International Journal of Innovative Research & Growth
E-ISSN: 2455-1848
homepage: http://www.ijirg.com/ijirg/
Volume: 14 Issue: 2, April 2025

Comparative Evaluation of Fast Dissolving Films Vs Conventional Oral Dosage Forms of Antihistamine in Terms of Drug Dissolution

Rizwan Ahmedhusain Bhaijamal[1]*, Machhi Yashkumar Virabhai[2], Maisuriya Aakashkumar B[3], Sonu Kachhiya M[4]
[1,2,3,4]Genezen Institute of Pharmacy Delol, Kalol-389310, Gujarat, India

CORRESPONDING AUTHOR

Rizwan Ahmedhusain Bhaijamal
e-mail: rbhaijamal.rb@gmail.com

KEYWORDS

Antihistamine, Mouth dissolving films, Allergy, Solvent Casting, Dissolution

ARTICLE DETAILS

Received 22 February 2025; revised 20 March 2025; accepted 06 April 2025

DOI: 10.26671/IJIRG.2025.2.14.115

CITATION
Bhaijamal, R. A., Virabhai, M. Y., B, M. A., M, S. K. (2025). Comparative Evaluation of Fast Dissolving Films Vs Conventional Oral Dosage Forms of Antihistamine in Terms of Drug Dissolution. *Int J Innovat Res Growth*, 14(2), 14240-14258. DOI

Abstract

Introduction: Rapidly dissolving oral films (RDOFs) and "mouth-melting" or "dissolve-in-mouth" (DIM) tablets represent novel pharmaceutical delivery systems engineered to dissolve or disintegrate when coming into contact with saliva. They present a convenient and hydration-independent approach to administering medications, proving particularly advantageous for individuals such as children and those facing difficulties with conventional tablet consumption. These pharmaceutical forms are applicable to a wide range of drugs and are manufactured through diverse methodologies, including patented technologies like Zydis and OraSolv. They offer benefits such as enhanced patient adherence, swift onset of drug action, increased drug absorption, and prolonged stability.
Discussion: Fast-dissolving oral films (FDOFs) are slender strips designed to dissolve rapidly, providing benefits such as swift drug onset and user-friendliness, particularly for pediatric and geriatric populations. While they do have certain constraints, FDOFs excel in terms of dissolution rates and bioavailability when compared to traditional tablets, positioning them as a promising choice for managing conditions like allergic rhinitis.
Conclusion:
It has been determined that fast-dissolving oral films (FDOFs) provide a patient- friendly, rapid drug delivery method with improved bioavailability, making them well- suited for individuals facing difficulties with conventional tablets. Despite encountering formulation complexities, FDOFs exhibit superior performance in comparative research, ensuring swifter and more predictable drug release, resulting in quicker therapeutic outcomes. They hold substantial potential for addressing a wide range of medical conditions, contributing to better patient adherence and expedited drug delivery, and are poised to drive further innovations in healthcare.

1. Introduction

A rapidly dissolving oral film is described as "an extremely thin film containing an active ingredient that rapidly dissolves or disintegrates in saliva, typically within a matter of seconds, without the need for water or chewing." This quick release mechanism is attributed to the film's larger surface area and reduced thickness in comparison to traditional tablets. The presence of hydrophilic polymers in the film ensures that saliva in the oral cavity quickly wets the film and leads to its rapid dissolution. Consequently, the oral mucosal tissues are highly vascularized, allowing the drug to be absorbed through the saliva. Creating formulations specifically for kids has proven to be a difficult task. Although adults and adolescents readily accept solid dosage forms, younger children frequently favor liquid formulations due to their ease of swallowing. Fast-dissolving oral films (FDOFs) have been developed by the pharmaceutical research community in response to the growing importance of ease of administration and swallowing. Traditional tablets and capsules have given way to modified-release versions, oral disintegrating tablets (ODTs), wafers, and, most recently, fast-dissolving oral films in the evolution of oral drug delivery research and development. FDOFs are essentially ultra-thin strips with an active pharmaceutical ingredient and multiple excipients, about the size of a postage stamp. Accompanying the release of FDOFs onto the market are educational initiatives aimed at educating consumers with warnings such as "do not swallow" or "do not chew."[1]

Tablets are the most commonly used pharmaceutical dosage form because of their easy self-administration, small size, and simple manufacturing procedures. However, older and younger patients frequently have trouble swallowing traditional tablets, which leads to less-than-ideal patient adherence. Researchers have developed novel drug delivery methods known as "mouth-melting" or "dissolve-in-mouth (DIM)" tablets in response to this challenge. These are a new kind of tablet that dissolves, disperses, or disintegrates in saliva. Their unique benefits, such as the flexibility to take them anytime, anywhere, and without water, make them especially appropriate for elderly and young patients. They also assist those who might be bedridden, mentally ill, or have restricted access to water. Due to their advantages over other pharmaceutical administration options, such as better patient adherence, quick onset of action, improved drug absorption, and strong stability, these tablets are now widely used in the market [2,3].

Many drugs can be thought of as good candidates for this dosage form, including those for bacterial infections, allergies, narcolepsy, cardiovascular disorders, and pain management. Many methods, including tablet molding [4], spray drying [5], lyophilization [6], sublimation [7], and the addition of disintegrants [8], are used in the formulation of fast-dissolving tablets. Notably, several patented technologies are available for the production of tablets that dissolve quickly, such as Wow tab (without water), Zydis [9,10], OraSolv [11], DuraSolv, Flash Dose [12], and Flashtab [13].

2.1 Aim

Comparative evaluation of fast dissolving films Vs conventional oral dosage forms of antihistamine in terms of drug dissolution.

2.2 Objectives

• For the research - to design a quality product and its manufacturing process to consistently deliver the intended performance of the product.
• To develop a pocket friendly formulation.
• To develop Improved Patient Compliance Product
• To develop formulation which give Rapid Onset of Action
• To develop easily administered product
• To develop mouth dissolving film for increased Bioavailability
• To create a product that masks unappealing taste or odor.

2.3 Rationale

About Diseases (Allergic rhinitis)
• The disease is Widely spread.
• There is No public awareness.
• Adults, children, and geriatric are affected by the allergic rhinitis.
• Management and treatment both are important.

About drug (Chlorpheniramine maleate)
• The drug is Potent.
• It has Low incidence of side effects.
• It Can be consumed by all age group.

About dosage form (Mouth Dissolving Film)
• Increase Bioavailability.
• Increase Solubility & permeability of API.
• Low dose required for formulation.

• Rapid onset of action.
• Patient Acceptance and Compliance
• Minimized Gastrointestinal Issues

2.4 Review of Literature

1. Pawar Rajat et al; Mouth dissolving films are a highly advanced form of oral medication that offers flexibility and convenience. These films disintegrate and dissolve in the mouth within a minute without the need for water or chewing. This unique dosage form allows medication to bypass first-pass metabolism, potentially improving the medication's bioavailability. Additionally, mouth dissolving films can enhance the onset of action, reduce the required dosage, and eliminate the fear of choking. The formulation of these films involves using plasticized hydrocolloids, taste masking agents for the active pharmaceutical ingredient (API), and laminating them through solvent casting and semisolid casting methods. Among these methods, solvent casting is preferred due to its ability to produce films with uniform thickness, a glossy appearance, and better physical properties. These films are evaluated for parameters such as thickness, folding endurance, disintegration, and dissolution time. This review provides insights into the formulation techniques, evaluation criteria, an overview of packaging, and some commercially available mouth dissolving film products.
2. Dr. Manish Kumar Gupta et al; Mouth dissolving films, which typically dissolve within seconds to release active agents, can be customized to control the drug release rate based on film thickness and polymer selection. These films are considered a dosage form that utilizes water-soluble polymers, facilitating rapid hydration, adhesion, and dissolution on the tongue or in the oral cavity for swift local or systemic drug delivery. After complete disintegration, the active pharmaceutical ingredient (API) can be absorbed through the buccal mucosa. Additionally, esophageal absorption may occur when swallowing saliva containing the dissolved API. However, the majority of the dose eventually reaches the stomach and is absorbed in a manner similar to traditional tablets, where stomach fluids gradually dissolve the entire tablet or capsule. This review article focuses on the formulation aspects and additives used in mouth dissolving films.
3. Poornima Sirohi et al; The aim of this study was to create a mouth dissolving film that rapidly disintegrates in the mouth, using a tasteless drug resin complex (DRC) of Chlorpheniramine maleate (CPM) with Tulsion-335 as an ion exchange resin. The formulated drug resin complex was evaluated for its taste and percentage drug loading and characterized using infrared spectroscopy. Multiple batches were developed using the optimized DRC through the solvent casting method. In simulated salivary fluid, more than 95% of Chlorphenaramine maleate was released from the formulation within 2 minutes. The taste masking and in vivo disintegration results were within acceptable limits. Among the different batches, the F1 batch was deemed suitable, as it exhibited low disintegration time and good physicomechanical properties when combined with the drug-resin complex. These findings suggest that by optimizing various formulation variables, the disintegration and drug release of Chlorphenaramine maleate can be significantly enhanced.
4. Quazi Bilal et al; The oral route is a widely used and convenient method for administering various pharmaceutical dosage forms, including tablets, capsules, syrups, suspensions, and emulsions. Fast Dissolving Drug Delivery systems have introduced fast-disintegrating preparations such as mouth dissolving films and MDT (Mouth Dissolving Tablets). Oral thin films are a novel dosage form made from hydrophilic polymers, which disintegrate rapidly in the mouth or buccal cavity upon placement. Mouth dissolving films are preferred over mouth
dissolving tablets due to their lower production cost. These films are particularly beneficial for geriatric and pediatric patients who may have difficulty swallowing tablets and capsules. They offer advantages such as self-administration, fast dissolution, and rapid absorption, making them a versatile dosage form. The primary focus of this study is to explore various polymers, their concentrations, and applications in oral films. The study also examines the use of plasticizers, polymers, sweeteners, different preparation methods, and various parameters used to evaluate the quality of the films.
5. Amarilla Mandola et al; Histamine, a bioactive amine, is a central player in allergic responses. Consequently, histamine receptor blockers (antihistamines) are vital in treating various atopic conditions like allergic rhinitis, conjunctivitis, and acute and chronic forms of urticaria. While immune cells and gut bacteria produce histamine, its influence extends beyond acute allergies, affecting the body through binding to its four pleiotropic G-protein coupled histamine receptors. In this discussion, we explore the roles of these histamine receptors, the clinical applications of antihistamines, their side effects, and innovative approaches for using antihistamines with different specificity, guided by established guidelines and recommendations.

3. Allergic Disease

One of the most prevalent conditions in the field of otorhinolaryngology is allergic rhinitis, which has a significant effect on people's quality of life. It can have serious repercussions if left untreated [14]. With a prevalence ranging from 10% to 40% and a rising rate, allergic rhinitis poses a significant global public health challenge [15– 18]. Between 20 and 40 million people are thought to be impacted in the US alone, which means that 3.5 million workdays are lost and 2 million school days are missed annually [19]. According to local

population-based studies, school-age children in Singapore have a 44% prevalence of allergic rhinitis [20]. Up to 30% of adults and 40% of children in the UK suffer from intermittent allergic rhinitis, commonly referred to as seasonal allergic rhinitis or hay fever, eventually in their lives [21].

Generally speaking, rhinitis is defined as inflammation of the nasal mucosa. It is a common condition that affects up to 40% of the population [22] Of the different types of rhinitis, allergic rhinitis is the most common, impacting roughly 10–20% of the population. There is mounting evidence that the condition is becoming more common [23]. It's important to remember that severe allergic rhinitis has been related to significant disturbances in sleep, productivity, and quality of life [23].

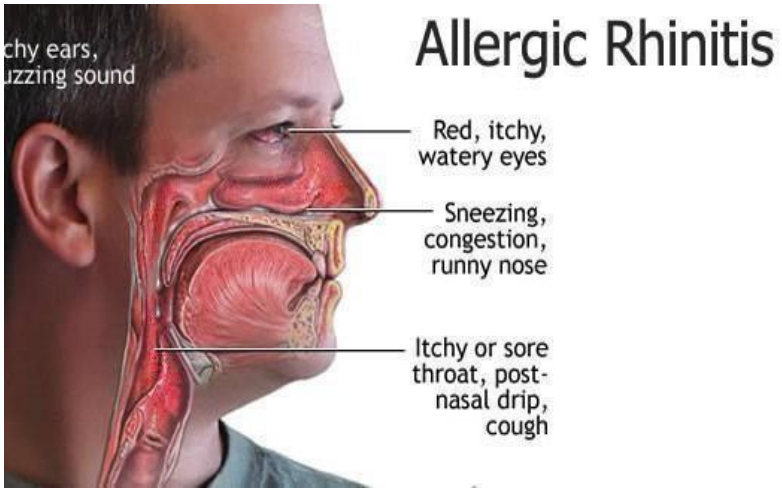

Fig.1: Allergic Rhinitis [24]

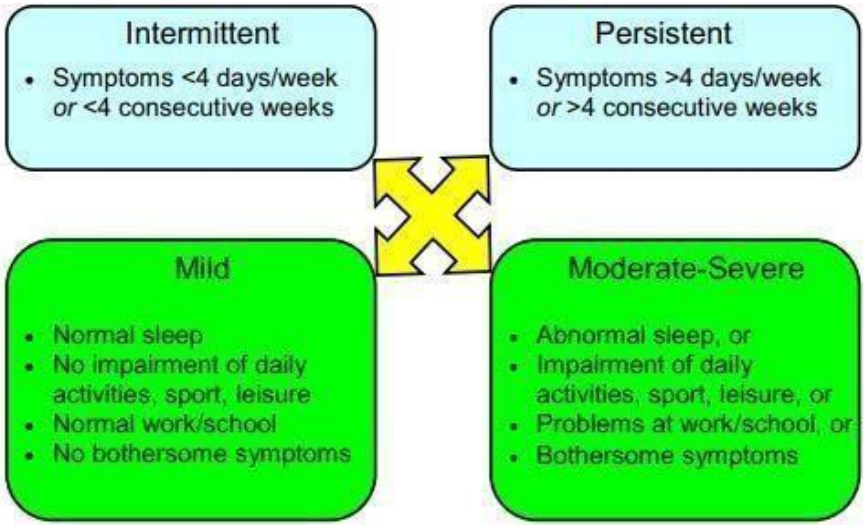

Fig.2: Classification of allergic rhinitis according to symptom duration and severity. [25]

Allergic arthritis, also referred to as reactive arthritis, is a form of inflammatory arthritis that may manifest following an infection originating from another body region, including the gastrointestinal system, urinary tract, or genital area. The infections most frequently associated with the development of allergic arthritis include:

- Chlamydia
- Salmonella
- Shigella
- Campylobacter
- Yersinia

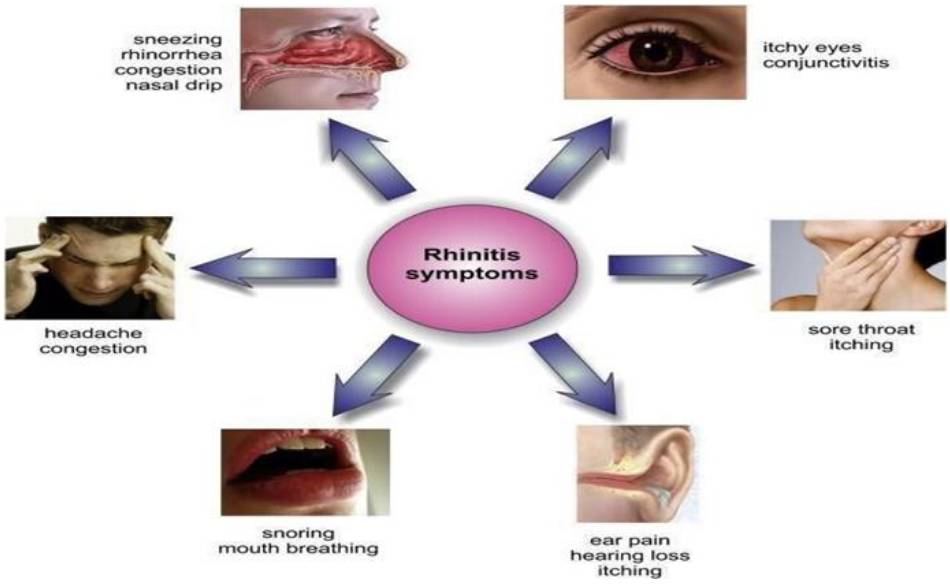

Fig.3: Symptoms of rhinitis [26]

The knees, ankles, and feet are among the lower extremity joints that are frequently affected by allergic arthritis. However, it can also affect joints in the upper extremities, such as the hands, wrists, and spine, so it is not just confined to these regions.

Fig.4: Allergy Symptoms [25]

Symptoms associated with allergic arthritis may encompass the following:
• Joint pain and swelling
• Stiffness
• Redness
• Tenderness
• Eye inflammation
• Skin rash

These symptoms often manifest suddenly and can persist for several weeks or months. In certain instances, they may exhibit a recurrent pattern, with symptoms appearing and disappearing over the course of several years.

When an individual is exposed to particular allergens, which are usually airborne particles such as dust mite feces, cockroach residues, animal dander, molds, and pollens, different types of inflammatory cells infiltrate the nasal lining and cause allergic rhinitis. Mast cells, CD4-positive T cells, B cells, macrophages, and eosinophils are some of these cells. The T helper 2 (T2) subtype accounts for the majority of T cells infiltrating the nasal mucosa in allergy sufferers. These T2 cells secrete cytokines, such as interleukin [IL]-3, IL-4, IL-5, and IL-13, which induce plasma cells to produce immunoglobulin E (IgE).

Histamine and leukotrienes are released as mediators when allergens and IgE bound to mast cells crosslink. Numerous physiological reactions, such as arteriolar dilatation, elevated vascular permeability, itching, rhinorrhea, mucous secretion, and smooth muscle contraction in the lungs, are brought on by these mediators [27, 28].

The subsequent cellular inflammatory response, known as the late-phase inflammatory response, occurs within the next 4–8 hours as a result of the mediators and cytokines released during the early phase of the immune response to the allergen incitation. Nasal congestion is a frequent and persistent symptom of this late-phase response, which frequently results in recurrent symptoms [27–30].

Table 1: Chemical and functional classification of H1 antagonist [31]

Derivatives	First generation	Second generation
Alkylamines	Chlorpheniramine, Pheniramine, Clemastine, Cyproheptadine, Diphenhydramine	Acrivastine
Piperazines	Hydroxyzine	Cetirizine, Levocetrizine
Piperidines	Cyproheptadine, Ketotifen	Astemizole, Desc, Loratadine, Mizolastine, Bilastine
Ethanolamines	Dimenhydrinate, Diphenhydramine, Doxylamine	-
Phenothizines	Promethazine	-
Others	Doxepin	Azelastine

An increase in vascular permeability is induced by the endogenous chemical messenger histamine, which causes fluid to flow from capillaries into the surrounding tissues. Blood vessels enlarge and swell more as a result of this process. By functioning as antagonists at the H-1 receptors, antihistamines reverse this effect and lessen allergy symptoms and their associated manifestations [32].

First-generation antihistamines can enter the central nervous system and irritate H-1 receptors with ease, even after passing through the blood-brain barrier. As such, their profile of side effects and therapeutic effects differs from that of second-generation antihistamines, which target peripheral histamine receptors specifically.

First-generation antihistamines usually take 4 to 6 hours to start working, whereas second-generation antihistamines work for 12 to 24 hours. The P450 cytochrome system is used by the liver to metabolize both kinds of antihistamines.

Mechanisms of allergic sensitization and allergen immunotherapy. (A) Upon inhalation of the allergen, ECs recruit DCs and polarize them to a pro-allergic DC2 phenotype. These cells uptake the allergen and migrate to lymph nodes, where they present it to naïve T cells and promote the development of TH2 and TFH subsets. TFH and TH2 cells collectively facilitate B cell maturation and class-switch recombination which leads to allergen-specific IgE production. These IgE molecules bind to high-affinity receptors on basophil and mast cell surfaces this way sensitizing the patient.

4. Mechanism of Action

Hydrochloric acid is secreted by parietal cells in the gastrointestinal tract, and it is controlled by histamine, gastrin, and acetylcholine. Enterochromaffin-like (ECL) cells secrete histamine. This sequence of events results in the phosphorylation of proteins involved in the transport of hydrogen ions, ultimately causing an increase in stomach acid secretion, particularly hydrochloric acid (HCl) [33].

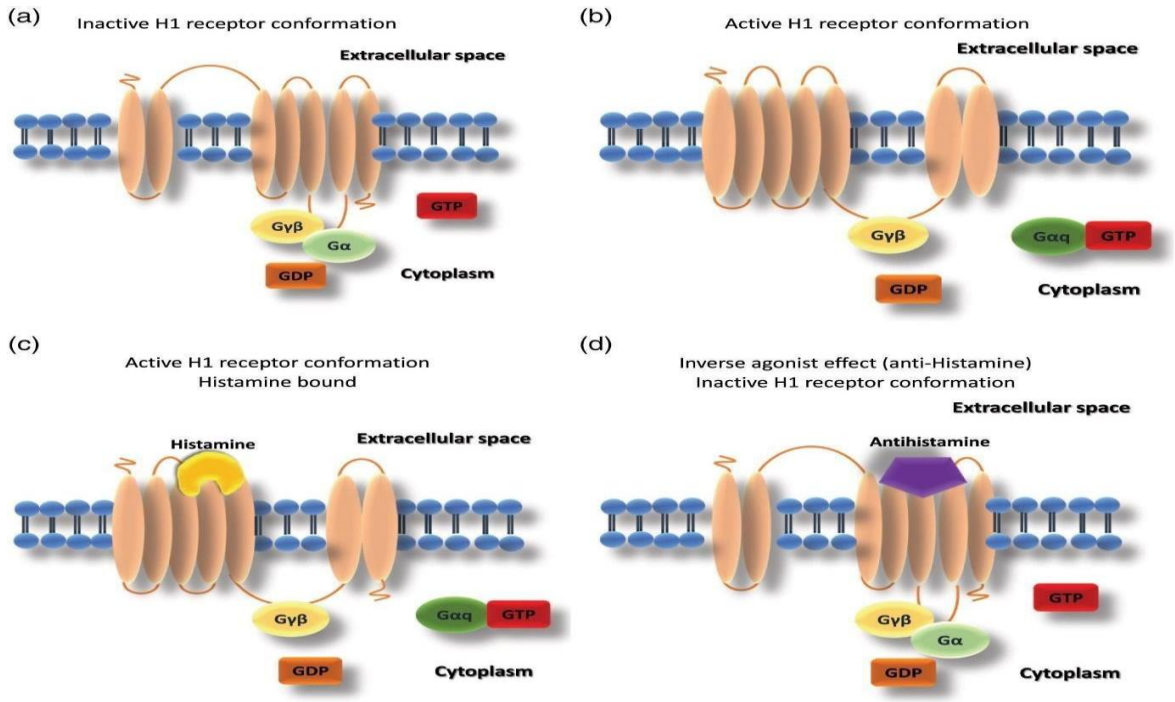

Fig.5: Mechanism of Action.

5. Method of Preparation of Fast Dissolving Film

The following procedures can be used alone or in combination to create mouth dissolving films:

5.1 Solvent Casting Method

Solvent casting is the most popular method for creating mouth dissolving films, or ODFs. In this method, the drug, polymers, and water-soluble excipients are dissolved in deionized water. It is possible to achieve homogeneity in a mixture by applying strong shear forces, which are typically produced by a shear processor.
The choice of solvent is contingent on the specific drug's physicochemical attributes, including factors such as its polymorphic form, sensitivity to shear, and melting point. Formulation considerations include ensuring compatibility between the drug and the solvent, as well as other excipients. To prevent the entrapment of air bubbles and maintain uniformity in the prepared films, a vacuum pump is employed for deaeration.
The solvent casting method has been successfully used to prepare various ODFs, such as tianeptine sodium and mosapride. An important factor in this process is the solution's viscosity. Different concentrations of pullulan, typically ranging from 2% to 8%, are used to create low-viscosity solutions that facilitate the casting of films. Additionally, the solvent casting method has been effectively applied to produce fast- disintegrating films containing substances like anastrozole, utilizing materials like Polyvinyl alcohol and HPMC (E5) [34,35]
This method involves dissolving the drug and other excipients in one suitable solvent and dissolving water-soluble polymers in another. After that, these two solutions are combined, agitated, and put into petri dishes to dry [34, 1, 35].

Polymer dissolved in solvent + Drug & excipient dissolved in suitable solven

↓

To form solution both solutions are mixed with rapid stirring

↓

homogenous solution is then spread on flat surface dried.

↓

Films formed.

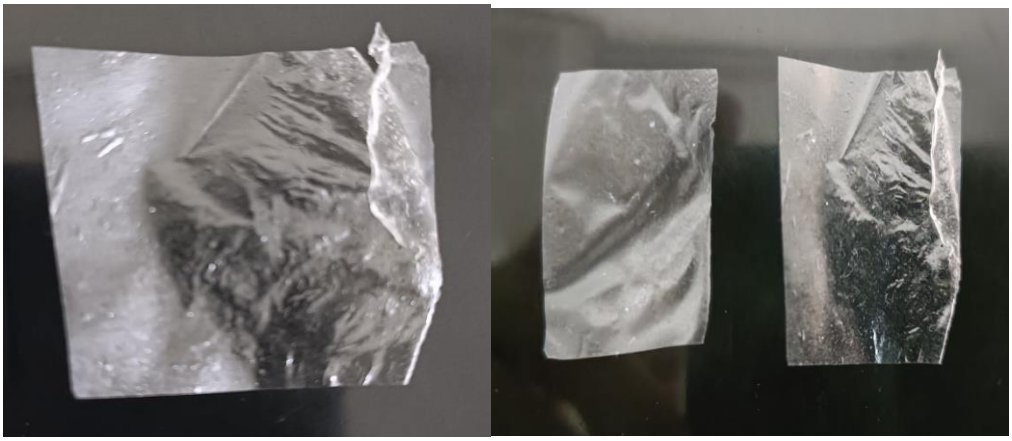

Fig.6: Mouth dissolving film.

5.2 Preparation of Fast Dissolving Films

For controlled solvent evaporation, the casting solution (20 ml) was put into a petri dish and set to the side. The film was peeled off and cut into squares of 2 × 2 cm (4 cm2), containing around 10 milligrams of medication per square. These films were sealed in self-sealing covers and placed in a desiccator for an additional two days to dry completely [5].

Table 2: Formulations of HPMC K4M

Formulation Code	Polymer(mg)	HPMC K4M(mg)	Drug (mg)	Propylene glycol (ml)	Aspartame (mg)
FA1	HPMC K4M	250	10	0.25	50
FA2	HPMC K4M	350	10	0.25	50
FA3	HPMC K4M	450	10	0.25	50

Table 3: Formulations of HPMC K4M and MCC combination

Formulation Code	HPMC K4M (mg)	MCC (mg)	Drug (mg)	Propylene glycol (ml)	Aspartame (mg)
FB1	250	200	10	0.25	50
FB2	300	150	10	0.25	50
FB3	350	100	10	0.25	50

6. Evaluation Parameters for Antihistamine MDFs

Physical Appearance:
The films were all visually examined for smoothness, homogeneity and color.
Uniformity of Weight:
Ten samples of each type of formulation had their individual weights measured, and the average weight was computed. Each batch of formulas' film weight was determined to be uniform, it was noted. Due to the viscosity (a greater concentration of polymer causes a higher viscosity) and the thickness of the films, among the HPMC K4M formulations, the weight rose with increased amount of polymer utilized. Table 5 provides the findings of all formulations.
Thickness: A screw gauge with a 0–10 mm range and a 0.001 mm revolution was used to measure the thickness of the film. After setting the anvil of the gauge to zero, the film was gently placed on it. The dial gauge's readings were noted. Three duplicates of each measurement were made.
Drug Content: A 1 cm2 film was dissolved in 5 mL of artificial saliva in a 10 mL volumetric flask in order to measure the drug content. Artificial saliva was then used to adjust the volume. After being suitably diluted, the samples underwent analysis. Three separate analyses of this data were performed.

Tensile Strength: The Mini Tech Tensiometer-UTM9051, equipped with a 500 N (50 kg) load cell, was used to measure the tensile strength, or the highest stress at which a film specimen fractures. Data was gathered using Test Bench II, the equipment's software. Tensile strength was measured while samples with the proper film thickness and fixed dimensions were held in place between pneumatic grips. For every sample, the experiment also computed the software's percent elongation data. Three separate tests were run for each of these.

$$\text{Tensile strength} = \frac{\text{Force at break}}{\text{Initial cross sectional area of the sample } (mm^2)}$$

Percent Elongation: Using the formula Percentage Elongation = ([L - L0] × 100) / L0, where L is the final length and L0 is the initial length, the percentage elongation was computed by measuring the increase in the film's length following the measurement of its tensile strength. The tensile strength measurement computations were derived in triplicate using the Test Bench II software.

$$\%\text{Elongation at break} = \frac{\text{Increase in length}}{\text{original length}} \times 100$$

Folding Endurance: The film was folded repeatedly at the same spot until it broke to determine the film's folding endurance, which indicates how brittle it is. These tests were performed in triplicate, and the number of folds before breakage was noted.

Surface pH: Wetting the created film with distilled water in a Petri dish and measuring the pH by contacting the film surface with an electrode from a pH meter allowed us to ascertain the pH of the films. As acidic or basic pH values can irritate the oral mucosa, determining the surface pH is essential [36, 37]

Content Uniformity: The content of the film was ascertained by employing conventional test techniques that are listed for each medication in different pharmacopeias. The Japanese pharmacopeia required the acceptance value of the test to be less than 15%, while USP27 specified a content range of 85% to 115% with a standard deviation of less than or equal to 6%. For the purpose of calculating the drug concentration in individual films, content uniformity was established [38, 39].

Table 4: Composition of Mouth Dissolving Film: [40]

Composition	Concentration
Drug	1-25%
Water soluble polymer	40-50%
Plasticizers	0-20%
Fillers, colors ,flavors	0-40%

7. Evaluation Parameters with Results

Physical Appearance:

The movie outside look was assessed. Indicating that the polymers utilized in the study were found to have good film forming capabilities as mentioned in the literature, all the films formed with various polymer concentrations were found to be flexible, smooth, transparent, non-sticky, and homogenous [19-21].

Uniformity of Weight:

Ten samples of each type of formulation had their individual weights measured, and the average weight was computed. Each batch of formulas' film weight was determined to be uniform, it was noted. Due to the viscosity (a greater concentration of polymer causes a higher viscosity) and the thickness of the films, among the HPMC K4M formulations, the weight rose with increased amount of polymer utilized. Table 5 provides the findings of all formulations.

Content Uniformity:

Table 7 displays the various formulations' % medication content. All formulations had a percentage drug content that was found to be between 91 and 98%.

Tensile Strength Measurement:

Tensile strength was assessed, which is the highest stress the film specimen can sustain before cracking. This important parameter was computed by dividing the load at the rupture site by the film's cross-sectional area. A Mini Tech Tensiometer-UTM9051, outfitted with a 500N (50kg) load cell and data gathering software, was

utilized to do the measurement. Films with the proper thickness and set dimensions (LxW10x2 cm) were firmly held in place between pneumatic grips spaced 3 cm apart. The program correctly input the dimensions and calculated the cross- sectional area. To avoid any loose folds, the film was carefully placed in between the pneumatic grips. Up until the film broke, the device ran at a pace of 5 mm per minute. For every sample, data on percent elongation was also taken out of the program. To guarantee dependability, this extensive experiment was conducted in triplicate [42].

Table 5: Results of tensile strength, percentage elongation and percentage drug content of formulations.

Formulation Code		Tensile strength* (kg/cm^2)	% Elongation*	Percentage Drug content in 4 cm^2
FA	FA1	1.155±0.032	31.85 ±0.475	98.25
	FA2	1.330 ±0.022	34.26 ±0.359	98.08
	FA3	1.479 ±0.022	41.15 ±0.406	93.95
FB	FB1	0.365 ±0.016	20.96 ±0.589	97.35
	FB2	0.505 ±0.023	25.78 ±0.412	95.50
	FB3	0.625±0.022	28.89±0.408	93.55

Percentage Elongation:

The percentage elongation was studied, which indicates how much the film deforms under stress. Higher concentrations of plasticizer often lead to greater elongation, and this metric is correlated with that concentration. Using the following formula, the % elongation was calculated by calculating the length increase of the film after the tensile strength evaluation:

Percentage Elongation = ([L - L0] × 100) / L0, where L represents the final length and L0 represents the initial length.

To guarantee accuracy and uniformity, the complete operation was carried out in duplicate. The % elongation data was estimated using the Test Bench II program [43].

Film Thickness:

Micro meter screw gauge was used to measure the thickness of 6 films of each formulation, and an average thickness was calculated. The findings for all formulations are shown in Table 5, and they are shown to be within the permitted range for rapid dissolving films [8] of 100 m to 200 m. additionally, each formulation's film thickness (HPMC K4M) was found to be consistent. The thickness of the films with more polymer content rose just little.

Folding Endurance Assessment: The test for folding endurance, which measures a film's brittleness, involved repeatedly folding the film at the same spot until it broke. The folding endurance value was determined by counting the number of folds made

before the film broke. To guarantee the accuracy of the findings, this crucial assessment was also carried out three times [44].

Disintegration Test: A film with a surface area of 2 x 2 cm (4 cm2) was laid on a glass petri dish containing 10 ml of pH 6.8 phosphate buffer. In vitro disintegration time was recorded as the amount of time needed to break the film [40].

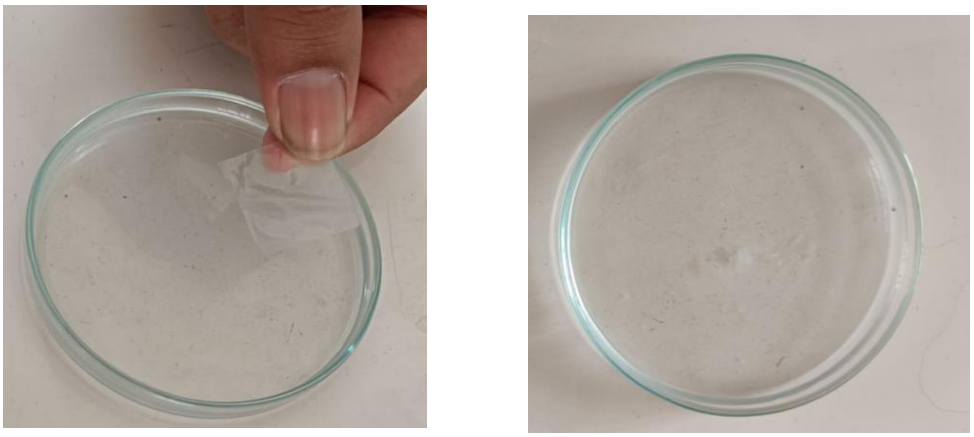

Fig.7: Disintegration test

Table 6: Data related to physicochemical properties

Formulation Code		Weight (mg)*	Thickness (mm)*	Surface pH#	Folding endurance	Disintegration time (s)
FA	FA1	57.56±0.578	0.135 ±0.005	6.33 ±0.007	>300	8.04±1.08
	FA2	64.55 ±0.805	0.140 ±0.007	6.65 ±0.022	>300	8.35±2.10
	FA3	73.20±0.669	0.135±0.008	6.57 ±0.009	>300	8.70±2.11
FB	FB1	61.80±0.975	0.150 ±0.010	6.49 ±0.029	>300	7.03±2.15
	FB2	62.85 ±0.752	0.166 ±0.012	6.71 ±0.020	>300	7.30±2.19
	FB3	74.30 ±0.905	0.145 ±0.082	6.68 ±0.012	>300	8.10±1.35

In-vitro Dissolution Test:

Chlorpheniramine maleate fast-release films' dissolution profile was tested in a beaker with 20–30 ml of simulated salivary fluid (pH 6.8) acting as the dissolving medium and being kept at 37±0.5°C. At 100 rpm, the medium was swirled. Every 5 s, aliquot (5 ml) of the dissolving media were removed and replaced with the equivalent volume of fresh medium. By using a UV spectrophotometer set to 262 nm, the amount of medication in the withdrawn samples was calculated. All samples underwent three trials, and an average value was calculated. The amount of medication that was dissolved on average during different time periods was quantified and shown against time. [41]

Fig.8: Dissolution test.

Table 7: In vitro drug dissolution profile data

Time(s)	Percentage drug release					
	FA			FB		
	FA1	FA2	FA3	FB1	FB2	FB3
00	0.000	0.000	0.000	0.000	0.000	0.000
10	22.68	27.07	23.68	25.48	24.51	22.69
20	30.27	31.73	31.25	37.78	32.01	35.09
30	51.15	51.73	52.10	44.71	44.71	41.15
40	71.44	62.88	66.42	47.98	65.96	60.76
50	84.80	75.09	82.30	65.19	84.42	75.28
60	95.52	94.03	91.5	85.09	91.13	94.90

*Average of 3 determinations

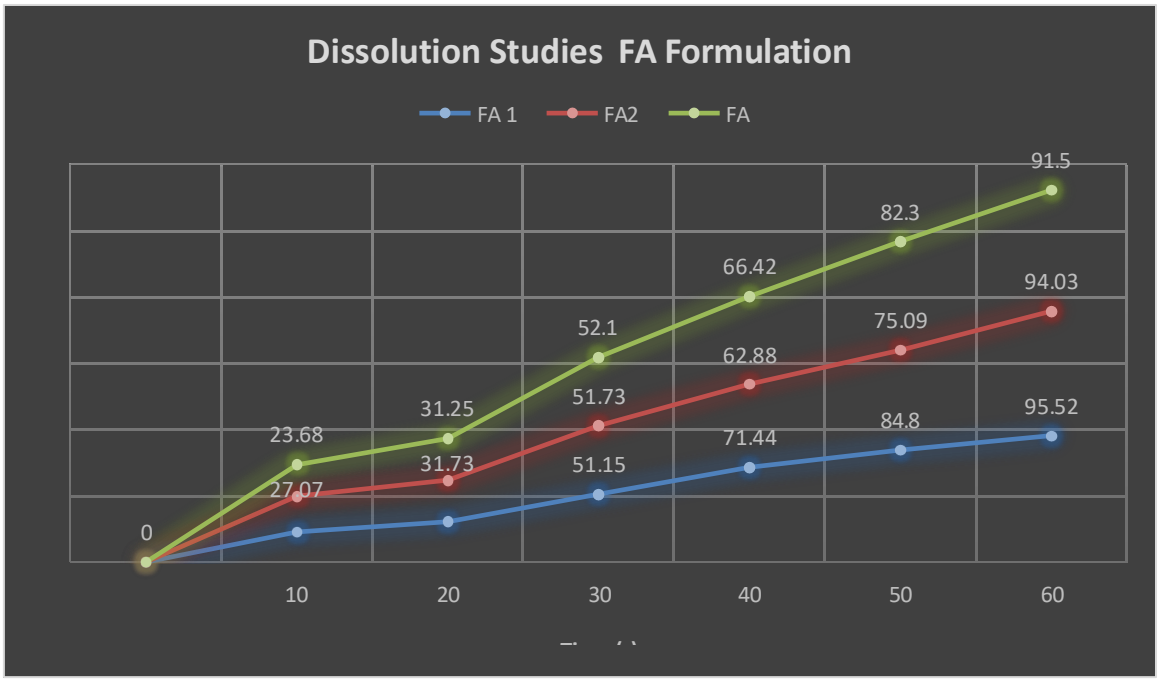

Fig.9: Dissolution profile of formulations FA.

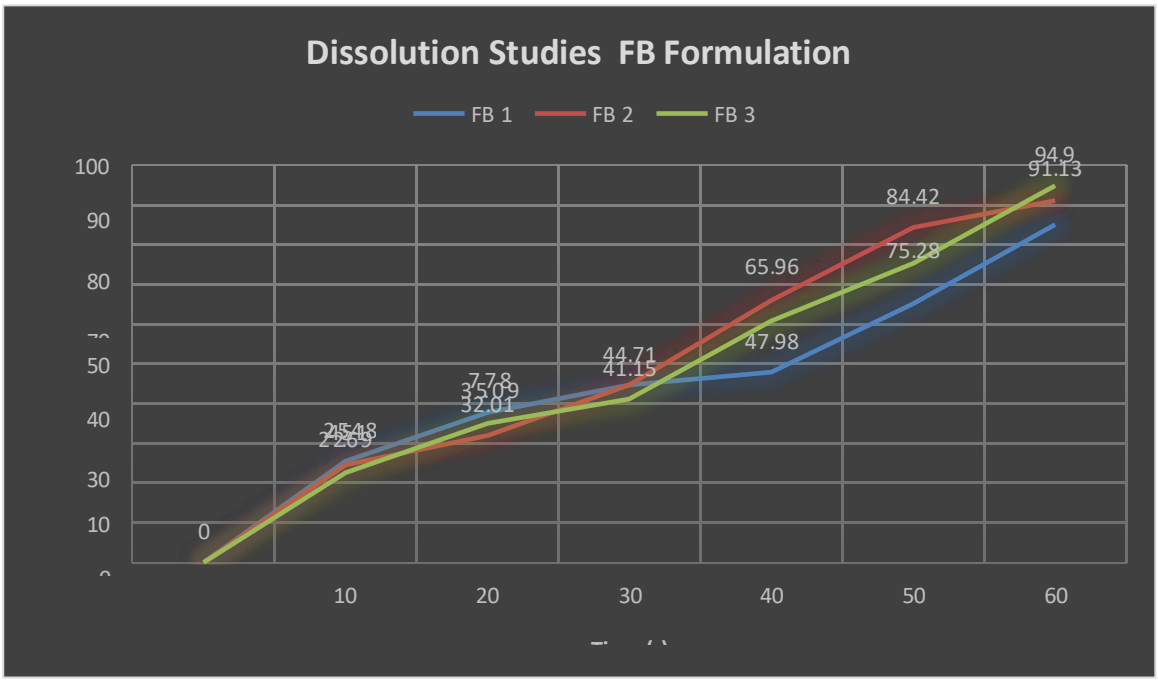

Fig.10: Dissolution profile of formulations FB.

Stability Studies: Studies on the stability of MDFs with 0.6% w/w Chlorpheniramine maleate and HPMC E3 were carried out. For six months, the films were kept in an atmosphere that was kept at 40℃ and 75 ± 5% relative humidity, enclosed in aluminum pouches to ensure airtightness. In order to determine the stability of the films over time, an assessment of their weight, appearance, and drug content was conducted as part of the inspection.

Table 8: Stability study data (Drug content)

Formulation Code	Initial % drug content	2-8°C (45% RH)			25-30°C (60% RH)		
		15 days	30 days	45 days	15 days	30 days	45 days
FA1	94.49	94.42	94.30	94.25	94.43	94.37	94.36
FA2	97.01	96.99	96.95	96.92	96.81	96.79	96.75
FA3	94.25	94.19	94.12	94.05	94.10	94.07	93.98
FB1	93.88	93.82	93.78	93.75	93.83	93.70	93.65
FB2	96.20	95.99	95.91	95.88	95.98	95.89	95.85
FB3	95.04	94.98	94.92	94.88	94.83	94.82	94.75

Table 9: Stability study data (in vitro release)

Formulation Code	Initial % drug release	2-8°C (45% RH)			25-30°C (60% RH)		
		15 days	30 days	45 days	15 days	30 days	45 days
FA1	89.50	89.46	89.42	89.35	89.45	89.40	89.35
FA2	75.80	75.80	75.73	75.67	75.76	75.70	75.65
FA3	65.85	65.83	65.75	76.74	65.89	86.80	65.79
FB1	78.28	78.25	78.19	28.15	78.25	78.21	78.18
FB2	83.90	83.85	83.80	83.79	83.85	83.84	83.78
FB3	92.80	92.75	92.68	92.65	92.72	92.65	92.60

Content Uniformity: In order to ensure content homogeneity, a film's contents had to be assessed using standard assay procedures that were listed for each medication in different pharmacopoeias. Twenty samples were tested in this manner using analytical methods. The findings had to meet the following acceptance criteria: they had to follow USP27 norms and fall between 85% and 115% with a standard deviation of less than or equal to 6%, or they had to show a variation of less than 15%, as per the Japanese pharmacopeia. To determine the number of drugs in each movie, content consistency was evaluated [38, 39].

8. Comparison With Marketed Product

Additionally, the drug release profile of the commercially available version of Chlorpheneramine maleate 4 mg (CPM-4) was established and compared to the most effective formulation across all batches. The medication release from fast-dissolving film was found to be substantially quicker than that from tablets (Table 10).

Fig.11: Marketed tablet.

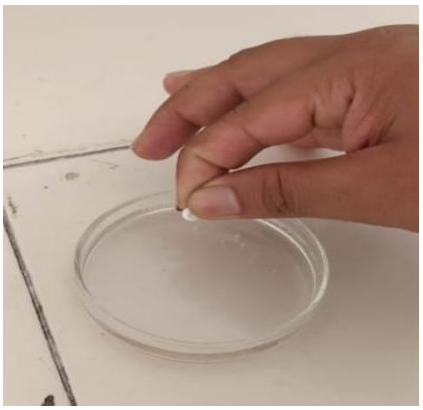

Fig.12: Disintegration test of tablet.

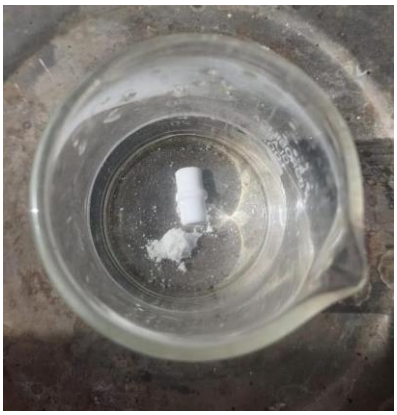

Fig.13: Dissolution test of tablet.

Table 10: In vitro drug release profile data of marketed tablet

Time (s)	Concentration (µg/ml)	% drug released
00	0.000	0.00
10	0.567	5.07
20	0.913	8.28
30	1.322	11.85
40	1.798	16.12
50	2.408	21.71
60	3.103	27.97

*Average of 3 determination

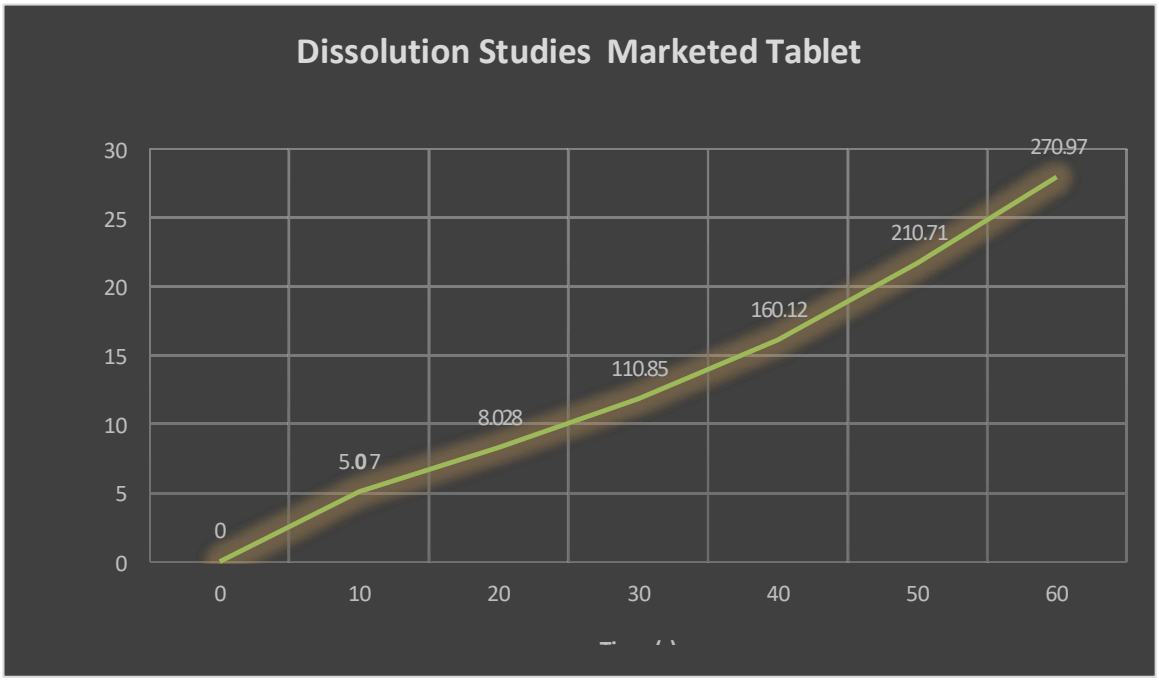

Fig.14: Dissolution profile of Market formulations.

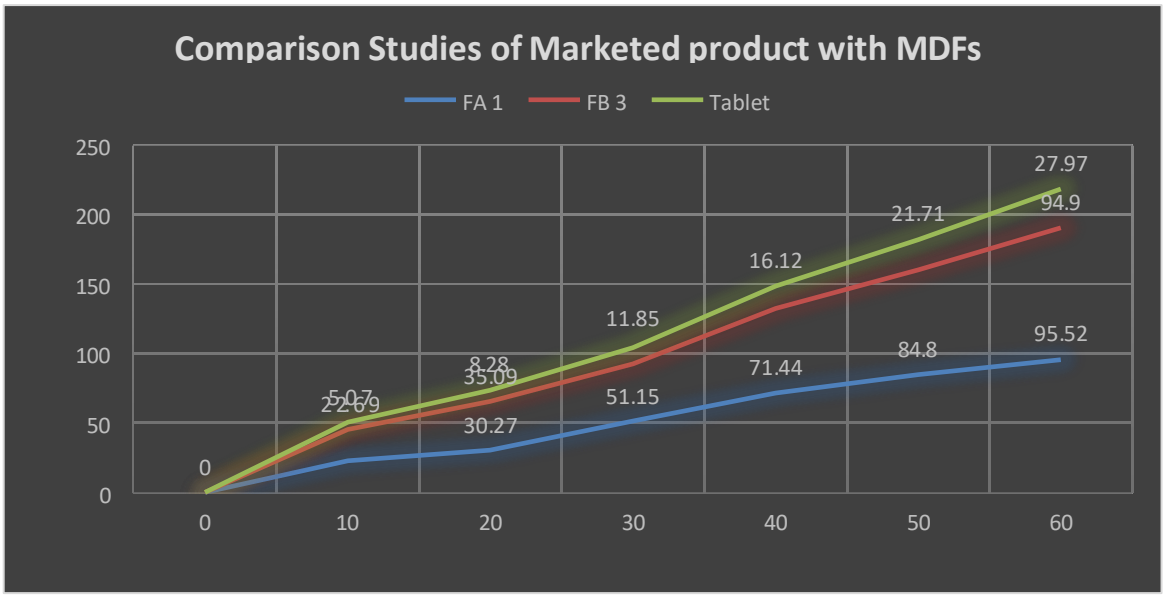

Fig.15: Comparison Studies of Marketed product with MDFs.

9. Compatibility Studies

To understand the interaction between the drug and the polymers, IR tests were conducted on the pure drug, HPMC K4M, MCC, and the formed films Figure (NUMBER). lists the values for the IR spectrum. The main peaks in the IR spectra of the pure medication "Chlorphenaramine maleate" were seen at 1682 cm-1 owing to carbonyl group stretching in the C=O direction, 1516 cm-1 in the C=N direction, 1341 cm-1 in the C=C direction, and 1060 cm-1 in the C-N vibration direction. Peak at 81 cm-1 is caused by stretching of the C-Cl bond. When mixed with polymers for the formulation, it was seen that there was no appreciable change in the major peaks of Clorpheniramine maleate, indicating that there was no drug-polymer interaction.

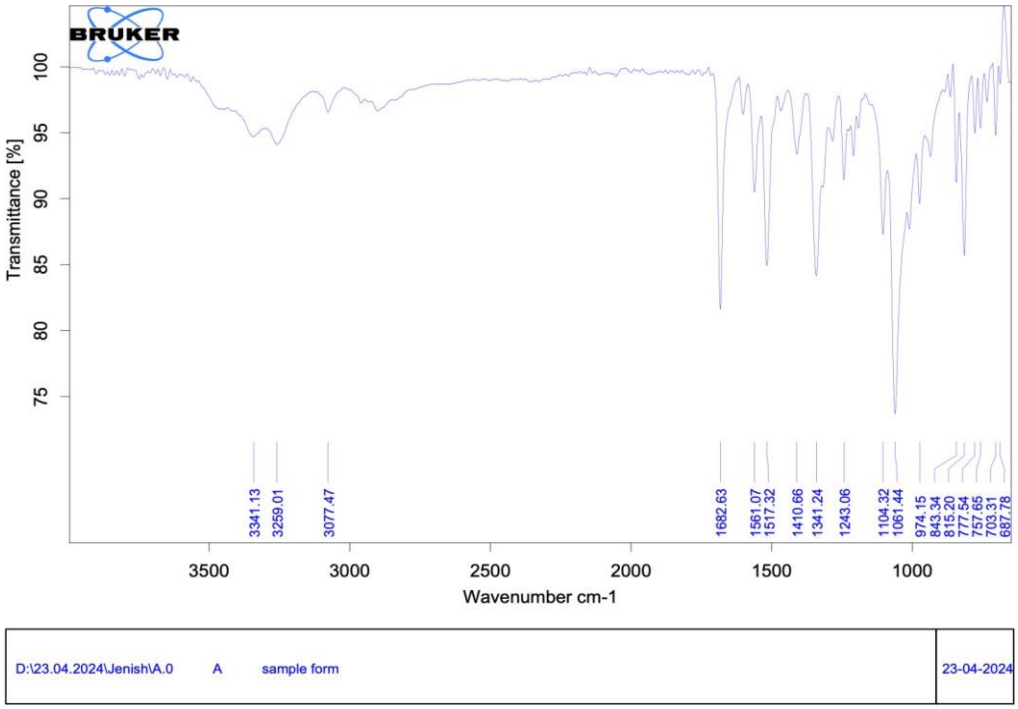

Fig.16: FTIR spectrum of CPM.

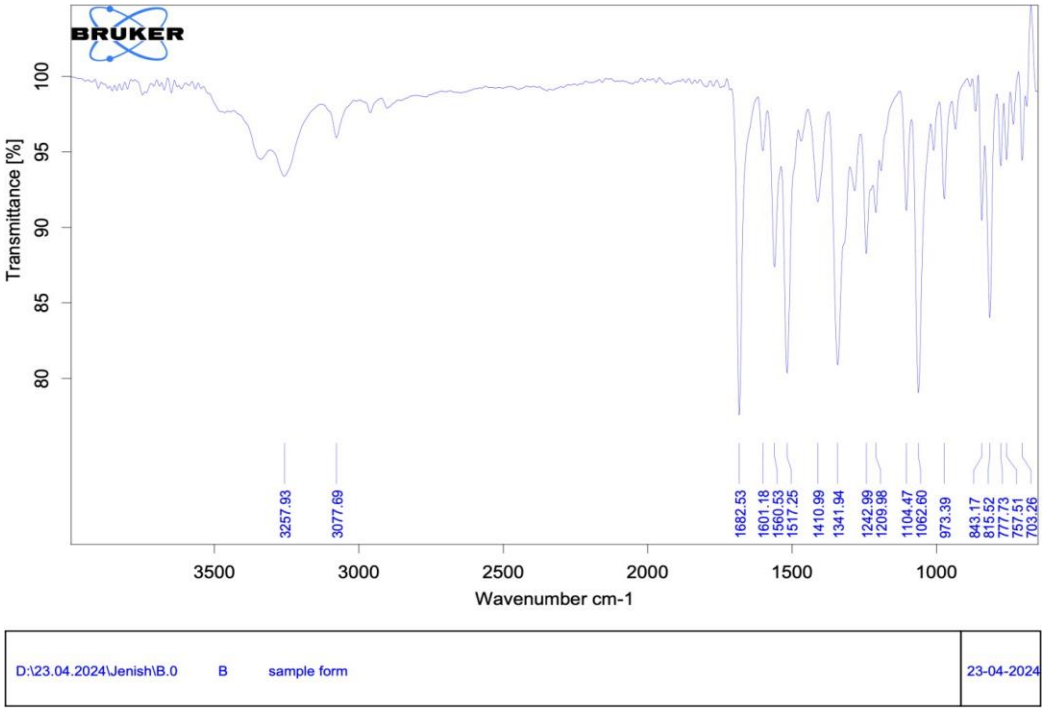

Fig.17: FTIR spectrum of HPMC+CPM.

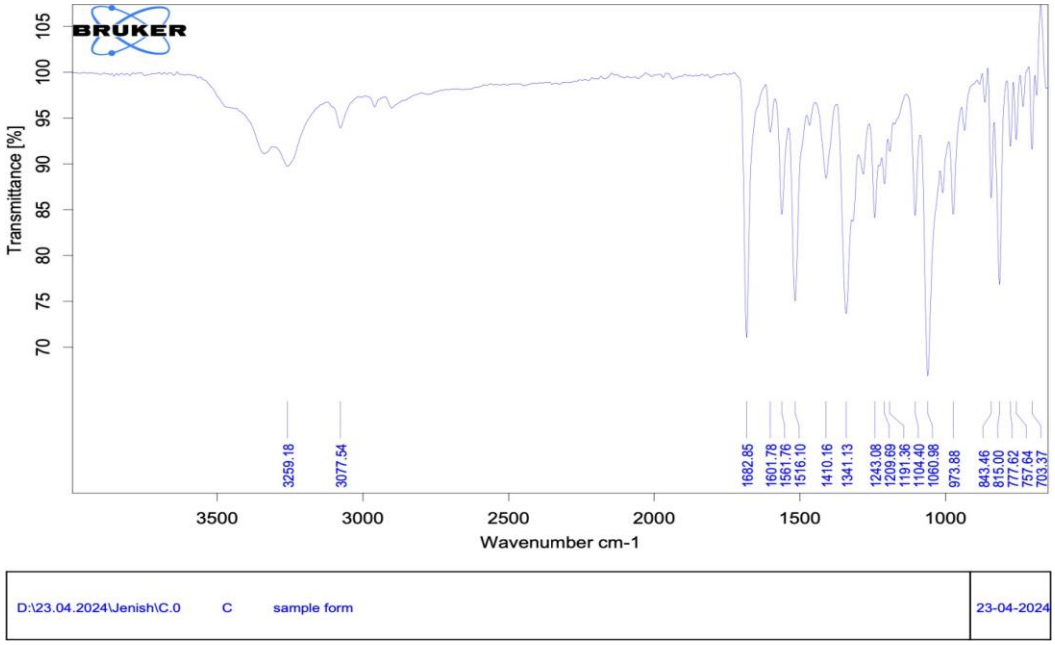

Fig.18: FTIR spectrum of MCC+CPM.

9. Discussion

The provided text discusses the merits of fast-dissolving oral films (FDOFs) and their relevance in treating allergic rhinitis. FDOFs are ultrathin strips designed to dissolve swiftly in saliva, making them an ideal drug delivery option, especially for individuals who may struggle with swallowing conventional tablets, such as children and the elderly. The text outlines various methods for preparing FDOFs and essential criteria for assessing these films. It underscores the advantages of FDOFs, including their ease of administration, rapid onset of action, enhanced bioavailability, and stability. These films are convenient, require no water for ingestion, offer precise dosing, and are well- suited for pediatric and geriatric patients. They also impart a mouth- refreshing effect. Nonetheless, the text acknowledges some limitations of FDOFs, such as challenges associated with formulating high-dose drugs and constraints with protein-based medications. It also mentions the limited availability of suitable polymers and potential issues related to thermal processes. Comparative analyses with traditional tablets reveal that FDOFs yield faster dissolution rates, resulting in more consistent

drug release profiles and, consequently, more predictable drug concentrations in the bloodstream. The increased bioavailability of FDOFs is attributed to their ability to bypass first-pass liver metabolism, as they are directly absorbed through the oral mucosa into the bloodstream, leading to a swifter onset of action. Furthermore, a pharmacokinetic study demonstrates that FDOFs can be a viable alternative to conventional tablets, delivering similar therapeutic outcomes in terms of drug administration. In summary, the text imparts valuable insights into the advantages, formulation, evaluation, and relative effectiveness of fast-dissolving oral films. These films represent a promising drug delivery approach, especially in conditions like allergic rhinitis, where rapid drug response and patient compliance are of paramount importance. These films represent a promising drug delivery approach, especially in conditions like allergic rhinitis, where rapid drug response and patient compliance are of paramount importance. It has also been discussed that the given formulations FA 1 and FB 3 exhibit higher drug release percentages compared to the tablet. FA 1 has the highest release rate at 95%, followed by FB 3 at 91%, while the tablet only achieves 27% release. This suggests that both FA 1 and FB 3 formulations are more effective in releasing the drug compared to the tablet. However, further analysis is needed to understand the differences in formulation and factors affecting drug release rates. The disintegration parameters indicate the ability of a formulation to break down into smaller particles for drug release. The lower drug release percentage of the tablet suggests a potential delay in disintegration compared to formulations FA 1 and FB 3, which exhibit higher release rates. This highlights the importance of optimizing disintegration parameters to enhance drug delivery efficiency.

10. Conclusions

In conclusion, the comparison of drug release percentages among the three formulations indicates that FA 1 and FB 3 are more efficient in releasing the drug compared to the tablet. FA 1 formulation demonstrates the highest drug release at 95%, followed by FB 3 at 91%, while the tablet only achieves a 27% release rate. These findings suggest that both FA 1 and FB 3 formulations could be preferable options for drug delivery due to their higher release rates also conclude that, the comparison of disintegration parameters suggests that formulations FA 1 and FB 3 likely have shorter disintegration times compared to the tablet, leading to higher drug release percentages. However, further investigation into formulation characteristics and their impact on drug release kinetics would be beneficial for optimizing drug delivery systems. The research findings indicate that fast-dissolving oral films (FDOFs) serve as a patient-friendly drug delivery method characterized by rapid dissolution, providing advantages like user- friendliness, improved bioavailability, and increased stability. Their utility is particularly noteworthy for individuals facing challenges in swallowing conventional tablets, a demographic that includes children and the elderly. Although there are formulation complexities and certain limitations, FDOFs demonstrate superiority in comparative investigations by ensuring quicker and more consistent drug release. Their capacity to bypass first-pass metabolism leads to expedited therapeutic effects. FDOFs stand as a promising development in drug delivery, offering potential applications across various medical conditions, including the treatment of allergic rhinitis. This contributes to improved patient compliance and faster medication administration. The ongoing research endeavors hold the promise of yielding further innovative solutions in healthcare delivery.

Conflict of Interest

The authors declare that there is no conflict of interest related to this research work.

Source of Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

[1] Kothapuvari, P. K., Rawat, S., Kadimpati, K. K. (2016). Preparation of fast dissolving oral films of new generation antimigraine drugs by solvent casting method. *Int J Curr Res.,* 8(5), 30704–10.
[2] Chang, R., Guo, X., Burnside, B., Couch, R. (2000). A review of fast dissolving tablets. Pharm Tech (North America), 24, 52-8.
[3] Bi, Y., Sunada, H., Yonezawa, Y., Dayo, K., Otsuka, A., Iida, K. (1996). Preparation and evaluation of a compressed tablet rapidly disintegrating in the oral cavity. *Chem Pharm Bull*, 44, 2121-7.
[4] Van, Scoik, K. G. (1992). Solid pharmaceutical dosage in tablet triturate form and method of producing same. US Patent No. 5082667.
[5] Allen, L. V., Wang, B. (1998). Rapidly dissolving tablet. US Patent No. 5807576.
[6] Blank, R. G., Mody, D. S., Avension, M. C. (1990). Fast dissolving dosage forms. US Patent No. 4946684.
[7] Roser, B. J., Blair, J. (1998). Rapidly soluble oral solid dosage forms, methods of making same, and composition thereof. US Patent No. 5762961.
[8] Wehiling, F., Shuehle, S. (1996). Process of preparing a fraction having a high content of α-lactalbumin from whey and nutritional compositions containing such fractions. US Patent No. 5503864.

[9] Gregory, G. K., Peach, J. M., Du, Mayan, J.D. (1983). Articles for carrying chemicals. US Patent No. 4198371.
[10] Yarwood, R. J., Kearney, P., Thompson, A. R. (1998). Process for preparing solid pharmaceutical dosage forms. US Patent No. 5738875.
[11] Chang, R., Guo, X., Burnside, B., Couch, R. (2000). A review of fast dissolving tablets. *Pharm Tech (North America)*, 12:52-8.
[12] Misra, T. K., Currington, J. W., Kamath, S. V., Sanghvi, P. P., Sisak, J. R., Raiden, M. G. (1999). Fast dissolving comestible units formed under high speed/high pressure conditions. US Patent No. 5869098.
[13] Mizumoto, T., Masuda, Y., Fukui, M. (1996). Intrabuccally dissolving compressed moldings and production process thereof. US Patent No. 5576014.
[14] Nathan, R. A. (2007). The burden of allergic rhinitis. *Allergy Asthma Proc*., 28(1), 3-9.
[15] Rondon, C., Fernandez, J., Canto, G., Blanca, M. (2010). Local allergic rhinitis: concept, clinical manifestations, and diagnostic approach. *J Investig Allergol Clin Immunol*, 20(5), 364-371.
[16] Piau, J. P., Massot, C., Moreau, D., Ait-Khaled, N., Bouayad, Z., Mohammad, Y., Khaldi, F., Bah-Sow, O., Camara, L. et al. (2010). Assessing allergic rhinitis in developing countries. *Int J Tuberc Lung Dis*, 14(4), 506-512.
[17] Bousquet, J., Khaltaev, N., Cruz, A. A., Denburg, J., Fokkens, W. J. et al. (2008). Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). Allergy, 63, 8-160.
[18] Saleem, T., Khalid, U., Sherwani, U. U., Ghaffar, S. (2009). Clinical profile, outcomes, and improvement in symptoms and productivity in rhinitic patients in Karachi, Pakistan. *BMC Ear Nose Throat Disord*, 9, 12.
[19] Skoner, D. P. (2001). Allergic rhinitis: definition, epidemiology, pathophysiology, detection, and diagnosis. *J Allergy Clin Immunol*, 108(1), S2-S8.
[20] Lim, M. Y., Leong, J. L. (2010). Allergic rhinitis: evidence-based practice. *Singapore Med J*. 51(7), 542-550.
[21] Hammersley, V. S., Walker, S., Elton, R., Sheikh, A. (2010). Protocol for the adolescent hayfever trial: cluster randomized controlled trial of an educational intervention for healthcare professionals for the management of school-age children with hayfever. *Trials*, 11, 84.
[22] Small, P., Frenkiel, S., Becker, A., Boisvert, P., Bouchard, J. et al. (2007). The Canadian Rhinitis Working Group. Rhinitis: a practical and comprehensive approach to assessment and therapy. *J Otolaryngol*, 36, S5- S27.
[23] Dykewicz, M. S., Hamilos, D. L. (2010). Rhinitis and sinusitis. *J Allergy Clin Immunol*. 125, S103-S115.
[24] Lee, P., Mace, S. (2009). An approach to allergic rhinitis. *Allergy Rounds*, 1,1.
[25] Bourdin, A., Gras, D., Vachier, I., Chanez, P. (2009). Upper airway 1: allergic rhinitis and asthma: united disease through epithelial cells. *Thorax*, 64(11), 999-1004.
[26] Simons, F. E. (2004). Advances in H1-antihistamines. *N Engl J Med*., 351(21), 2203- 2217.
[27] Pirahanchi, Y., Sharma, S. (2022). Physiology, Bradykinin. StatPearls, Treasure Island (FL): Jul 25.
[28] Heda, R., Toro, F., Tombazzi, C. R. (2023). Physiology, Pepsin, StatPearls, Treasure Island (FL): May 1.
[29] Desu, P. K., Brahmaiah, B., Nagalakshmi, A., Neelima, K., Nama, S., Baburao, C. (2013). An overview of rapid dissolving films. *Asian J. Pharm. Res*., 3, 15-23.
[30] Dinge, A., Nagarsenker, M. (2008). Formulation and evaluation of fast dissolving films for delivery of triclosan to the oral cavity. *AAPS Pharm. Sci. Tech*., 9, 349- 356.
[31] Rekha, M. R., Sharma, C. P. (2007). Pullulan as a promising biomaterial for biomedical applications: a perspective. *Trends Biomater Artif Organs*, 20(2), 116- 121.
[32] U.S. Congress, Office of Technology Assessment, Biopolymers: Making Materials Nature's Way-Background Paper, OTA-BP-E102 (Washington, DC: U.S. Government Printing Office, 1993).
[33] Saini, S., Rana, A. C., Gupta, S. (2011). Optimization of formulation of fast dissolving films made of pullulan polymer. *Int J Pharm Sci Rev Res.*, 9(1), 127- 131.
[34] Claudia, A. R. B., Bello-Perez, L. A., Gacia, M. A., Martino, M. N., Solorza- Feria, J., Zaritzky, N. E. (2005). Carbohyd. *Polym*, 60, 235-244.
[35] Laohakunjit, N., Noomhorm, A. (204). Effect of plasticizers on mechanical and barrier properties of rice starch film. *Starch/Staerke*, 56, 348-356.
[36] Kunte, S., Tandale, P. (2010). Fast dissolving strips: A novel approach for the delivery of verapamil. *J Pharm Bio Sci.*, 2(4), 325-328.
[37] Nalluri, B. N., Sravani, B., Maheshwari, K, M., Saisri, A. V., Brahmini, S. R. (2013). Development and evaluation of mouth dissolving films of salbutamol sulfate. *J Chem Pharmaceut Res.*, 5(3), 53-60.
[38] Maheshwari, K. M., D, P. k., Sravanthi, D., Salma, S., Naga, Pravallika U., Nalluri, B. N. (2014). Development and evaluation of mouth dissolving films of amlodipine besylate for enhanced therapeutic efficacy. *Journal of Pharmaceutics*, 20949, 1-10.

[39] Parmar, D., Patel, U., Bhimani, B., Tripathi, A., Daslaniya, D., Patel, G. (2012). Orally Fast dissolving films as dominant dosage form for quick release. *IJPRBS*, 1(3), 27-41.
[40] Sapkal, N. P., Kilor, V. A., Daud, A. S., Bonde, M. N. (2011). Development of fast dissolving oral thin films of ambroxol hydrochloride: Effect of formulation variables. *JAPR*, 2(2), 102-109.
[41] Halnor, P. K., Gondkar, S. B., Saudagar, R. B. (2015). A short review: An innovative drug delivery system of fast dissolving oral films. *International journal of institutional pharmacy and life sciences*, 05(03), 381-393.