-based Rizatriptan Microemulsion for Intranasal Migraine Treatment.
11. Chaudhary SA, Mehta TA, Chaudhary AB. Formulation, development and evaluation of fast disintegrating tablets of rizatriptan benzoate using novel adjuvants. Int J Chem Tech Res. 2010;2(2):1026–30.
12. Satyanarayana T, Krishna JM, Kumar PS, Krishnan SN, Shaji G. Formulation and evaluation of rizatriptan benzoate orodispersible tablets. Sch Res Libr. 2011;3(6):125–30.
13. Mothilal M, Kota S, Babu SG, Kumar G, Manimaran V, Damodharan N. Formulation and Evaluation of Rizatriptan Benzoate Orally Disintegrating Tablets. Int J Drug Dev Res. 2012;4(2):117–23.