Exploring the Impact of Polymers on Trimetazidine Muco- Adhesive Buccal Tablets for Effective Management of Angina Pectoris

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Abstract:

There has been a rise in interest in buccal medication administration for its potential to produce either local or systemic effects. The buccal mucosa may be used to apply and remove dosing forms in emergency situations involving toxicity. Patients with insufficient control of, or intolerance to, first-line medications may benefit from prophylactic and symptomatic therapy with Trimetazidine for stable angina pectoris. Polymers like HPMC and Sodium Alginate were used to make the mucoadhesive buccal tablets. As a result of Response Surface analysis, the formulation has been fine-tuned. According to FTIR analyses, the pure medicine and excipients did not react chemically with one another. The tablets were made using a direct compression approach. Optimal Formulation F1 Has a High Mucoadhesive Property. According to the Optimizing research, after 9 hours, F1 shows a maximum of 89% drug release. And a 98.75% assay value was determined.

Key Words: *Buccal delivery, local and systemic effects, Trimetazidine, Stable angina pectoris, Response Surface methodology, Polymers, FTIR, Direct compression method.*

Introduction:

In recent years, there has been a growth in interest in buccal administration of drugs with the aim of obtaining both local and systemic effects. The goal of this kind of delivery is to achieve synergy between the local and systemic levels of treatment. This is because there are a variety of advantages that come along with the administration of drugs in this particular manner. [1]. The ingestion of pharmaceuticals via the oral route is the technique that is regarded as the safest as well as the most prevalent one. It is uncomplicated, makes it possible for patients to write their own prescriptions, and takes into account a titratable and regulated dosing plan that is compatible with the vast majority of other medication delivery systems. All of these qualities contribute to the positive impression that it gives. These are just some of the advantages associated with it. [2] Although the oral route is favoured for the administration of medications, it also has a number of significant drawbacks, such as the first-pass effect, gastrointestinal enzymatic degradation, and a delay between the time of administration and retention, which is unfavourable for medications that have requirements for a rapid onset of action. [3,4]

Mucoadhesive dosage forms are carefully engineered to attach to the surface of the mucosa. This increases the amount of time that the medication is retained at the site of administration, while also allowing for a regulated rate of drug release, which results in a superior therapeutic effect [5]. Mucoadhesive drug delivery systems include, but are not limited to, adhesive patches, adhesive gels, adhesive tablets, adhesive films, and adhesive discs, etc. [6]. The mucosal layer lines many areas of the body, including the gastrointestinal (GI) tract, the urogenital tract, the ear, the nasal route, and the airways. Other areas that are lined by the mucosal layer include the urogenital tract and the airways. The gastrointestinal tract, the lungs, and the intestines all have single-layered epithelium, whereas the oesophagus, the vagina, and the cornea all have multi-layered stratified epithelium. These are the prospective areas where mucoadhesive drug delivery devices might be effective.

Anatomy Buccal Mucosa:

In a manner similar to that of the skin, the major purpose of the buccal mucosa is to restrict the entry of individuals from the outside world to important tissues. An undulating cellar film acts as a barrier between the defined squamous epithelium of the buccal mucosa and the submucosal connective tissue, which consists of the lamina propria and the submucosa. When they move from the basal area to the superficial region, where they are shed, the cells (keratinocytes) that make up the squamous epithelium change in size, shape, and composition. This occurs as the cells migrate from the basal region to the superficial region. Under light microscopy, the epithelium of the human oral mucosa displays characteristic patterns of development; however, these patterns may vary depending on where in the mouth one looks. (a) non-keratinized surface in the mucosal covering of the delicate sense of taste, the ventral surface of the tongue, the floor of the mouth, alveolar mucosa, vestibule, lips, and cheeks; and (b) keratinized epithelium which is tracked down in the hard sense of taste and non-adaptable locales of the oral cavity. Both of these types of epithelium serve as a protective layer for the tissues that lie underneath. Throughout their journey to the surface, epithelial cells undergo development, reshaping, and enlargement beginning at the basal cells. [7].

Materials and methods:

Trimetazidine was obtained from Yarrow Chemicals, Mumbai, while HPMC and Sodium Alginate were Obtained from Loba Chemicals, Magnesium Stearate and Lactose were obtained from Fine chemicals. [8,9,10,11,12,13]

Formulation	Trimetazidine [mg]	HPMC [mg]	Sodium Alginate [mg]	Magnesium Stearate [mg]	Lactose [mg]	Talc [mg]
F1	38	3.5	2.0	1	54.5	1
F2	38	3.7	1.8	1	54.5	1
F3	38	4.0	1.5	1	54.5	1
F4	38	4.2	1.3	1	54.5	1
F5	38-	4.4	1.1	1	54.5	1

Optimization by DOE:

The Design of Experiments (DOE) is a technique that is used to identify the link between elements that influence a process and the output of that process in a methodical and organized manner. In other words, it is utilized to determine the links between causes and their effects. [19,20,21]

This information is essential for managing the process inputs in order to achieve maximum efficiency in the output. In an experiment or procedure, the input parameters that are possible to be altered are referred to as controllable input factors, sometimes written as x factors. (For example, polymer concentrate and binder concentrate. [13,16,17,21]

Fit Statistics – Lack of Fit & Anova

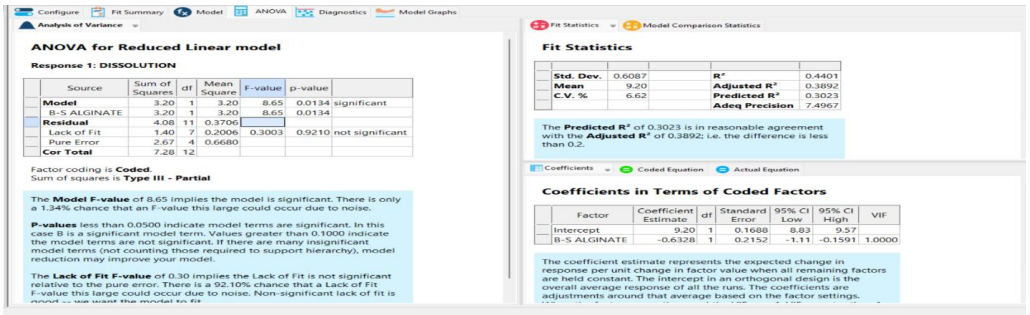
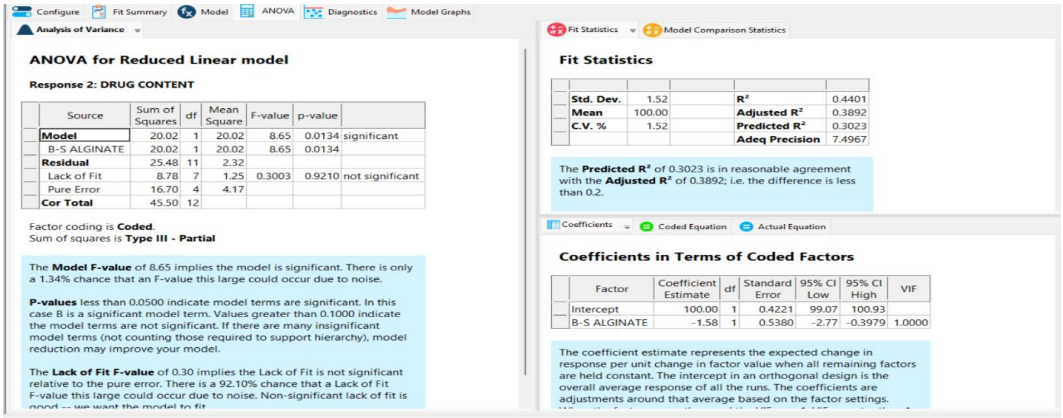
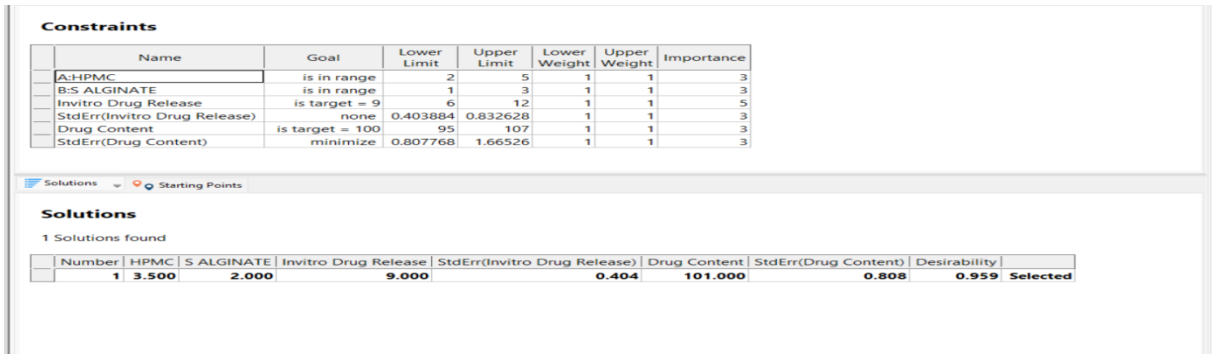


Figure no: 1 Fit Statistics - I

Figure no: 2 Fit Statistics - II



Constraints:



Constraints

	Name	Goal	Lower Limit	Upper Limit	Lower Weight	Upper Weight	Importance
	A:HPMC	is in range	2	5	1	1	3
	B:S ALGINATE	is in range	1	3	1	1	3
	Invitro Drug Release	is target = 9	6	12	1	1	5
	StdErr(Invitro Drug Release)	none	0.403884	0.832628	1	1	3
	Drug Content	is target = 100	95	107	1	1	3
	StdErr(Drug Content)	minimize	0.807768	1.66526	1	1	3

Solutions | Starting Points

Solutions

1 Solutions found

Number	HPMC	S ALGINATE	Invitro Drug Release	StdErr(Invitro Drug Release)	Drug Content	StdErr(Drug Content)	Desirability	
1	3.500	2.000	9.000	0.404	101.000	0.808	0.959	Selected

Figure no: 3 Constraints

Contour plot:

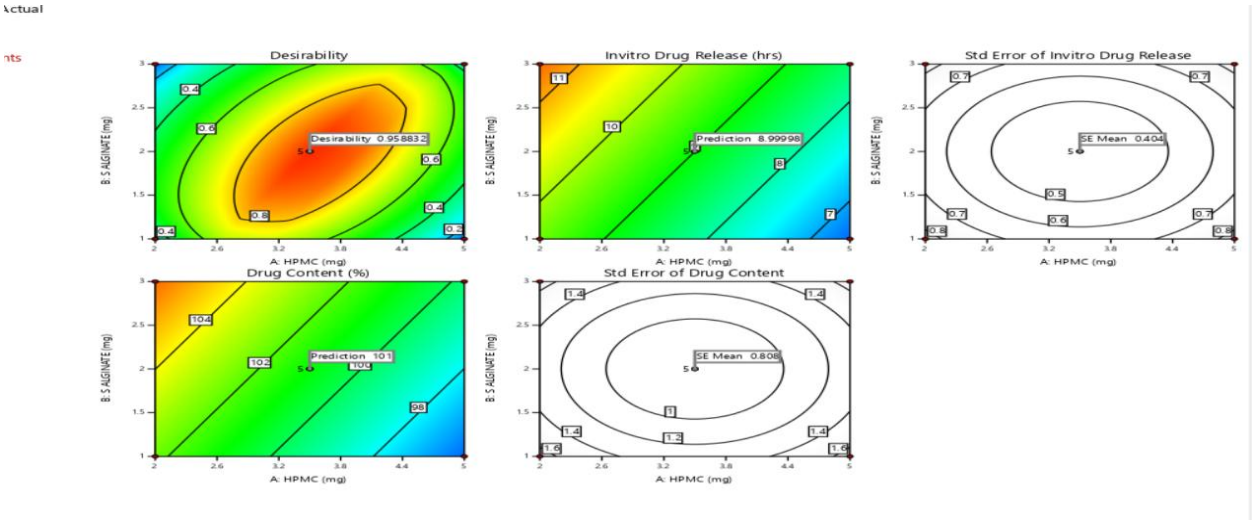


Figure no: 4 Contour plot

3D Interpretation Chart:

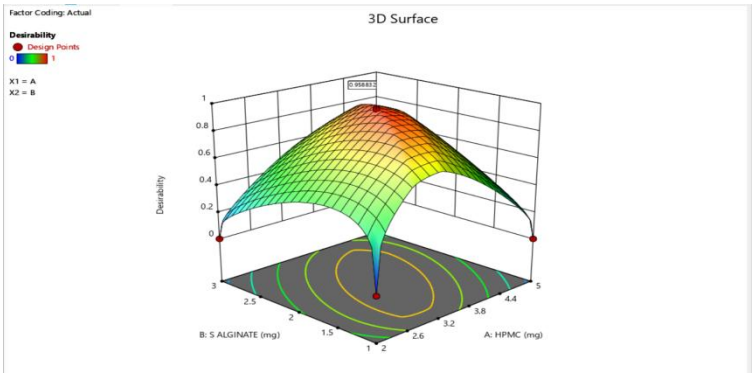


Figure no:5 3D Interpretation Chart

Interpretation of Optimization:

According to the findings of the ANOVA, the F value for the Significance is 0.0134, which indicates that it is not substantially relative to the pure experimental error. This finding suggests that the model corresponds well with the experimental data. The fact that there is a lack of fit that is not statistically significant is also a positive indicator, given that the main goal was to have the model correspond to the experimental data. The fact that the model developed had an R2 value of 0.920 demonstrated that it was able to provide an accurate estimation of the response of the system within the range.

FTIR Spectra: (Drug- Excipient Compatibility Studies)

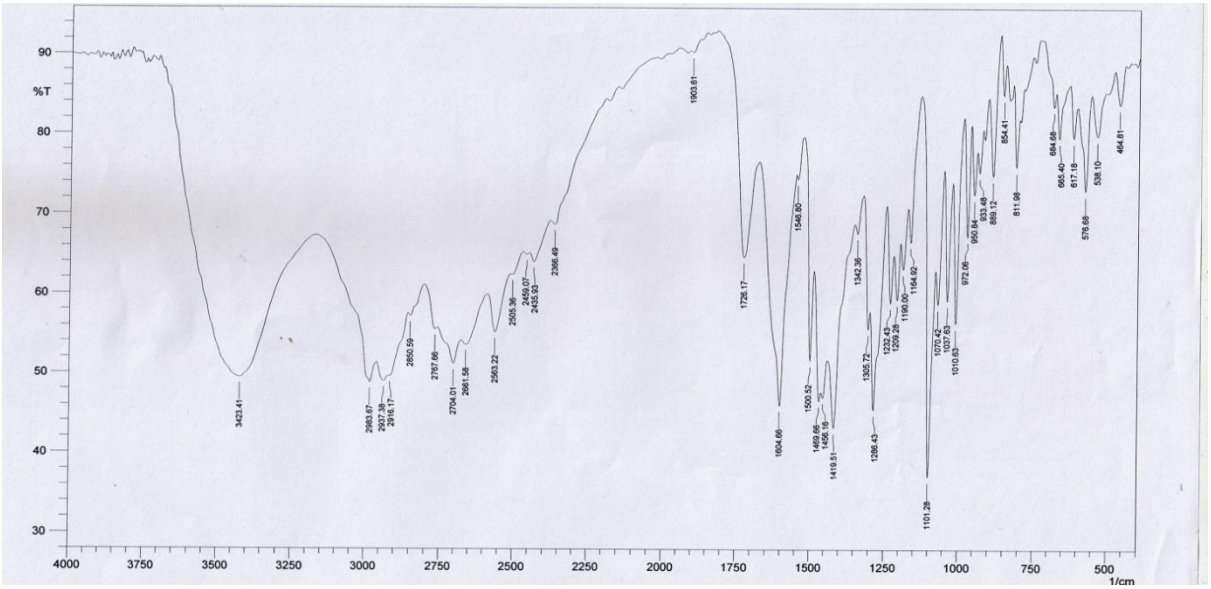


Figure no:6 IR Spectrum of Pure drug - Trimetazidine

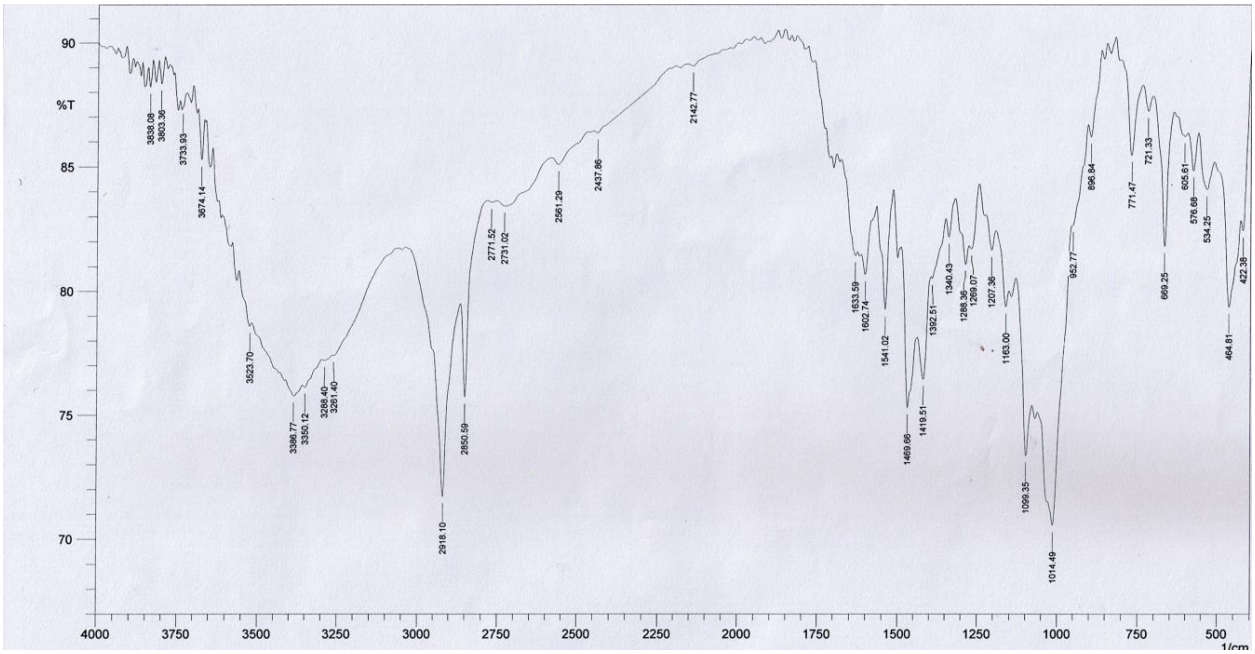


Figure no: 7 IR Spectrum of Trimetazidine and Excipients

An FT-IR spectrum analysis is performed on the Trimetazidine, together with the excipients. Since there were no discernible differences in the strength or location of the peaks in the spectrum, it was determined that the medicine was compatible with the excipients. A graph is used to display the findings.[18]

Calibration Curve of Trimetazidine:

Create a number of standard solutions of Trimetazidine with concentrations that are already established. It is possible to do this by dissolving a predetermined quantity of Trimetazidine in an appropriate solvent such as water or methanol. With a UV-visible spectrophotometer, one should determine the absorbance of each standard solution at a wavelength that is appropriate. It is possible for the measurement wavelength to change depending on the solvent and on the other circumstances of the experiment; nonetheless, 280 nm is a wavelength that is often employed for Trimetazidine. Create a graph that compares the absorbance of the standard solutions to their concentrations.

Post Compression Parameters:

1. Hardness
2. Friability
3. Assay (Percentage Drug Content)
4. Disintegration
5. Invitro Drug Release. [9,10]

Results:

Standard Curve Trimetazidine

Table No:1 Standard Curve Trimetazidine

S. NO	Concentration (µg/ml)	Absorbance (nm)
1	0	0
2	10	0.1010
4	20	0.213
5	30	0.325
6	40	0.410
7	50	0.510
8	60	0.608
9	70	0.691

Post compression parameters:

Hardness and Friability:

Table No:2 Hardness and Friability of the Formulation

Formulation	Hardness (kg/Cm2)	Friability (%)
F 1	3.76	0.44
F 2	3.86	0.76
F 3	3.79	0.85
F 4	3.89	0.79
F 5	3.90	0.68

Disintegration time, assay of the formulation

Formulation	Disintegration time (mins)	% Drug content (Assay)
F 1	02	98.7
F 2	03	97.3
F 3	03	95.5
F 4	04	93.5
F 5	03	95.6

Table no: 3 Disintegration time, assay of the formulation

Dissolution profile of Trimetazidine

Table no: 4 Dissolution profile of Trimetazidine

S. No	TIME (hrs)	F1 (%)	F2 (%)	F3 (%)	F4 (%)	F5 (%)
1	0	0	0	0	0	0
2	1	10.1	8.5	10.2	9.8	9.2
3	2	17.3	15.2	16.3	15.4	15.6
4	3	35.2	33.3	35.6	23.3	21.4
5	4	48.1	42.1	42.9	35.5	31.5
6	5	60.6	52.4	50.4	47.3	44.3
7	6	69.4	64.6	59.7	55.4	51.3
8	7	78.3	75.4	68.6	67.3	60.2
9	8	85.1	78.4	76.1	75.5	67.2
10	9	89.2	81.1	84.1	81.3	75.7

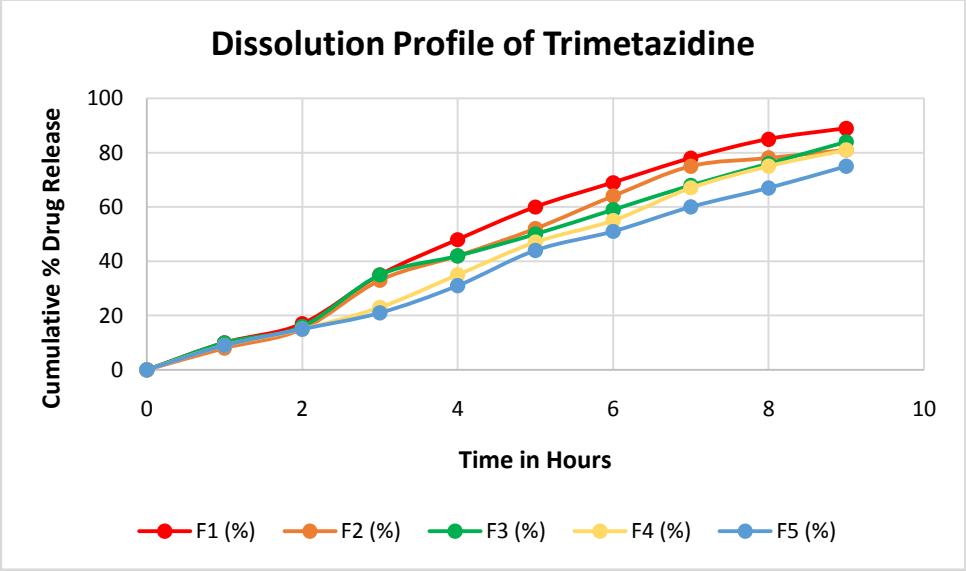


Figure no :8 Dissolution profile of Trimetazidine

Discussion

An effort has been made in the current research to create and construct Mucoadhesive Buccal tablets of Trimetazidine using Binders such as HPMC and chitosan. The technique used direct compression, with HPMC and sodium alginate serving as binders, talc facilitating flow, and magnesium stearate acting as a lubricant. FTIR analyses showed that the medication and polymer were compatible with one another. According to FTIR analyses, the pure medicine and excipients did not react chemically with one another. As a result of its low production cost and few requirements, the direct compression technique was used to create the tablets.

Thickness, hardness, friability, in vitro disintegration time, wetting time, and in vitro drug release are only some of the post-compression properties that were tested, and all came back within IP limits. The combination of HMPC and Sodium Alginate (F1) has excellent swelling and mucoadhesive properties. Trimetazidine tablets made with 3.50 percent HMPC and sodium alginate (F1) were shown to be more efficacious and better at meeting patient compliance.

CONCLUSION

The purpose of this study was to create a mucoadhesive buccal tablet for the prevention of myocardial infraction that is stable, safe, has a Extend release profile, and is easily administered. All five formulations (F1–F5) of mucoadhesive buccal tablets using HPMC and Sodium Alginate as a binder by direct compression method were successfully prepared after being optimised using design expert software. A variety of factors, including the formulations' hardness, friability, in-vitro disintegration time, and in-vitro drug release studies, were taken into account. According to the Optimizing research, after 9 hours, F1 shows a maximum of 89% drug release. And a 98.75% assay value was determined. We find that the improved formula F1 results in increased drug release and test value.

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