

Development and Evaluation of Hydrogel Based Mouth Dissolving film of Tizanidine: A Novel Muscle Relaxant Therapy

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Abstract

Background: The present study aimed to develop Tizanidine mouth dissolving films to provide a convenient and rapidly disintegrating dosage form.

Methods: Nine formulations (F1–F9) were prepared using different water-soluble polymers and plasticizers. The films were evaluated for physical appearance, thickness, weight variation, surface pH, folding endurance, tensile strength, disintegration time, drug content and in-vitro drug release. The optimized formulation was further evaluated for drug-release kinetics and three-month stability.

Results: All formulations showed smooth, uniform and flexible films with acceptable physical and mechanical properties. Disintegration time ranged from 42 to 23 seconds, while drug content ranged from 96.42–100.42%. Formulation F9 showed the highest drug release of 98.12% at 60 min, with a disintegration time of 23 seconds, folding endurance of 280 folds and tensile strength of 2.600. The Higuchi model showed the highest correlation ($R^2 = 0.9918$).

Conclusion: Tizanidine mouth dissolving films were successfully developed, and F9 was selected as the optimized formulation based on its satisfactory film characteristics, rapid disintegration and drug-release performance.

Keywords: Tizanidine; Mouth Dissolving Film; Film-Forming Polymers; In-vitro Drug Release; Formulation Optimization.

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Introduction

Tizanidine is a centrally acting muscle relaxant commonly used for the treatment of muscle spasticity. It is generally given by the oral route in conventional dosage forms. Although tablets are easy to use for most patients, some individuals may have difficulty swallowing them. This creates a need for dosage forms that are simple to administer and can break down quickly after administration. Mouth dissolving films are thin and flexible films that can be placed in the mouth, where they rapidly break down in the presence of saliva. They are easy to handle and do not require the use of water. The properties of these films depend largely on the type and amount of polymer and plasticizer used in their preparation. A suitable combination can provide a film with good flexibility, strength, uniformity and rapid drug release.

In the present work, Tizanidine mouth dissolving films were prepared using different water-soluble polymers such as HPMC E15, HPMC K100, PVP K25, PVP K30, sodium alginate and sodium CMC.

Different plasticizers and other excipients were also incorporated to obtain films with suitable characteristics. Nine formulations, coded F1 to F9, were prepared and evaluated for appearance, thickness, weight variation, surface pH, folding endurance, tensile strength, disintegration time, drug content and in-vitro drug release. The formulations were compared on the basis of their evaluation results, and the most suitable formulation was selected for further drug-release kinetic and stability studies. The study was carried out to develop a Tizanidine mouth dissolving film having good physical properties, sufficient mechanical strength, quick disintegration and satisfactory drug release.

Aim and Objectives

Aim: To develop and evaluate Tizanidine mouth dissolving films using different film-forming polymers and plasticizers to obtain a film with

good physical properties, rapid disintegration and satisfactory drug release.

Objectives

- To carry out pre-formulation studies of Tizanidine.
- To study the compatibility of Tizanidine with selected excipients.
- To prepare different Tizanidine mouth dissolving film formulations using suitable polymers and plasticizers.
- To evaluate the prepared films for physical and mechanical properties.
- To evaluate the stability of the optimized formulation during storage.

Materials And Methods

Materials and Instruments: Tizanidine and the required polymers, plasticizers and excipients were

used for preparation of mouth-dissolving films. The instruments used included UV-visible spectrophotometer, FTIR spectrophotometer, DSC, melting point apparatus, digital balance, micrometer, disintegrator, dissolution apparatus, magnetic stirrer and heating mantle.

Preformulation Studies: Melting point, physical compatibility, chemical compatibility and calibration curve studies of Tizanidine were performed. Drug–excipient compatibility was evaluated by physical observation and FTIR spectroscopy. The calibration curve was prepared in SGF in the concentration range of 5–25 µg/mL and absorbance was measured at 320 nm.

Formulation of Tizanidine Mouth-Dissolving Films: Nine formulations (F1–F9) were prepared using different polymers and plasticizers. Each formulation contained 500 mg of Tizanidine.

Table 1: Formulation design of Tizanidine mouth-dissolving films

Excipients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Tizanidine (mg)	500	500	500	500	500	500	500	500	500
HPMC E-15	25	-	-	-	25	-	-	-	-
HPMC K-100	-	25	-	-	-	25	-	-	-
PVP K-30	-	-	25	-	-	-	25	-	-
PVP K-25	-	-	-	25	-	-	-	25	-
Sodium alginate	25	25	25	25	-	-	-	-	25
Sodium CMC	-	-	-	-	25	25	25	25	25
Glycerin	25	-	-	12.5	-	12.5	12.5	-	-
PG	-	25	-	12.5	12.5	-	-	12.5	-
PEG-400	-	-	25	-	12.5	12.5	-	-	12.5
Citric acid	5	10	5	10	5	10	5	10	5
Xanthan gum	-	12	-	22	-	-	12	22	-
Sodium croscarmellose	22	-	12	-	12	22	-	-	22
SLS	5	10	5	10	5	10	5	10	5
Na Saccharin	10	10	-	10	-	-	10	10	10
Mannitol	-	-	10	-	10	10	10	10	-
Vanillin	10	10	10	10	10	10	10	10	10
Distilled water	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

Evaluation of Mouth-Dissolving Films: The prepared films were evaluated for appearance, thickness, weight variation, surface pH, folding endurance and tensile strength.

Results and Discussion

Pre-formulation Studies

Table 2: Melting Point Determination of Tizanidine

S. No.	Drug	Melting point observed	Reported melting point	Observation
1	Tizanidine	290°C	≈ 290°C	White crystalline powder; sharp melting point

Melting Point Determination: The melting point of Tizanidine was found to be 290°C, which was consistent with the reported value. The sharp melting point indicated the suitability of the drug for further formulation studies.

Drug–Excipient Compatibility: Physical compatibility studies showed no noticeable changes

in the colour, odour or appearance of the drug–excipient mixtures during the four-week

observation period. FTIR studies showed retention of the characteristic peaks of Tizanidine without major peak disappearance or appearance of new significant peaks.

This indicated that the selected excipients were compatible with Tizanidine.

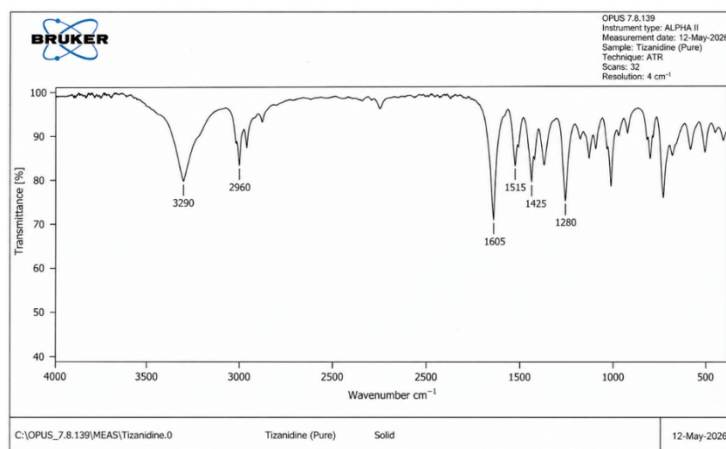


Figure 1:

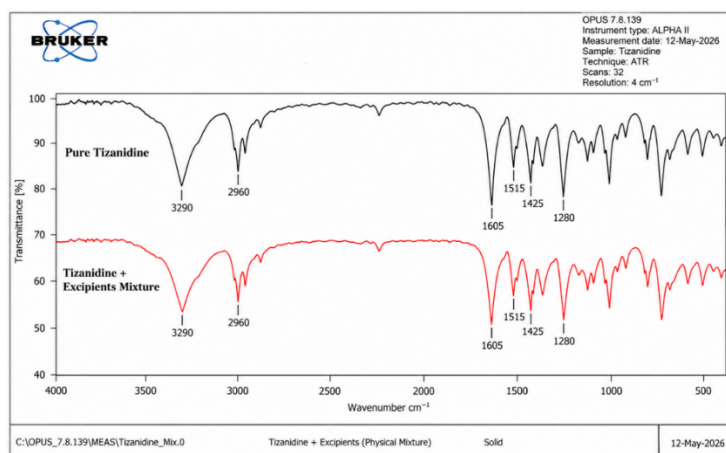


Figure 2:

Calibration Curve of Tizanidine: The calibration curve was prepared in SGF over the concentration range of 5–25 µg/mL at 320 nm. A linear relationship was obtained between drug concentration and absorbance, with an R^2 value of 0.999, indicating good linearity.

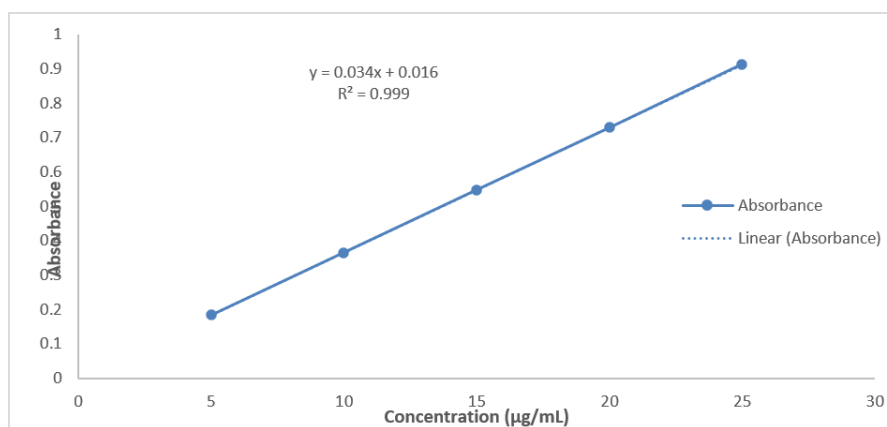


Figure 3:

Formulation Development: Nine Tizanidine mouth dissolving film formulations (F1–F9) were prepared using different film-forming polymers and

plasticizers. HPMC E15, HPMC K100, PVP K25, PVP K30, sodium alginate and sodium CMC were used as film-forming polymers, while glycerin,

propylene glycol and PEG-400 were used as plasticizers. All nine formulations were successfully prepared.

Physical and Mechanical Evaluation: All formulations produced smooth, uniform and flexible films. Film thickness ranged from 0.034–0.044 mm, weight from 18.2–25.0 mg, surface pH from 6.2–7.0, folding endurance from 250–280 folds, and tensile strength from 0.710–2.600. The results indicated satisfactory physical and mechanical properties of the prepared films. Increasing the polymer concentration from 25% to 50% resulted in an increase in film thickness, folding endurance and tensile strength, indicating the influence of polymer concentration on film properties.

Evaluation of Tizanidine Mouth Dissolving Films

Disintegration Time: The disintegration time ranged from 42 to 23 seconds among the formulations. F9 showed the shortest disintegration time of 23 seconds, indicating rapid breakdown of the film in the aqueous medium.

Drug Content: The drug content of the prepared films ranged from 96.42–100.42%. The relatively small variation indicated satisfactory distribution of Tizanidine throughout the films. F9 showed the highest drug content of 100.42%.

In-vitro Drug Release: The in-vitro dissolution study showed a progressive increase in Tizanidine release with increasing time. At 60 minutes, drug release ranged from 78.36% for F1 to 98.12% for F9. F9 showed the highest drug release among the prepared formulations.

The order of drug release at 60 minutes was:

F9 > F8 > F7 > F6 > F5 > F4 > F3 > F2 > F1

The higher drug release from F9 indicated that its polymer–plasticizer combination was favourable for Tizanidine release.

Selection of Optimized Formulation: Based on the overall evaluation, F9 was selected as the optimized formulation. It showed a thickness of 0.043 mm, surface pH of 6.8–7.0, folding endurance of 280 folds, tensile strength of 2.600, disintegration time of 23 seconds and cumulative drug release of 98.12% at 60 minutes.

Table 3: Selection of Optimized Formulation F9

Evaluation parameter	F9 result
Appearance	Smooth and uniform
Thickness	0.043 mm
Weight	24–25 mg
Surface pH	6.8–7.0
Folding endurance	280 folds
Tensile strength	2.600
Disintegration time	23 sec
Cumulative drug release at 60 min	95.64%
Overall selection	Optimized formulation

Drug Release Kinetics: The drug-release data of the optimized formulation F9 were fitted to zero-order, first-order, Higuchi and Korsmeyer–Peppas models. The Higuchi model showed the highest correlation coefficient ($R^2 = 0.9918$), suggesting that drug release from F9 predominantly followed a diffusion-controlled mechanism.

Stability Study: The optimized formulation F9 was subjected to a three-month stability study. The

film remained smooth, uniform and flexible throughout the study period. Drug content decreased from 100.42% to 98.96%, while cumulative drug release at 60 minutes decreased from 98.12% to 96.84%. Folding endurance decreased from 280 to 276 folds. These minor changes indicated satisfactory stability of the optimized formulation during the three-month study period.

Table 4: Three-Month Stability Study of Optimized Formulation F9

Evaluation Parameter	Initial	1 Month	2 Months	3 Months	Change at 3 Months
Physical appearance	Smooth, uniform	Smooth, uniform	Smooth, uniform	Smooth, uniform	No significant change
Thickness (mm)	0.043	0.043	0.044	0.044	2.33%
Weight (mg)	24.5	24.6	24.6	24.7	0.82%
Folding endurance (folds)	280	279	277	276	1.43%
Drug content (%)	100.42	99.96	99.48	98.96	1.45%

Summary

The present study was carried out to develop and evaluate Tizanidine mouth dissolving films using different film-forming polymers and plasticizers. Pre-formulation studies were performed to assess the melting point and compatibility of Tizanidine with the selected excipients. The drug showed a melting point of 290°C, and the compatibility studies indicated no significant interaction with the selected excipients. Nine formulations, coded F1–F9, were prepared using different polymers and plasticizers. The prepared films were evaluated for physical appearance, thickness, weight, surface pH, folding endurance, tensile strength, disintegration time, drug content and in-vitro drug release. All formulations showed acceptable physical and mechanical properties.

The disintegration time of the films ranged from 42 to 23 seconds, while drug content ranged from 96.42–100.42%. In the in-vitro drug release study, F9 showed the highest drug release of 98.12% at 60 minutes. Based on the overall results, F9 was selected as the optimized formulation. The drug-release data of F9 were evaluated using different kinetic models. The Higuchi model showed the highest correlation ($R^2 = 0.9918$), suggesting diffusion-controlled drug release. The optimized formulation was also subjected to a three-month stability study and showed only minor changes in its evaluated properties.

Conclusion

The study concluded that Tizanidine mouth dissolving films were successfully developed using suitable polymer and plasticizer combinations. The developed films showed satisfactory physical and mechanical properties, rapid disintegration and good drug content. Among the nine formulations, F9 was selected as the optimized formulation because it showed the best overall performance, with a 23-second disintegration time, 100.42% drug content and 98.12% drug release at 60 minutes. The optimized formulation also maintained satisfactory characteristics during the three-month stability study.

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