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FORMULATION AND EVALUATION OF FAST DISSOLVING BUCCUAL FILM OF SUMATRIPTANT SUCCINATE

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ABSTRACT
Current research is focused on formulation and evaluation of fast dissolving buccal film of sumatriptant succinate used for treatment of migraine. The design of developing drug delivery system is to provide patient with more convenient means of drug administration and maximum drug dissolution in oral cavity to by passing the first metabolism, to increase the convention. The delivery system consist of the oral film, which is simply placed on the patient tongue and any oral mucousal tissue (buccal / sublingual). The film following polymer HPMC E15 used of film forming. The film evaluated for disintregration, dissolution, tensile streght, thickness, folding endurance and elastic modules. Following single subcutaneous or oral dosage of drug in healthy individuals, the terminal estimation half-life of drug is 1.5-2.6 hours.

KEYWORDS: Fast dissolving buccal film sumatriptant succinate, HPMC E15,propylen glycol, methanol, bioavaibility enhancement.

INTRODUCTION
Among the different routes, the most agreeable route for the patients is oral route. Most of the pharmaceutical companies have directed their research activity in developing viable dosage alternatives from oral route for pediatrics, geriatric, noncompliant or nauseous patients. Research in the oral drug delivery segment has led to evolution of dosage forms from simple conventional tablets and capsules to modified release tablets and capsules to oral disintegrating tablet to wafer to the recent development of fast dissolving oral films.[1]

Fast dissolving oral film and fast dissolving buccal films, a novel drug delivery system for the oral delivery of the drugs is an ultra-thin film prepared.

The delivery system consists of a very thin oral strip, which is simply placed on the patient's tongue or any oral mucosal tissue, instantly wet by saliva the film rapidly hydrates and adheres onto the site of application. It then rapidly disintegrates in a matter of seconds and dissolves to release medication for oromucosal absorption.

Oral dissolving films design permits to incorporate a variety of drugs for their pharmacological effects e.g. anti-tussive, anti-epileptic, anti-asthmatic, expectorant, etc. High temperature and moisture sensitivity necessitating expensive packaging and inability of high dose loading are some disadvantages of Oral dissolving films.[2]

Advantages and Disadvantage
Fast dissolving oral film being an advanced evolution of fast dissolving drug delivery system over conventional dosage forms and orally disintegrating tablets.[3]

Formulation ingredients
Drug, polymer, pasticizers, surfactant, sweeting agent, saliva stimulating agent, flavoring agent, coloring agent used of formulation.[4,8]

Evaluation Tests
Thickness
Thickness of film is directly concern it can measured by micrometer screw gauge or calibrated digital vernier calipers at different strategic location.[9]

Dryness test and tack tests
About eight stages of film drying process have been identified and they are set-to-touch, dust-free, tack-free (surface dry), Dry-to touch, dry-hard, dry-through (dry-to-handle), dry-to-recoat and dry print-free.[10]

Folding endurance
The number of folds i.e. how many times the film being folded at same place that required to disrupt the film sample or developing a noticeable cracks, this is known

as folding endurance. This term provide an indication of film brittleness, that a strip has been subjected to this test through film folding at same point repeatedly for many times until a noticeable crack was detected, the values are stated.[11]

Assay and Content uniformity

This is determined by any standard assay method described for the particular API in any of the standard pharmacopoeia. Content uniformity is determined by estimating the API content in individual strip. Limit of content uniformity is 85–115 percent and more stringent limit is 95.0% to 105.0%.[13,14]

Dissolution test

Dissolution testing can be performed using the standard basket or paddle apparatus described in any of the pharmacopoeia. Many times the dissolution test can be difficult due to tendency of the strip to float onto the dissolution medium when the paddle apparatus is employed. Migraine is a chronic, episodic, neurological disorder, which usually begins in childhood, adolescence or early adult life, characterized by unilateral headache often accompanied by nausea and vomiting.[12]

MATERIAL AND METHOD

The polymer was dissolved in purified water accurately weighted and transfer the stated amount as per above formulation table, the HPMC E15 in glass beaker and was dissolve properly with continuous stirring use magnetic stirrer if require to dissolve properly. Dissolute the API and other processing ingredients in purified water weight accurately and transfer the stated amount as per above formulation table, the Sumatriptan in glass beaker add the weighted amount of other remaining ingredients to it and dissolve properly with continuous stirring. Mix the above two solutions to form a thick mass mix the above two portion of solutions with continuous stirring to form a thick mass than can be rolled to from a strips. Rolling to form a thin film: taking the above thick mass and rolled on the glass slide to form a thin film of that mass. Cutting of films in required sizes: Cut the thin film so obtained into the suitable size and shape by using surgical blade and scale. Optimization of formulation: same procedure is followed for all the formulations F1 to F9 and the formulation with all the acceptable properties and parameters to be selected table.1

Table 1: Formula for optimization of oral dissolving buccal film.

Formulations	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Polymer conc. % (By Weight)	**20%**	**25%**	**30%**	**35%**	**40%**	**45%**	**50%**	**55%**	**60%**
Sumatriptan Succinate(mg)	25	25	25	25	25	25	25	25	25
HPMC E15(mg)	8	10	12	14	16	18	20	22	24
Glycerin(mg)	10.7	9.8	8.7	7.7	6.7	5.7	4.7	3.55	2.55
PEG 400(mg)	10.3	9.2	8.3	7.3	6.3	5.3	4.3	3.45	2.45
Menthol(ml)	0.2	0.2l	0.2	0.2	0.2	0.2	0.2	0.2	0.2
citric acid(mg)	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8	1.8
Aspertame(mg)	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Sodium Starch Glycolate(mg)	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5	3.5
Purified water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.
Total weight per strip	60	60	60	60	60	60	60	60	60

The final weight of strips = 60.00 mg
Dimensions (L X W) = 250mm X 200 mm

Evaluation of formulation

Organoleptic evaluation

For evaluation of psychophysical evaluation of the product, special controlled human taste panels are used. In-vitro methoral dissolving strips of utilizing taste sensors, specially designed apparatus and drug release by modified pharmacopoeia methoral dissolving strips are being used for this purpose. These in-vitro taste assessment apparatus and methodologies are well suited for high-throughput taste screening of oral pharmaceutical formulations.

Drug content

The drug content in the strip was calculated by UV spectrophotometer at the Lambda max. of 227nm. The standard and sample solutions of sumatriptan succinate was prepared as per the following method and the absorbance was taken.

Standard solution of drugcontent

Weigh and dissolved 100 mg of Sumatriptan Succinate accurately in small amount of acetonitrile in 100 ml volumetric flask and then the volume is to be adjusted with acetonitrile resultant solution gives the concentration of 1mg/ml ie.1000 µg/ml (stock –I solution). From there pipette out 10 ml solution and then

diluted up to 100 ml with same solvent in a volumetric flask and then the concentration of this stock was 100µg/ml (II stock solution). Further pipette out 5 in 50 ml of volumetric flask and diluted to volume with acetonitrile. Further pipetted out 5 in 25 ml of volumetric flask and diluted to volume with acetonitrile.

Determination of absorbance maxima □□max)

The stock solution was further diluted this solution was then scanned at wavelength of 200 to 400 nm against blank. The wavelength of maximum absorbance was found at 227nm which is used for preparation of calibration curve

Sample solution

Weighed and transferred accurately 4 strips Equivalent to 100 mg of Sumatriptan Succinate transfer in 100 mL of volumetric flask. Added about 70 mL of acetonitrile shaken for 15 minute and diluted to volume with acetonitrile Pipetted out 10.0 mL of resulting solution in 100 mL volumetric flask, diluted to volume with acetonitrile (100 µg/mL).). Further pipette out 5 in 50 ml of volumetric flask and diluted to volume with acetonitrile. Further pipette out 5 in 25 ml of volumetric flask and diluted to volume with acetonitrile.

Calibration curve for standard

The standard solution was diluted serially to get the concentrations 2, 4,6,8,10,12,14,16,18, and 20 respectively. The absorbance of these solutions was measured at 227 nm. The standard calibration curve was obtained for data of concentration v/s absorbance. The results are depicted in the below table.

Calibration curve

Sumatriptan Succinate (100mg) of was accurately weighed and dissolved in small amount of acetonitrile in 100 ml volumetric flask and then the volume was adjusted with acetonitrile, the resultant solution gives the concentration of 1mg/ml ie.1000 µg/ml (stock –I solution). From this 10 ml solution was taken and then diluted up to 100 ml with the same solvent in a volumetric flask and then the concentration of this stock will be 100µg/ml (II stock solution). From this II stock solution, 2, 4,6,8,10,12,14,16,18,and 20 ml solutions were pipetted and volume was made to 100 ml using acetonitrile as a solvent to get concentrations 2,4,6,8,10,12,14,16,18,and 20 respectively. The absorbance of these solutions was measured at 227 nm. The standard calibration curve was obtained for data of concentration v/s absorbance.

pH

Prepared 1% solution of strips and determined the pH using pH meter.

Disintegration time

The single strip was hold in 100 mL of water and recorded the time required to disintegrate the strip.

Thickness

Determined the thickness of 5 units by Screw Gauge and Digital Micrometer

Dryness test and tack tests

Strips should not adhere to each other or to an accessory if it can be remove easily from each other. The test was performed by taking 5 strips together.

Tensile strength

Tensile strength is the maximum stress applied to a point at which the strip specimen breaks. It is calculated by the applied load at rupture divided by the cross-sectional area of the strip as given in the equation below:

$$TensileStrength = \text{Load at breakage/Strip thickness} \times \text{Strip Width}$$

Folding endurance

Folding endurance is determined by repeated folding of the strip at the same place till the strip breaks. The number of times the film is folded without breaking is computed as the folding endurance value.

RESULT & DISCUSSION

FTIR sumatriptant succinate

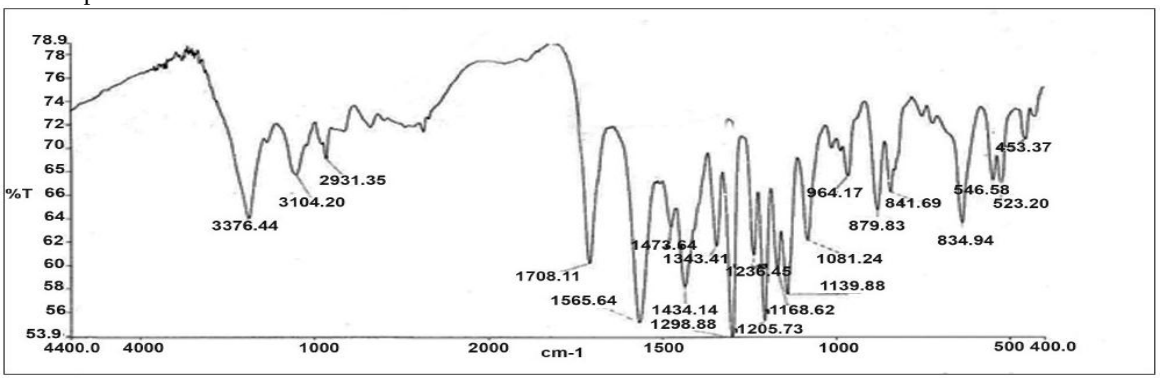
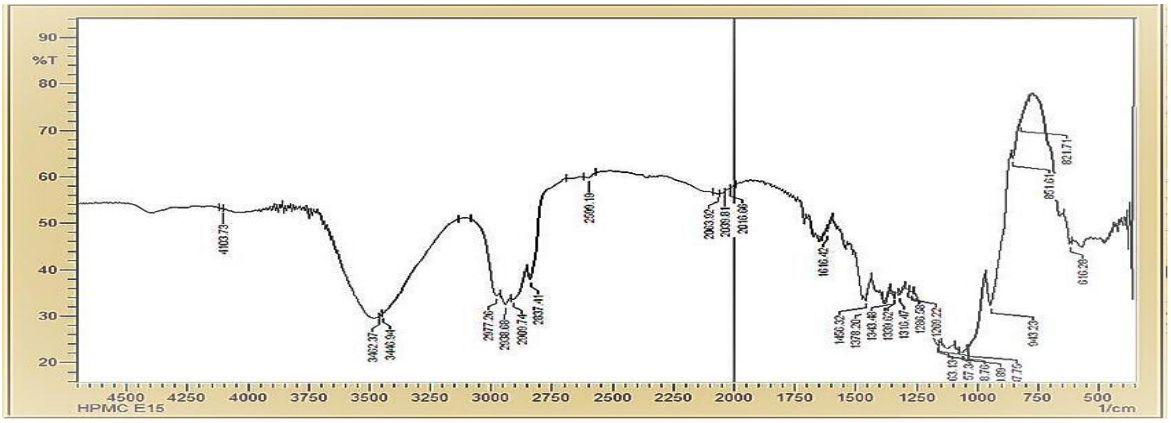


Fig 1. FTIR Spectrum of Sumatriptan Succinate. HPMC E15



HPMC E15
Fig 2. FTIR spectra of HPMC.

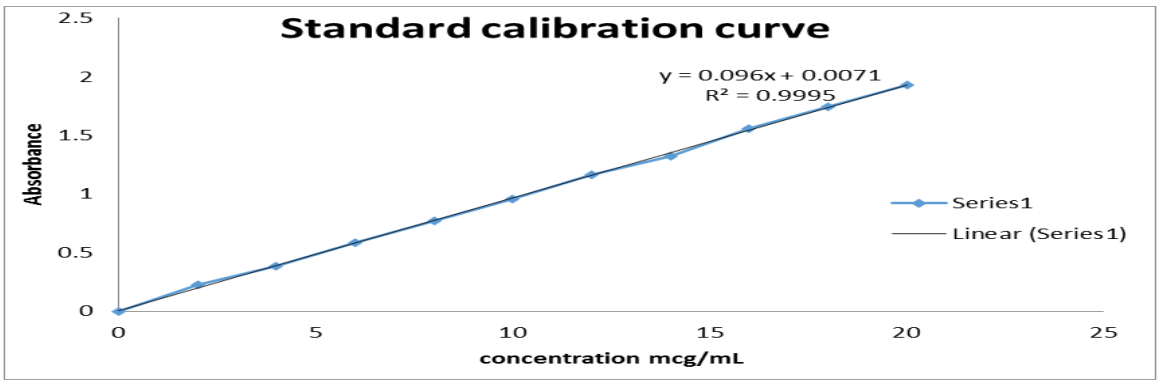


Figure 3: Standard Calibration Curve.

Table 2: Calibration curve for Standard and.

Sr. No	Concentration (µg/ml)	Absorbance at 227nm
1	0	0
2	2	0.226
3	4	0.386
4	6	0.581
5	8	0.768
6	10	0.958
7	12	1.165
8	14	1.326
9	16	1.555

From the above results it can be seen that the % content of formulations F1 to F5 are on lower side considering the acceptance criteria for % assay 95 % to 105%. Hence these formulations cannot be considered suitable. From the remaining formulations F6 shows the results on Lower side and F9 shows on higher side results.

The results of formulations F7 and F 8 are well within the limit i.e. **98.1% and 100. 5 %.** So these formulations are to be considered suitable for further study.

Table 3: Absorbance and results of samples.

Formulations	Absorbance	% Content
F1	0.196	92.4
F2	0.200	94.3
F3	0.196	92.4
F4	0.183	86.3
F5	0.189	89.1
F6	0.203	95.7
F7	0.208	98.1
F8	0.213	100.5
F9	0.219	103.3

Table 4: The formulations are given in the following table.

Formulations	Ph	Disintegration time (seconds)	Thickness (mm)	Tack test	Folding endurance test
F1	6.2	16	0.079	Does not Complies	Complies
F2	6.5	15	0.086	Does not Complies	Complies
F3	7.3	11	0.092	Does not Complies	Complies
F4	6.9	09	0.076	Does not Complies	Complies
F5	7.1	12	0.065	Does not Complies	Complies
F6	6.8	09	0.067	Does not Complies	Complies
F7	6.5	10	0.080	Complies	Complies
F8	6.9	12	0.069	Complies	Complies
F9	6.3	08	0.075	Complies	Complies

From the above table it is seen that due to the presence of high concentrations of plasticizer, the strips are adhered to each other which are difficult to separate. The right concentration of plasticizer gives the tack test positive. So the formulations **F7, F8 and F9** shows tack test and folding endurance test positive. So these formulations are to be considered for further study.

In the present study, the fast dissolving buccal films of Sumatriptan succinate 25 mg was prepared by rolling method using HPMC E-15 as a film forming polymer, PEG 400 and Glycerine as a plasticizer, Sodium starch glycolate as a super-disintegrant. Other formulation ingredients are also used in the formulation. Total nine formulations (F1 to F9) were prepared by rolling method. The strategy for formulation development was to optimize the concentration of polymer HPMC E15 at which all the evaluation parameters and percent drug content would be in limit.

The nine formulations were prepared keeping the weight of strip to 60 mg and the concentrations of HPMC E-15 was taken from 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55% and 60%, the weights of strips adjusted with plasticizer concentration.

The stripes was evaluated for various parameters like color, size& shape, % drug content, pH, disintegration time, thickness, tack test and folding endurance test.

All the strips were colorless and rectangular in shape, based on % drug content the formulations F1, F2, F3, F4, and F5 failed in the test, so the formulations F6, F7, F8 and F9 were to be taken into consideration. Among these four formulations F6 show lower results and F9 show results on higher side. So, the formulations F7 and F9 were taken as optimize formulations in this study.

All the formulations passed the pH, DT and thickness folding endurance test. The tack test passed by only F7, F8 & F9, this might be due to the optimize level of plasticizer and polymer.

From the present study, it is concluded that the optimum level of polymer in the fast dissolving buccal film and orally disintegrating strip formulation should be as high as 50%-60% to pass all the tests and drug content too.

CONCLUSION

Oral drug delivery is considered to be an important alternative to the pre-oral route for the systemic administration of drugs, as it considered the most convenient, east, safest route of administration. Oral mucosa has rich vasculization, offers better permeability to many drugs and it act as an excellent site for the absorption of drugs. Fast dissolving oral thin film is used as a novel approach, as it dissolve rapidly in mouthand directly reaches to the systemic circulation.

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