

<https://doi.org/10.56770/jcp2025915>

FAST DISSOLVING FILM OF TIZANIDINE HYDROCHLORIDE FOR ORAL DOSAGE FROM SEMI-SYNTHETIC AND SYNTHETIC POLYMER

Sadia Shehzad, Ali Zafar, Abdul Basit *

University College of Conventional Medicine, Faculty of Medicine and Allied Health Sciences, The Islamia University of Bahawalpur, Pakistan

Submitted: December 21, 2024; Revised: April 3, 2025; Accepted: April 27, 2025; Published: June 30, 2025

ABSTRACT

Tizanidine Hydrochloride is commonly used to treat multiple sclerosis spastic diplegia, backache, and injuries to central nervous system (CNS). **Objective:** This study aimed to develop quick-release films of tizanidine HCl to create a dosage form that provides a rapid onset of action. This formulation enhances bioavailability and offers convenient administration without the need to swallow or use water. **Methods:** The tizanidine hydrochloride films were prepared by means of polymers for example polyvinyl alcohol (PVA) and hydroxypropyl methylcellulose (HPMC), either in combination or individually, through a solvent casting method. The films were assessed for physical properties. The formulations underwent disintegration and *in vitro* drug release tests. **Results:** The films were repeatedly folded at the same point, and after an average of 95 folds, they began to break at that location, indicating a folding endurance of 95. The percentage elongation was measured at four springs. Disintegration and dissolution studies showed favorable results, with disintegration occurring within no time and a dissolution rate of 99%. **Conclusions:** These films are suitable in alleviating diplegia, backache, and spinal injuries, where a immediate onset of action, rapid release, and convenient administration are essential.

Keywords: Tizanidine Hydrochloride, Fast dissolving tablets, Dosage form.

*Corresponding Author. E-mail: abdulbasit81402@gmail.com

INTRODUCTION

Tizanidine hydrochloride is primarily used for the management of neurological disorders. Due to its short half-life and other extensive properties, Tizanidine requires frequent dosing, which can compromise patient compliance, particularly among the elderly and those with difficulty in swallowing conventional tablets or capsules.

Mouth-dissolving films provide an appealing method for systemic drug delivery. They are highly favourable because of their higher systemic bioavailability and by passing property of first metabolism. This in turn provides better permeability. These films also have well-supplied vascular and lymphatic drainage. Additionally, the oral mucosa offers a large absorption surface area, ease of ingestion and swallowing, and pain avoidance, making it a highly practical [1].

The delivery mechanism involves a thin oral strip that is placed in mouth on the tongue or any area of oral mucosa. As soon as it comes into contact

with saliva present in mouth, the film rapidly absorbs moisture and sticks to the place of application. It then breaks down and results in the dissolution of drug contents so the release of medication takes place. [2].

An significant advantage of orally disintegrating films (ODFs) is their precise dosing therefore it is most conveniently used dosage form for pediatric patients or individuals with dysphagia [3]. They also contain additional ingredients like plasticizers and sweeteners and some other excipients like flavoring agents, coloring agents etc. [4]. Rapidly dissolving films are suitable for nicotine replacement therapy, as well as for antiulcer and antihistamine medications. Antipsychotic and medicines used for treating sleep disorders also show a promising behaviour as contenders for this delivery method [5].

Recently, there has been a notable increase in the creation of innovative drug delivery systems



aimed at improving efficacy, safety, and patient acceptance [6]. Considering that the discovery of new chemical agents is a complex, and prolonged process, the emphasis has shifted to creating innovative delivery systems for existing drugs. These thin, flexible, and rapidly disintegrating films are placed on the tongue, where they dissolve quickly and release active pharmaceutical ingredient (API) directly into the oral cavity for systemic absorption or pre-gastric delivery [2]. Among these systems, orally disintegrating films (ODFs) are particularly advantageous for both pediatric and geriatric populations. These fast-dissolving films have advantages over fast-dissolving tablets, which carry risks of choking and friability. ODFs can be administered to dysphagic and schizophrenic patients, as they disintegrate in no time, releasing medication directly in the mouth.

The formulation of Tizanidine hydrochloride into a fast dissolving film offers significant advantages, like rapid onset of action, bypassing the first-pass metabolism, improved bioavailability, and better patient adherence. The selection of polymers have a critical role in the function and characteristics of ODFs. Both semi-synthetic polymers such as HPMC and NaCMC, and synthetic polymers have been widely employed in the development of fast dissolving films due to their marvellous film-forming characteristics, biocompatibility, and due to the effective facilitation of rapid disintegration and drug release [7].

This study aims to formulate a fast dissolving film of Tizanidine hydrochloride using selected semi-synthetic and synthetic polymers, with a focus on optimizing film characteristics such as mechanical strength, disintegration time, drug release profile, and patient acceptability.

MATERIALS AND METHOD

Pre Formulation Studies

The solubility of Tizanidine Hydrochloride in water decreases as the pH increases. It is freely soluble in a 0.1 N hydrochloric acid solution and in a mixture of dichloromethane and methanol. A 4% W/V solution of Tizanidine Hydrochloride in methanol has a pH of 4.68. The moisture content of Tizanidine Hydrochloride is 0.39%, and its melting point ranges from 280 to 290 °C [8].

SOLVENT CASTING METHOD

Among the different techniques for film manufacturing, solvent casting is a practical and commonly utilized method, mainly because of its simple process and affordability. It is crucial to take into account the rheological characteristics of

the polymer blend, as these characteristics affect the drying speed, film thickness, structure, and uniformity of content in the films. The mixing process can unintentionally trap air bubbles within the liquid; thus, de-aeration is vital for obtaining a uniform product. Once the solution is cast onto an appropriate substrate, it is permitted to dry, which allows the solvent to evaporate and results in a polymeric film that contains the drug [9].

Deaeration was done by placing the films at room temperature for 1 day. In the separate container remaining water soluble excipients, citric acid, peppermint oil and tizanidine are dissolved. solutions are mixed on magnetic stirrer. After settling, cast the resulting formulation onto a suitable platform and dry it to form a film. It is preferable to air-dry the film or use an oven for drying, after which the film can be carefully removed. Films are cut into desired shapes and sizes but the cutting must be done with such considerations that each strip must contain an estimated and desired quantity of the drug tizanidine in order to have the desired pharmacological effect [10].

EVALUATION OF TIZANIDINE HYDROCHLORIDE MOUTH DISSOLVING FILMS

Appearance, Shape, and Thickness

Films were evaluated for their physical characteristics and the thickness was measured at five different locations using a micrometer [11].

Surface pH

The next step Was the determination of surface pH. It was done by placing a film in a petri dish and moistening it with distilled water, allowing it to soak for one hour. Afterward, the pH meter was used to calculate the pH and it was then recorded. [11].

Folding Endurance

It was assessed by repeatedly folding it at the same location until it broke. The number of folds that the film can endure at that specific spot without breaking indicates its folding endurance [12].

% Elongation

When stress is applied to a sample strip, it stretches, a phenomenon known as strain. Strain is defined as the deformation of the strip divided by its original dimensions. Typically, as the concentration of plasticizer increases, the elongation of the strip also increases. The % elongation at break was calculated using the given formula.

$\% \text{ Elongation} = (\text{Increase in length} / \text{Initial length}) \times 100$ [12]

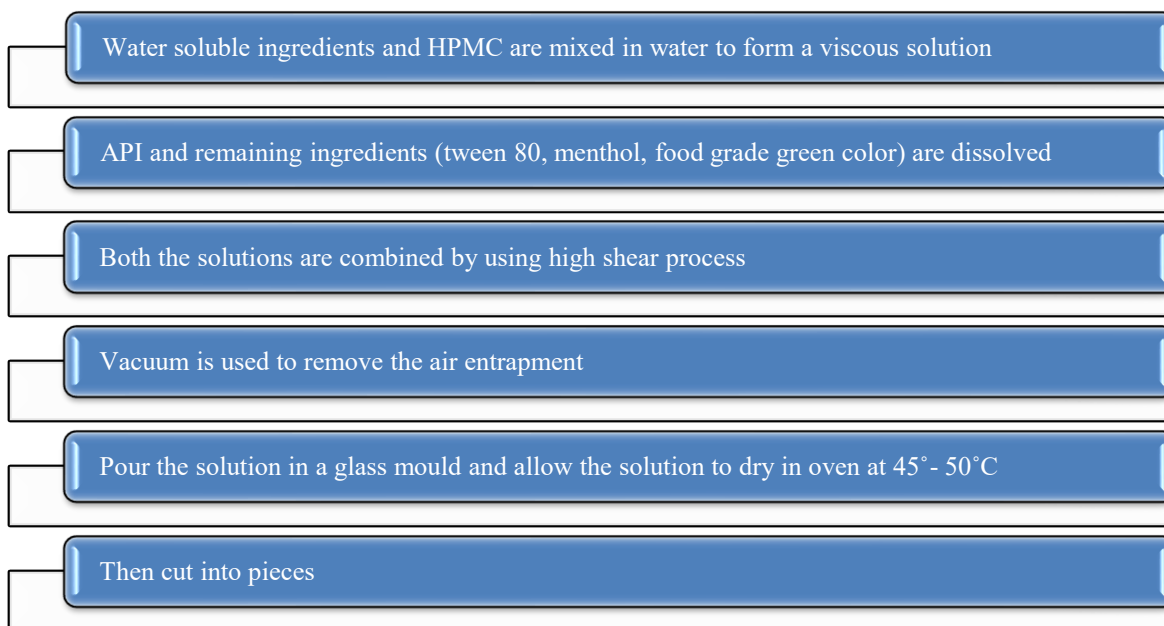


Figure 1: Schematic preparation of fast dissolving films.

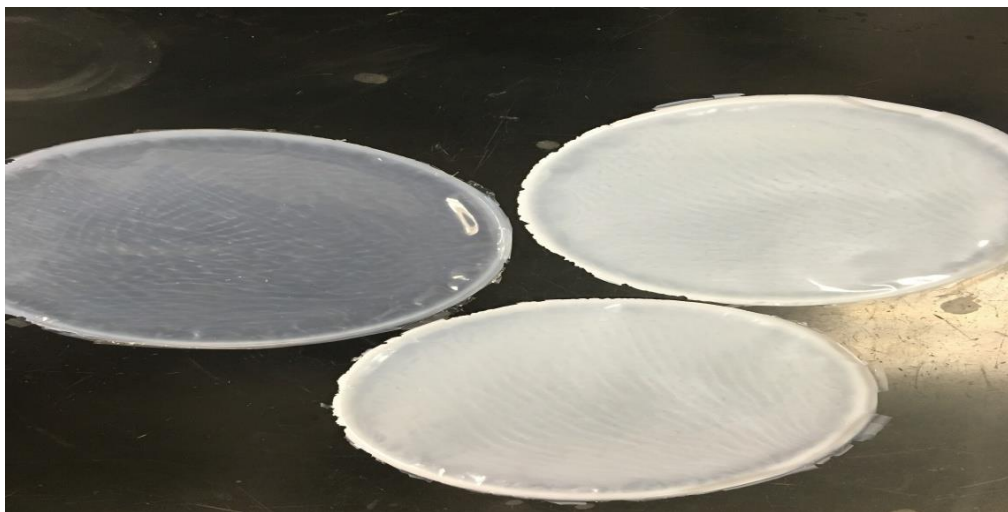


Figure 2: Real freshly prepared films of tizanidine.

Assay/ Content Uniformity

It was assessed by estimating the API content in individual strips, with an acceptable range of 85–115%. The samples were carefully prepared and the absorbance was measured at 230 nm [12].

Drug Content

The film (area 2x2 cm²) was placed in a beaker. The film was then applied by satisfactory amount of phosphate buffer. The pH of buffer was set at 6.8. Filtered and the absorbance of solution was measured at 230 nm using UV spectrophotometer. The experiment was performed in triplicate. And readings were noted carefully [11].

Disintegration Time

It was assessed by placing a 2x2 cm² film in a beaker containing 10 ml of phosphate buffer at pH 6.8. The mixture was swirled every 5 seconds, and the time was recorded [11].

In Vitro Dissolution Study

USP dissolution test apparatus (USP type II) was used at a temperature of 37±0.5°C. Rotation speed was kept at 50 rpm, with phosphate buffer at pH 6.8. The absorbance of each sample was measured at 230 nm using a LABINDIA 3000+ UV-VIS spectrophotometer. standard calibration curve was applied [13].

Tensile strength and dryness tack tests were also performed.

RESULTS AND DISCUSSION

Appearance, Shape and Thickness

Films had a smooth appearance, films were in rectangular or square shapes, each with an area of 6 square centimeters. The thickness, was found to be 0.15 ± 0.03 mm. All films exhibited the same appearance, shape, and thickness.

Surface pH

pH meter was used. Each film was dissolved in 100 ml of water, and after allowing one film to dissolve, the pH was determined to be 6.5, which is close to neutral pH.

Dryness/Tack Test

The strips were thoroughly dried and non-sticky.

Tensile Strength

The tensile strength of the film was calculated and it was of 1 kg/millimeter square to 1.5 ± 0.02 kg.

Folding Endurance

The films were repeatedly folded, and after 95 folds, they began to break. Therefore, the folding endurance was considered to be 95 folds.

% Elongation

%elongation refers to the point at which the films undergo deformation before breaking, specifically before reaching their plastic limit. The average %elongation was found to be four stretches, indicating that the films became deformed after being stretched four times.

Assay/Content Uniformity

After performing this assay it was found to be 98.6%.

Disintegration Time

The disintegration time estimated to be 23 ± 3 seconds. This short disintegration time is intentional, as the films are designed for rapid dissolution.

In-Vitro Dissolution Study

USP paddle apparatus was used. Phosphate buffer was prepared as the dissolution medium, mimicking the pH of the mouth (6.8). The temperature was at 37°C, at 50 rpm. Samples were analyzed using a UV spectrophotometer at a wavelength of 230 nm. The results showed that 99% of the drug was released within the first 20 seconds.

CONCLUSION

In conclusion the films are stable and meet standards. The demonstrated compatibility, indicates that the formulation is safe for use. So these can be easily and safely suggested to be formulated and used for clinical purpose for treating neurological disorders.

Author(s) Contribution: Conceptualization and supervision, A. Basit; writing-up and editing, S. Sadia; data analysis, Z. Ali.

Funding: Nill

Ethical Approval: NA

Conflict of Interest: There is no conflict of interest.

Consent for Publication: All authors approved the manuscript for publication and agreed to be responsible for all aspects of this article.

REFERENCES

1. Kunte S, Tandale P. Fast dissolving strips: A novel approach for the delivery of verapamil. *Journal Pharm. Bioavailability Science* 2010; 2, 4:325-328.
2. Edith M, Donald EC and Claus ML. *Bioadhesive Drug Delivery Systems*. Marcel Dekker Inc., New York, (1999), 541-562.
3. Pham T. Design and characterisation of orally dissolving films as a potential new dosage form for paediatrics (Doctoral dissertation, Aston University).
4. Yuan C, Sha H, Cui B. Orally disintegrating film: A new approach to nutritional supplementation. *Food and Bioprocess Technology*. 2022 Dec;15(12):2629-45.
5. Jacob S, Boddu SH, Bhandare R, Ahmad SS, Nair AB. Orodispersible films: current innovations and emerging trends. *Pharmaceutics*. 2023 Dec 11;15(12):2753.
6. Baryakova TH, Pogostin BH, Langer R, McHugh KJ. Overcoming barriers to patient adherence: the case for developing innovative drug delivery systems. *Nature Reviews Drug Discovery*. 2023 May;22(5):387-409.
7. Park H, Otte A, Park K. Evolution of drug delivery systems: From 1950 to 2020 and beyond. *Journal of Controlled Release*. 2022 Feb 1;342:53-65.
8. Hutchinson DR. Modified release tizanidine: a review. *J Int Med Res* 1990; 18: 20-25.
9. Remington, *The Science and Practice of pharmacy*, 19th Edn, vol. I,
10. Gururaj S. Kulkarni and P.R.Sateesh Babu, Design and Evaluation of Tizanidine Buccal Mucoadhesive Patches, *Journal of Applied Pharmaceutical Science*; Vol:02 (04); 2012: 74-81
11. Baichwal MR., *Advances in drug delivery system*, proceedings of the international symposium on advances in drug delivery systems: Bombay, Polymer films as drug delivery systems 1984.
12. Khanna R, Agrawal SP and Ahuja A. Preparation and evaluation of buccal films of clotrimazole for oral Candida infections: *Ind J Pharm Sci* 1997; 59, 299-305.
13. Samuelav Y, Donbrow M, Friedman M. Sustained release of drugs from ethylcellulose- polyethylene glycol films and kinetics of drug release. *J. Pharm. Sci.*, 1979; 68, 352-29.