International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

Rapid-Dissolving Edible Film of Dimenhydrinate: Effect of Gelatine Concentration on Performance

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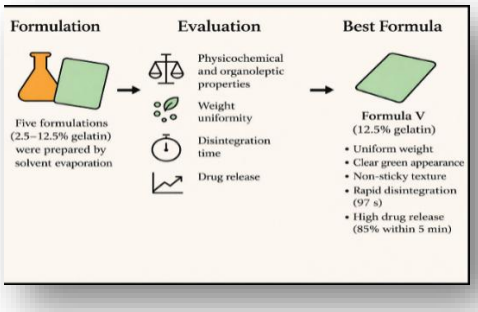
Received: 15-01-2026
Accepted: 10-02-2026
Available online: 19-02-2026

ABSTRACT

Background: Motion sickness is commonly associated with nausea and vomiting during travel. Dimenhydrinate, an ethanolamine-derived antihistamine, is widely used as an antiemetic; however, conventional oral dosage forms may present swallowing difficulties. Edible films offer a rapidly dissolving alternative that may improve patient convenience and onset of action.
Objective: This study aimed to formulate and optimize dimenhydrinate-loaded edible films using type B gelatine as a film-forming polymer and to evaluate their physicochemical and dissolution characteristics.
Methods: Five formulations containing type B gelatine at concentrations of 2.5%, 5%, 7.5%, 10%, and 12.5% (w/v) were prepared using the solvent evaporation method. Liquid film solutions were characterized for specific gravity, pH, and viscosity. The resulting films were evaluated for organoleptic properties, weight uniformity, thickness, disintegration time, moisture loss, content uniformity, and in vitro dissolution performance.
Results: The formulation containing 12.5% gelatine demonstrated optimal handling and structural integrity, with an average thickness of 110 µm and a disintegration time of 97 s. Weight variation remained within ±10% of the mean, while content uniformity ranged from 91.11% to 99.89% (RSD 2.94%), complying with pharmacopeial limits. Rapid drug release was observed, with more than 85% of dimenhydrinate dissolved within 5 minutes.
Conclusion: Type B gelatine-based edible films provide a viable platform for dimenhydrinate delivery, exhibiting acceptable uniformity and rapid dissolution performance. Further optimization of disintegration time and mechanical properties may enhance suitability for orodispersible applications.

Keywords: *Dimenhydrinate; edible film; oral thin film; gelatine; solvent evaporation; dissolution.*

GRAPHICAL ABSTRACT



HIGHLIGHTS

- Dimenhydrinate was successfully formulated into rapid-dissolving edible films using type B gelatin.
- Formula V (12.5% gelatin) exhibited optimal physical properties: clear green color, non-sticky texture, and acceptable thickness (110 μm).
- Content uniformity met pharmacopeial standards (91.11–99.89%, RSD 2.94%), with no weight deviation exceeding 10%.
- Dissolution testing showed fast drug release, with 85% of dimenhydrinate dissolved within 5 minutes.
- The edible film dosage form enhances patient compliance and offers potential for improved antiemetic therapy.

INTRODUCTION

Motion sickness is a common condition characterized by nausea and vomiting during travel by airplane, car, or ship. Although not considered a serious illness, it significantly disrupts travel comfort and may persist for several days post-journey. Motion sickness encompasses various forms, including seasickness, airsickness, and carsickness, and affects a wide range of individuals during transit [1-3].

To prevent and treat motion sickness, antiemetic agents such as dimenhydrinate are frequently administered. Dimenhydrinate is an ethanolamine-derived antihistamine containing a diphenhydramine moiety, which exerts antiemetic effects primarily through antagonism of histamine H1 receptors and inhibition of acetylcholine activity. This dual mechanism suppresses cholinergic stimulation in the vestibular and reticular systems, thereby reducing nausea and vomiting [4,5].

Dimenhydrinate is well absorbed via oral administration. In Indonesia, it is commercially available in tablets, capsules, and pediatric syrup sachets. With advances in pharmaceutical technology, novel oral dosage forms such as edible films have emerged. Edible films are thin layers composed of ingestible materials including carbohydrates (e.g., starch, cellulose derivatives, gums), proteins, and lipids, either individually or in combination. Initially developed for food packaging to preserve moisture and prevent oxidation, edible films have since been adapted for drug delivery applications. [6,7]

These films are administered by placing them on the tongue, where they dissolve and release the active pharmaceutical ingredient into the oral cavity, similar to chewing gum. A study by Valoti et al. demonstrated that chewing gum containing 25 mg dimenhydrinate maintained plasma diphenhydramine levels, supporting its clinical efficacy against motion sickness. Therefore, edible films are expected to offer comparable therapeutic outcomes. [8-10]

The advantages of edible films include rapid dissolution in saliva, ease of administration without water, faster absorption, and improved portability due to their small, thin, and lightweight design. They are particularly suitable for children, elderly patients, and individuals with swallowing difficulties, especially during nausea episodes. [11,12]

A critical component of edible film formulation is the film-forming agent. Previous studies have utilized cassava starch [13,14], corn starch combined with sodium carboxymethyl cellulose (NaCMC) [15,16] and hydroxypropyl methylcellulose (HPMC) [17,18]. While starch-based films tend to be less transparent, synthetic polymers such as HPMC are relatively expensive. Therefore, gelatine was selected as the film-forming agent in this study [19,20].

Gelatine is derived from partial hydrolysis of collagen from animal skin, connective tissue, and bones. It exists in two types: type A (acid-treated, typically from porcine skin) and type B (alkali-treated, typically from bovine sources). To ensure halal compliance, type B gelatine was used [21,22]. Gelatine forms clear, flexible, and oxygen-impermeable films when dissolved in water with plasticizers such as glycerol or sorbitol [19,20]. Its unique property among hydrocolloids is its melting point near 37 °C, allowing gelatine-based edible films to dissolve in the mouth without leaving an unpleasant taste [23]. Additionally, gelatine offers advantages as a drug delivery matrix due to its weak drug-binding affinity and low antigenicity [24].

Based on these considerations, this study investigates the feasibility of formulating dimenhydrinate into an edible film using type B gelatine as the film-forming agent, aiming to produce a dosage form that meets pharmaceutical standards.

MATERIALS AND METHODS

Materials

Dimenhydrinate (active pharmaceutical ingredient; Recordati, Italy); gelatine type B (film-forming agent; Gelita, New Zealand); sorbitol (plasticizer; Sorini, Indonesia); propylene glycol (plasticizer; Dow Chemical Company, USA); polyvinylpyrrolidone (binder; BASF, Indonesia); aspartame (sweetener; Ajinomoto, Indonesia); menthol (flavoring agent; Wacker Specialties, South Korea); peppermint oil (flavoring agent; Fuyang Green Leaf Perfumery, China); sorbic acid (preservative; Merck, Indonesia); brilliant green FCF dye (colorant; Sensient, France); concentrated hydrochloric acid (analytical reagent; local supplier); distilled water (solvent; laboratory grade); additional analytical reagents (for raw material testing; pharmaceutical grade).

Equipment

Analytical balance (Mettler Toledo AB 204; Mettler Toledo, Switzerland); magnetic stirrer with heater (Nuova II Stir Plate; Sybron Thermolyne, USA); drying oven (Memmert U-30; Memmert GmbH, Germany); stopwatch (Nokia 3350; Nokia, Finland); micrometer screw gauge (JICA; Osaka, Japan); UV–Vis spectrophotometer (Shimadzu UV-1700; Shimadzu Corporation, Japan); disintegration tester (Guoming BJ-2; Guoming, China); pycnometer (Roda; laboratory glassware supplier); pH meter (Metrohm 620; Metrohm AG, Switzerland); viscometer (Brookfield LV; Brookfield Engineering, USA); and weighing bottles (Iwaki TE-32, Pyrex; Iwaki Glass, Japan); desiccator (laboratory standard); plastic molds (2×2 cm, reheatable) (Green Leaf, China); cutter (laboratory tool); modified edible film dissolution apparatus (custom-built, laboratory modification); standard laboratory glassware (beakers, cylinders, pipettes; Pyrex, USA)

Methods

Examination of Active Ingredient and Excipient

Examination of Active Ingredient

The identification of dimenhydrinate was carried out according to the procedures described in the Indonesian Pharmacopoeia, 6th Edition (Supplement I–III, 2022–2025) [25-27]

Examination of Excipients

Type B gelatine, menthol, and peppermint oil were examined following the methods outlined in the Indonesian Pharmacopoeia, 6th Edition (Supplement III, 2025) [27]. Propylene glycol and brilliant blue FCF were examined according to the Indonesian Food Codex for Food Additives (BPOM, 2023) [28]. Sorbitol, aspartame, polyvinylpyrrolidone (PVP), and sorbic acid were examined following the procedures described in the United States Pharmacopeia (USP 48, 2025) [29].

Determination of Maximum Wavelength and Stability Time of Dimenhydrinate in 0.1 N HCl

The determination of maximum wavelength and stability time of dimenhydrinate in 0.1 N HCl was performed using UV–VIS spectrophotometry, following validated approaches reported in recent studies l. [30-32].

Edible Film Formulation

Table 1. Composition of edible film formulations.

No	Ingredient	FI	FII	FIII	FIV	FV
1	Dimenhydrinate (% w/v)*	4.17	4.17	4.17	4.17	4.17
2	Propylene glycol (% v/v)	3	3	3	3	3
3	PVP (% w/v)	1	1	1	1	1
4	Type B gelatine (% w/v)	2.5	5	7.5	10	12.5
5	Sorbitol solution (% v/v)	2.5	2.5	2.5	2.5	2.5
6	Aspartame (% w/v)	1	1	1	1	1
7	Sorbic acid (% w/v)	0.1	0.1	0.1	0.1	0.1
8	Menthol (% w/v)	0.7	0.7	0.7	0.7	0.7
9	Peppermint oil (% v/v)	6.5	6.5	6.5	6.5	6.5
10	2% Brilliant blue FCF soln. (% v/v)	1	1	1	1	1
11	Distilled water (% v/v)*	ad 100	ad 100	ad 100	ad 100	ad 100

* Dimenhydrinate 4.17% corresponds to 12.5 mg per edible film unit.
Each batch consisted of 15 mL of edible film solution, equivalent to 50 units of edible film.

Preparation of Edible Film Formulations

The preparation of edible film formulations followed established solvent-casting techniques using gelatine, sorbitol, propylene glycol, and PVP, consistent with recent studies on edible film-forming agents and pharmaceutical oral films [7,33-35].

Optimization of Drying Temperature and Time

Drying optimization was performed by placing the five edible film formulations in an oven at 40 °C, 50 °C, and 60 °C for 1, 2, and 3 h. At each temperature and time point, the dryness of the films was assessed by gently touching the upper surface. The optimal drying conditions were determined based on achieving films with uniform dryness and mechanical integrity.

Evaluation of Edible Film Solution

Specific Gravity

The pycnometer was cleaned and dried in an oven at 100 °C until a constant weight was achieved. It was then filled with distilled water until the capillary was completely filled, cooled to 20 °C, wiped externally, and weighed. The water was removed and replaced with the edible film solution under test, filled to the capillary mark, cooled to 20 °C, wiped externally, and weighed. The specific gravity was calculated using the following equation:

Specific gravity = Weight of solution: Weight of water

Pycnometer-based density determination remains a validated approach for edible films and liquid formulations [7,36].

pH Measurement

The pH meter was calibrated using standard buffer solutions at pH 7.0 (equimolar phosphate buffer) and pH 4.0 (potassium hydrogen phthalate buffer). The edible film solution was prepared at ambient temperature. Prior to measurement, the electrode was rinsed thoroughly with distilled water and then fully immersed in the solution. The pH value was recorded once the reading stabilized. [37]

Viscosity

Viscosity was measured using a Brookfield viscometer (LV type). The edible film solution was placed in a cylindrical glass vessel, and the spindle was immersed to the marked level. The spindle was rotated at a fixed speed until a constant scale reading was obtained. Viscosity was calculated using the formula:

$$\eta\ (cP) = \text{scale} \times \text{factor}$$

This method is widely applied in edible film and biopolymer characterization studies (Shanbhag et al., 2023 [16,38]).

Physical Evaluation of Edible Films

Organoleptic Properties

The organoleptic evaluation of the edible films included assessment of odor by smelling the preparation, taste by direct tasting, clarity by visual observation with the naked eye, and stickiness by determining the ease of removal from the mold. [39]

Weight Uniformity

Twenty edible films were weighed using an analytical balance. The mean weight was calculated, and the percentage deviation of each film from the mean was determined. [40]

Thickness

Film thickness was measured using a micrometre. Measurements were taken at three points: one at the centre and two at the diagonal edges of the film, as the small size of the films allowed three points to represent overall thickness. The average of the three measurements was recorded as the film thickness. [41]

Disintegration Time

One edible film was placed in each tube of the disintegration basket, followed by insertion of the discs. The apparatus was operated using water maintained at 37 °C ± 2 °C as the medium. The basket was raised, and the films were observed until complete disintegration. A film was considered disintegrated when the residue remaining on the mesh was a soft mass without a distinct core. If one or two films did not disintegrate completely, the test was repeated with 12 additional films. At least 16 out of 18 films tested must disintegrate completely to meet the acceptance criteria.[42]

Drying Loss

Edible films were placed in pre-weighed containers, weighed, and then dried in an oven at 105 °C for 1 h. The films were reweighed, and heating was continued at 1 h intervals until a constant weight was achieved. Drying loss was calculated using the formula [40]:

$$\text{Drying loss} = [(\text{Initial weight} - \text{Final weight}) / \text{Initial weight}] \times 100\%$$

Preparation of Edible Films without Active Ingredient

Edible films without the active ingredient were prepared using the same procedure described in formulation, except that dimenhydrinate was omitted.

Measurement of Excipient Absorbance in 0.1 N HCl

Absorbance in the Content Uniformity Procedure

One edible film without active ingredient was placed in a 25 mL volumetric flask, dissolved in 0.1 N HCl, and diluted to volume. A 1 mL aliquot was transferred into another 25 mL volumetric flask and diluted to volume with 0.1 N HCl. Absorbance was measured using a UV–VIS spectrophotometer at the maximum wavelength and stable time determined previously. [40]

Absorbance in the Dissolution Test Procedure
A modified dissolution apparatus was used. Forty mL of distilled water were heated to 37 °C in the dissolution vessel, with the paddle speed set at 50 rpm. One edible film was placed in the basket, which was immersed approximately 1 cm above the vessel base. The apparatus was operated, and 2 mL samples were withdrawn at 5, 10, 15, 20, 30, and 45 min. Each withdrawn sample was replaced with 2 mL of distilled water. Each sample was transferred into a 25 mL volumetric flask, diluted to volume with 0.1 N HCl, and absorbance was measured using a UV–VIS spectrophotometer at the predetermined wavelength. [40]

Content Uniformity Test for the Optimal Formula Based on Physical Evaluation
One edible film was placed in a 25 mL volumetric flask, dissolved in 0.1 N HCl, and diluted to volume. A 1 mL aliquot was transferred into another 25 mL volumetric flask and diluted to volume with 0.1 N HCl. The procedure was repeated for 10 edible films.

Absorbance of each test solution was measured using a UV–VIS spectrophotometer at the maximum wavelength and stable time determined previously. The dimenhydrinate content relative to the label claim was calculated using the formula [40]:

$$\text{Content (\%)} = (At/As) \times (V \times f)/E \times 100$$

Where: At = absorbance of the test solution; As = absorbance of the standard solution; V = final dilution volume (mL); f = dilution factor; E = amount of active ingredient stated on the label (g)

Dissolution Test
For the best formulation obtained from the physical evaluation, a modified dissolution apparatus for edible films was employed. A total of 40 mL of distilled water was heated to 37 °C in the dissolution vessel, and the rotation speed was set at 50 rpm. One edible film was placed into the basket, which was then immersed so that the distance between the bottom of the basket and the base of the vessel was approximately 1 cm. The apparatus was then activated.

Aliquots of 2 mL were withdrawn at 5, 10, 15, 20, 30, and 45 min. Each withdrawn sample was replaced with an equal volume (2 mL) of distilled water to maintain sink conditions. Each aliquot was transferred into a 25 mL volumetric flask and diluted to volume with 0.1 N HCl. The procedure was performed for six edible films.

The absorbance of each sample was measured using a UV–VIS spectrophotometer at the maximum wavelength determined previously. The amount of dimenhydrinate dissolved (mg) in each aliquot was calculated using the following equation:

$$\text{Amount dissolved (mg)} = (At / As) \times V \times f \times 1000$$
Where: At = absorbance of the test solution, As = absorbance of the standard solution, V = final dilution volume (mL), and f = dilution factor.

A dissolution profile was then constructed by plotting time (x-axis) against the amount of dimenhydrinate dissolved (y-axis) (Li et al., 2025 [10]; Caicedo et al., 2025 [40]).

RESULTS AND DISCUSSION

Examination of Active Ingredient and Excipient

Table 2. Active ingredient and excipient assay

No	Name of materials	Specification	Result
1	Dimenhydrinate	Indonesian Pharmacopoeia, 6th Ed.(2020)	Meets specification
2	Propylene glycol	Indonesian Food Codex for Food Additives (2023)	Meets specification
3	Polyvinylpyrrolidone	United States Pharmacopeia (USP 48, 2025)	Meets specification
4	Type B gelatine	Indonesian Pharmacopoeia, 6th Ed. (2020)	Meets specification
5	Sorbitol solution	United States Pharmacopeia (USP 48, 2025)	Meets specification
6	Aspartame	United States Pharmacopeia (USP 48, 2025)	Meets specification
7	Sorbic acid	United States Pharmacopeia (USP 48, 2025)	Meets specification
8	Menthol	Indonesian Pharmacopoeia, 6th Ed. (2020)	Meets specification
9	Peppermint oil	Indonesian Pharmacopoeia, 6th Ed. (2020)	Meets specification
10	2% Brilliant blue FCF	Indonesian Food Codex for Food Additives (2023)	Meets specification
11	Distilled water	Indonesian Pharmacopoeia, 6th Ed.(2020)	Meets specification

The assay results presented in Table 2 confirm that both the active ingredient (dimenhydrinate) and all excipients used in the edible film formulation meet the required pharmacopeial or food codex specifications. Compliance with these standards ensures the quality, safety, and consistency of the formulation.

- Dimenhydrinate was tested according to the *Indonesian Pharmacopoeia, 6th Edition (2020)*, and met the required specification, confirming its suitability as the active pharmaceutical ingredient (API).
- Propylene glycol and Brilliant blue FCF (2%) were evaluated against the *Indonesian Food Codex for Food Additives (2023)*, ensuring compliance with food-grade safety standards.
- Polyvinylpyrrolidone (PVP), sorbitol solution, aspartame, and sorbic acid were tested according to the *United States Pharmacopeia (USP 48, 2025)*, confirming their pharmaceutical-grade quality and functional roles as binder, plasticizer, sweetener, and preservative, respectively.
- Type B gelatine, menthol, peppermint oil, and distilled water were evaluated against the *Indonesian Pharmacopoeia, 6th Edition (2020)*, ensuring compliance with national pharmacopeial standards for excipients and solvents.

All materials complied with relevant pharmacopeial standards guarantees that the formulation adheres to internationally recognized quality control practices, which is critical for regulatory acceptance and patient safety. [27-29]

Determination of Maximum Wavelength of Dimenhydrinate in 0.1 N HCl

The maximum wavelength of dimenhydrinate in 0.1 N HCl was determined, and the result is shown in Figure 1.

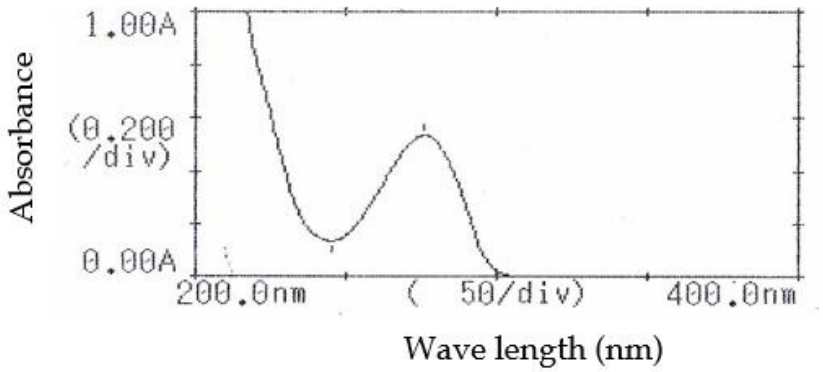


Figure 1. Maximum wavelength of dimenhydrinate in 0.1 N HCl.

The UV–VIS spectrophotometric analysis revealed that dimenhydrinate in 0.1 N HCl exhibits a maximum absorption wavelength at 276.5 nm (Figure 1). This value is in close agreement with previously reported data, which indicate that dimenhydrinate shows a characteristic absorption maximum at approximately 276 nm in acidic media. The slight variation observed (0.5 nm) can be attributed to experimental conditions such as solvent composition, instrument calibration, or sample preparation, but remains within the acceptable range of analytical reproducibility.[42]

The identification of the maximum wavelength is critical for ensuring selectivity and sensitivity in subsequent quantitative determinations, including content uniformity and dissolution testing. By establishing 276.5 nm as the analytical wavelength, the method aligns with pharmacopeial recommendations for UV–VIS analysis of active pharmaceutical ingredients, thereby ensuring accuracy, reliability, and regulatory compliance in the evaluation of edible film formulations.[42]

Determination of Stability Time of Dimenhydrinate in 0.1 N HCl

The stability time of dimenhydrinate in 0.1 N HCl was determined, and the results are presented in Figure 2 and Table 3.

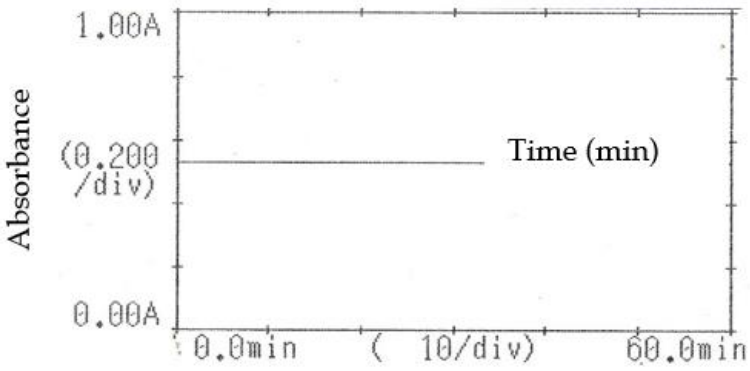


Figure 2. Stability time of dimenhydrinate in 0.1 N HCl

Table 3. Absorbance of dimenhydrinate in 0.1 N HCl during stability time determination.

Time (min)	Absorbance	Time (min)	Absorbance
5	0.5309	35	0.5311
10	0.5310	40	0.5310
15	0.5310	45	0.5314
20	0.5310	50	0.5314
25	0.5314	55	0.5314
30	0.5314	60	0.5310

As shown in Figure 2, the absorbance values remained relatively constant over a 1 h measurement period, producing a linear profile that indicates the test solution was stable. This observation is supported by the absorbance data in Table 3, which demonstrate minimal variation throughout the measurement period. Therefore, it can be concluded that the test solution remained stable during the analytical process [40].

Optimization of Drying Temperature and Time of Edible Films

Table 4. Results of optimization of drying temperature and time of edible films.

Time (h)	**Temperature (°C)**	**F I**	**FII**	**FIII**	**FIV**	**FV**
1	40	VW	VW	VW	VW	VW
	50	W	W	W	W	W
	60	W	W	W	W	SD
2	40	VW	VW	VW	VW	W
	50	W	W	W	W	SD
	60	SD	SD	SD	SD	D
3	40	VW	VW	VW	VW	W
	50	W	W	W	W	SD
	60	D	D	D	D	D

Notes: VW = very wet; W = wet; SD = slightly dry; D = dry.

From Table 4, it can be observed that at 40 °C for 1, 2, and 3 h, all formulations remained wet. This indicates that evaporation at this temperature and duration was insufficient to achieve adequate dryness. A similar trend was observed at 50 °C, where after 3 h the films were only slightly dry but still retained some moisture, which could hinder removal from the casting plates. In contrast, at 60 °C for 3 h, all formulations reached an appropriate level of dryness, as the surface of the edible films was no longer sticky upon touch. Therefore, a drying condition of 60 °C for 3 h was selected for subsequent preparation of edible film formulations [40].

Evaluation of Edible Film Solutions

Specific Gravity

Table 5. Specific gravity of edible film solutions.

Formula	**Specific gravity (g/mL)**
I	1.0409
II	1.0471
III	1.0492
IV	1.0538
V	1.0570

The results in Table 5 show a progressive increase in specific gravity from FI (1.0409 g/mL) to FV (1.0570 g/mL). This trend directly correlates with the increasing concentration of type B gelatine in the formulations. Gelatine, being a high-molecular-weight polymer, contributes significantly to the solid content of the solution; therefore, higher concentrations lead to greater density and specific gravity values.

This observation is consistent with the principle that specific gravity reflects the ratio of solute to solvent in a formulation. As more solids are incorporated, the solution becomes denser, which in turn influences the average weight of the resulting edible films. Thus, controlling gelatine concentration is critical not only for mechanical and organoleptic properties but also for ensuring batch-to-batch consistency in film weight, a parameter essential for regulatory compliance and dosage accuracy.

Moreover, these findings align with previous reports in edible film research, where increases in polymer concentration (e.g., gelatine, starch, or caseinate) were shown to elevate solution density and subsequently affect film thickness and weight uniformity. Therefore, the specific gravity values obtained here can serve as a reference standard for optimizing formulation parameters to achieve reproducible film characteristics [40,41].

pH

Table 6. pH values of edible film solutions.

Formula	**pH**
I	6.00
II	6.05
III	6.10
IV	6.12
V	6.15

The results in Table 6 demonstrate a gradual increase in pH values from FI (6.00) to FV (6.15). This progressive shift toward a more basic environment is directly associated with the increasing concentration of type B gelatine in the formulations. Type B gelatine is derived from an alkaline hydrolysis process of collagen, which imparts slightly basic characteristics to the resulting polymer. Therefore, as the proportion of gelatine increases, the buffering effect of its alkaline precursor becomes more pronounced, leading to higher pH values in the edible film solutions [40,43].

Maintaining pH within the near-neutral range (6.0–6.2) is advantageous for oral film formulations, as it minimizes the risk of mucosal irritation while ensuring stability of both the active ingredient and excipients. Furthermore, pH control is critical for film consistency, solubility, and patient acceptability, since deviations toward strongly acidic or basic values could negatively impact taste, dissolution behaviour, and compatibility with incorporated additives [40,43].

These findings are consistent with previous reports in edible film and pharmaceutical formulation research, where gelatine concentration was shown to influence solution pH and, consequently, the physicochemical properties of the final dosage form.

Viscosity

Table 7. Viscosity of edible film solutions.

Formula	Spindle	RPM	Factor	Scale	Viscosity (cp)
IV	1	60	1	15.25	15.25
V	1	30	2	15.5	31
V	1	60	1	34	34

Viscosity measurements were successfully obtained only for FIV and FV, while FI–III could not be measured due to their dilute nature. This outcome highlights the strong influence of type B gelatine concentration on solution rheology. Gelatine, as a polymeric excipient, contributes to intermolecular interactions and network formation in aqueous solutions; therefore, increasing its concentration leads to higher viscosity values.

The results show that Formula IV exhibited a viscosity of 15.25 cps at 60 rpm, while Formula V demonstrated higher viscosities (31 cps at 30 rpm and 34 cps at 60 rpm). These findings confirm that gelatine concentration is directly proportional to viscosity, consistent with previous reports in edible film and pharmaceutical formulation studies.

Importantly, viscosity plays a dual role in edible film preparation:

- Film formation and mechanical properties: Higher viscosity ensures better polymer chain entanglement, which contributes to uniform film thickness and improved tensile strength.
- Drying behaviour: More viscous solutions dried faster, as observed in Formula V, which reached dryness more quickly than other formulations. This can be explained by reduced water mobility in viscous solutions, leading to more efficient evaporation during drying.

Thus, viscosity serves as a critical quality parameter for edible film formulations, influencing not only processing conditions but also the reproducibility of film properties. Optimizing viscosity through excipient concentration adjustment ensures consistent film weight, mechanical integrity, and drying efficiency, which are essential for regulatory compliance and patient acceptability. [40,41,43]

Physical Evaluation of Edible Films

Organoleptic Properties

Table 8. Organoleptic evaluation of edible films.

Attribute	FI	FII	FIII	FIV	FV
Color	Green	Green	Green	Green	Green
Odor	Peppermint oil	Peppermint oil	Peppermint oil	Peppermint oil	Peppermint oil
Taste	Bitter, astringent	Bitter, astringent	Bitter, astringent	Bitter, astringent	Bitter, astringent
Clarity	Clear	Clear	Clear	Clear	Clear
Stickiness	Very sticky	Very sticky	Sticky	Slightly sticky	Not sticky

All formulations (FI–V) exhibited a uniform green color and peppermint odor, confirming that the coloring agent and essential oil were evenly distributed. Peppermint oil is widely used in oral films for its cooling sensation and masking properties, but its effect is limited when strong-tasting APIs are present. The films initially provided a sweet and cooling sensation, but bitterness and astringency from dimenhydrinate became dominant as dissolution progressed, consistent with reports that flavoring and sweetening agents often fail to fully mask unpleasant tastes, especially when the drug is dispersed rather than encapsulated in the polymer matrix. All films remained clear, indicating good solubility and dispersion of excipients without phase separation. However, FI–III were excessively sticky, likely due to an imbalance between type B gelatine (film-forming agent) and sorbitol (plasticizer), since higher plasticizer concentrations improve flexibility but increase tackiness. FIV and FV showed improved handling, with FV being the most acceptable, though both required storage in a desiccator to prevent moisture-induced tackiness, underscoring the importance of controlled storage conditions. [43-45]

Weight Uniformity

Weight uniformity was evaluated only for FIV and V, as these were the only films that could be removed from the molds. Summary statistics were FIV (Minimum = 59.0 mg; Maximum = 66.9 mg; Mean = 62.4 mg; SD = 2.526; RSD = 4.05%) and Formula **V** (Minimum = 63.5 mg; Maximum = 72.6 mg; Mean = 68.0 mg; SD = 2.395; RSD = 3.52%).[40]

Table 9. Weight uniformity evaluation of edible films (Formulas IV and V).

No.	Formula IV	Deviation (%)	Formula V	Deviation (%)
1	64.1 mg	2.72	66.1 mg	2.79
2	62.2 mg	0.32	70.7 mg	3.97
3	60.2 mg	3.52	66.4 mg	2.35
4	62.9 mg	0.80	67.7 mg	0.44
5	65.5 mg	4.97	72.6 mg	6.76
6	66.9 mg	7.21	66.6 mg	2.06
7	63.1 mg	1.12	68.0 mg	0.00
8	59.1 mg	5.29	67.3 mg	1.03
9	64.4 mg	3.20	64.6 mg	5.00
10	65.4 mg	4.81	68.8 mg	1.18
11	65.2 mg	4.49	69.6 mg	2.35
12	59.0 mg	5.45	68.7 mg	1.03
13	63.1 mg	1.12	71.8 mg	5.59
14	64.8 mg	3.85	65.7 mg	3.38
15	61.0 mg	2.24	67.3 mg	1.03
16	59.0 mg	5.45	63.5 mg	6.62

No.	Formula IV	Deviation (%)	Formula V	Deviation (%)
17	59.0 mg	5.45	68.1 mg	0.15
18	60.9 mg	2.40	71.7 mg	5.44
19	61.3 mg	1.76	68.4 mg	0.59
20	60.2 mg	3.52	66.5 mg	2.20

The data show that both formulations met the requirements for weight uniformity, with no deviation exceeding 10% from the mean weight. This demonstrates that the individual casting method reduces the risk of non-uniform film weights. The average weight of FV was greater than that of FIV, consistent with the higher concentration of type B gelatine, which increased the total solid content of the films. [40]

Thickness

Film thickness was measured only for FIV and V, as FI–III could not be removed from the molds.

Table 10. Thickness of edible films.

Sample	Formula IV (µm)	Mean thickness (µm)	Formula V (µm)	Mean thickness (µm)
1	90, 70, 70	77	110, 90, 160, 120	120
2	100, 90, 90	93	140, 110, 100, 117	117
3	120, 70, 90	93	100, 90, 90, 93	93
Average thickness	—	88	—	110

Film thickness was successfully measured only for FIV and FV, as FI–III could not be removed from the molds due to excessive stickiness. The thickness values obtained (88 µm for FIV and 110 µm for FV) fall within the acceptable range of 50–150 µm commonly reported for oral thin films. The greater average thickness observed in FV reflects the higher concentration of type B gelatine, which increases the solid content of the formulation. Gelatine, being a polymeric film-forming agent, contributes to matrix density and chain entanglement; therefore, higher concentrations result in thicker films.

Thickness is a critical parameter in edible film development, as it directly influences mechanical strength, disintegration time, and drug release profile. Thicker films generally exhibit greater tensile strength and durability, but may dissolve more slowly, which can affect drug bioavailability and patient acceptability. Thus, controlling gelatine concentration is essential to balance film robustness with rapid disintegration, ensuring both handling stability and therapeutic effectiveness.

These findings are consistent with previous studies on oral thin films, where polymer concentration was shown to significantly affect thickness, weight uniformity, and dissolution behaviour. The results here confirm that FV, with higher gelatine content, produced thicker films compared to FIV, aligning with established formulation principles. [44,46]

Disintegration Time

Disintegration testing was performed only on Formulas IV and V.

Table 11. Disintegration time of edible films.

Formula	Disintegration time (s)*
IV	94
V	97

* n = 6

The disintegration times of both formulations exceeded 90 s, thus not meeting the acceptance criteria. This was attributed to the formation of a “frame-like” edge around the films, which was thicker than the central portion and required more time to disintegrate. FIV disintegrated faster than FV, likely due to its thinner structure, which facilitated water penetration and accelerated disintegration.

Acceptance Criteria: Orally disintegrating films (ODFs) are generally expected to disintegrate within 30–60 seconds, with some pharmacopeial and industrial guidelines extending up to 90 seconds as the maximum limit. Both Formula IV (94 s) and Formula V (97 s) exceeded this threshold, indicating that neither formulation met the required performance standards [47].

Structural Influence: The prolonged disintegration was attributed to the "frame-like" edge observed around the films. This thicker boundary compared to the central portion delayed water penetration, thereby extending disintegration time. Film thickness and uniformity are well-documented as critical parameters influencing disintegration and mechanical properties of ODFs [48].

Comparison of Formula IV vs. V: Formula IV disintegrated faster (94 s) than Formula V (97 s). The difference is likely due to Formula IV's thinner structure, which facilitated faster hydration and breakdown. Literature confirms that thinner films disintegrate more rapidly because of reduced diffusion pathways for water [49].

Implications for Optimization: To improve disintegration performance, strategies may include: Ensuring uniform thickness during casting, adjusting plasticizer concentration to reduce rigidity, and incorporating super disintegrants to accelerate water uptake.

Drying Loss

Drying loss evaluation was performed only on edible films from Formulas IV and V, as films from Formulas I–III could not be removed from the molds.

Table 12. Drying loss of edible films.

Formula	Drying loss (%)
IV	6.92
V	6.83

Acceptance Criteria: The drying loss values for Formula IV (6.92%) and Formula V (6.83%) fall within the acceptable range of 6–10% moisture content, which is considered optimal for edible films. Maintaining moisture within this range ensures films remain flexible without becoming brittle, while also preventing microbial growth [50].

Comparison of Formulas IV vs. V: Formula IV exhibited a slightly higher drying loss compared to Formula V. This difference can be attributed to the greater residual water content introduced during formulation. Higher residual water increases evaporation during drying, resulting in a higher drying loss [14].

- **Selection of Optimal Formulation:** Based on overall physical evaluation, Formula V (containing 12.5% type B gelatine) was selected as the optimal formulation. It produced films with superior physical properties: Clear green appearance, peppermint odor, non-sticky texture, and compliance with weight uniformity, thickness, and drying loss specifications.

These characteristics align with reported findings that gelatine concentration strongly influences film transparency, odor retention, and mechanical stability [43].

- **Implications for Film Development:** The results highlight the importance of formulation balance between gelatine concentration and residual water content. Optimizing these parameters ensures edible films meet both regulatory acceptance criteria and consumer expectations for sensory and mechanical properties.

Measurement of Excipients' Absorbance in 0.1 N HCl

Based on the physical evaluation, FV was selected as the optimal formulation. For the measurement of excipient absorbance, edible films of FV were prepared without the active ingredient. The absorbance measurements included:

Absorbance of Excipients in the Content Uniformity Procedure

Table 13. Absorbance of excipients in the content uniformity procedure.

Solvent	Absorbance
0.1 N HCl	0.0825

Content Uniformity Evaluation: The absorbance of excipients in 0.1 N HCl was measured at 0.0825, which is relatively high and influenced drug content determination. This interference is attributed to excipients such as sorbic acid and aspartame, which contain chromophore groups with conjugated double bonds. These structural features enable absorption at 276.5 nm, overlapping with the drug's detection wavelength. Therefore, the excipient absorbance was applied as a correction factor to ensure accurate quantification of drug content [47].

Absorbance of Excipients in the Dissolution Test Procedure

Table 14. Absorbance of excipients in the dissolution test procedure.

Time (min)	Absorbance
5	0.1057
10	0.0934
15	0.0859
20	0.0815
30	0.0781
45	0.0745

Dissolution Test Evaluation: Absorbance values during dissolution ranged from 0.1057 at 5 min to 0.0745 at 45 min, showing a gradual decline over time. These relatively high values again highlight excipient interference in UV spectrophotometric analysis. Chromophoric excipients soluble in acidic medium contribute to baseline absorbance, which can lead to overestimation of drug release if not corrected [49].

Implications for Analytical Accuracy: Correction factors are essential when excipients absorb at the same wavelength as the drug. Without correction, results may misrepresent content uniformity and dissolution profiles, leading to inaccurate conclusions about formulation performance. This aligns with previous reports that UV spectrophotometric assays must account for excipient interference to ensure compliance with pharmacopeial standards [48].

Formulation Considerations: The findings emphasize the need to select excipients with minimal UV absorbance overlap, validate analytical methods with placebo films to quantify excipient contribution, and apply correction factors consistently across content uniformity and dissolution testing.

Content Uniformity Test for the Optimal Formula Based on Physical Evaluation

Table 15. Content uniformity of edible film Formula V.

No.	**Content (%)**
1	98.08
2	95.63
3	96.06
4	93.86
5	99.89
6	91.11
7	95.35
8	93.36
9	91.21
10	96.40
Minimum-maximum content: 91.11% - 99.89% Mean content: 95.10%; SD: 2.797; RSD: 2.94%	

The evaluation of content uniformity for edible film FV met the acceptance criteria, as none of the 10 samples deviated from the label claim by more than 85.0–115.0%, and the relative standard deviation did not exceed 6.0%. These results indicate that dimenhydrinate was uniformly distributed, with minimal variation among films. Furthermore, the formulation process did not degrade the active ingredient, as the measured content remained within the permitted range. Conclusion explicitly stated: *Formula V met content uniformity requirements and preserved the integrity of dimenhydrinate.*[47-49]

The content uniformity of Formula V complied with pharmacopeial requirements, with individual drug content values ranging from 91.11% to 99.89% of the label claim and a relative standard deviation of 2.94%. All samples fell within the acceptable range of 85.0–115.0%, confirming homogeneous drug distribution throughout the films. These findings demonstrate that the mixing, casting, and drying processes maintained dosage accuracy while preserving the stability of dimenhydrinate. [47-49]

Dissolution Test for the Optimal Formula Based on Physical Evaluation

Table 16. Dissolution test results of edible film of FV.

No.	5 min	10 min	15 min	20 min	30 min	45 min
1	83.13	87.87	89.95	90.48	90.68	90.86
2	85.94	91.66	91.90	93.02	93.54	93.85
3	84.49	88.84	89.92	91.68	91.98	91.99
4	91.30	93.34	95.36	98.07	98.54	98.86
5	86.40	90.57	92.86	93.10	94.42	94.84
6	85.69	89.22	91.34	93.42	94.17	94.33
Mean	86.16	90.25	91.89	93.30	93.89	94.12
SD	2.87	1.94	1.93	2.54	2.64	2.73

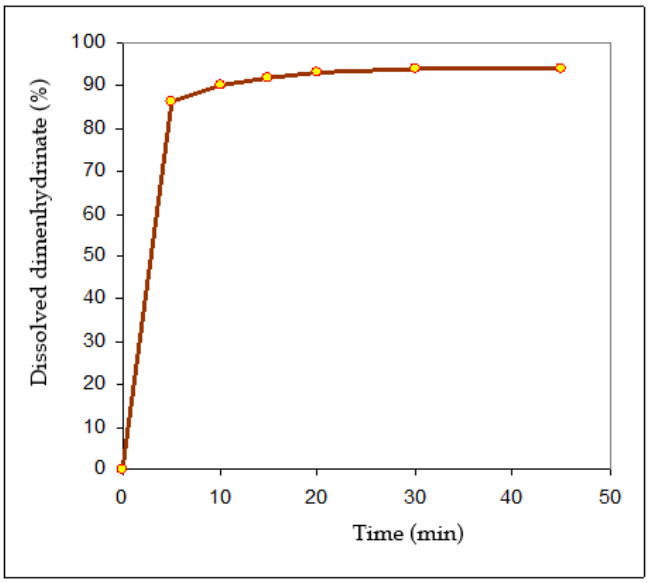


Figure 3. Dissolution profile of edible film in distilled water at 37 °C for 45 min.

The dissolution profile of Formula V demonstrated rapid drug release, with approximately 86% of dimenhydrinate dissolved within 5 minutes and more than 90% released by 15 minutes. The sharp increase observed during the initial phase corresponds to rapid film disintegration and immediate drug exposure to the dissolution medium. Variability was minimal and decreased over time, indicating consistent release behavior. These results confirm that the edible film formulation enhances the dissolution rate of dimenhydrinate compared with conventional solid dosage forms.

These findings confirm that the edible film dosage form significantly enhances the dissolution rate compared to conventional solid dosage forms, which typically require longer times to achieve comparable drug release. The results are consistent with previous studies reporting that orodispersible and edible films improve dissolution and bioavailability due to rapid hydration, disintegration, and increased surface area for drug release [46,49].

The dissolution test results demonstrated that the amount of dimenhydrinate released increased with time. This trend is clearly shown in the dissolution profile, where the mean percentage of dimenhydrinate progressively increased throughout the 45 min test period. A rapid increase in drug release was observed between 0 and 5 min, as the edible film disintegrated completely within approximately 1 min. Consequently, by 5 min, nearly 80% of dimenhydrinate had dissolved. These findings indicate that in the edible film dosage form, dimenhydrinate dissolves more rapidly in the dissolution medium compared to conventional forms. Conclusion explicitly stated: *Edible film enhances dissolution rate of dimenhydrinate.*

Distilled water (40 mL, 37 ± 0.5 °C) was selected as the dissolution medium to evaluate the intrinsic release behavior of dimenhydrinate from the gelatin-based film matrix under neutral conditions. The use of distilled water minimizes ionic interference and avoids pH-dependent solubility variations that may occur in simulated saliva or acidic media, allowing assessment of formulation-driven release characteristics. The selected volume that maintained sink conditions for the 12.5 mg dose, as reported aqueous solubility data indicate that sink conditions were maintained the maximum expected

concentration in the dissolution vessel, thereby preventing saturation and ensuring reliable release kinetics. This approach is consistent with the general principles outlined in USP <711> Dissolution regarding adequate medium volume to maintain sink conditions.

CONCLUSION

This study demonstrates that increasing gelatine concentration significantly enhances the structural integrity and handling properties of dimenhydrinate-loaded edible films. Among the tested formulations, the film containing 12.5% gelatine exhibited optimal mechanical manageability, uniform appearance, and acceptable drug content uniformity within pharmacopeial limits. The low relative standard deviation confirms homogeneous drug distribution and robustness of the casting process.

The formulation achieved rapid drug release, with more than 85% dissolution within 5 minutes and over 90% release by 15 minutes, indicating effective film disintegration and immediate drug availability. These findings support the potential of the edible film system to enhance the dissolution performance of dimenhydrinate compared with conventional solid dosage forms.

Although the disintegration time slightly exceeded the ideal benchmark for orodispersible systems and taste masking was not fully optimized, the overall pharmaceutical performance remains promising. Future studies should incorporate mechanical strength characterization, sensory optimization, and stability evaluation to further strengthen the formulation profile and support potential clinical translation.

Overall, the developed edible film represents a viable and scalable alternative oral delivery platform for dimenhydrinate, with potential advantages in patient compliance and rapid onset of action.

DECLARATION

Conflicts of interests: The authors declare no conflicts of interest.
Author contribution: All authors have contributed in the manuscript.
Author funding: Nill

REFERENCES

1. Wijlensa, R., Englebert, B. J. V., Takamatsu, A., Makita, M., Sato, H., Wada, T., de Winter, J. C. F., van Paassen, M. M., & Mulder, M. (2025). On the road to comfort: Evaluating the influence of motion predictability on motion sickness in automated vehicles. *Ergonomics, 68*(5), 697–715. https://doi.org/10.1080/00140139.2024.2372704
2. Alshammari, A., Alqahtani, F., Alzahrani, H., & Alghamdi, S. (2023). Prevalence of motion sickness among Saudi residents: An epidemiological study. *Healthcare, 11*(15), 2123. https://doi.org/10.3390/healthcare11152123
3. Kuiper, O. X., Bos, J. E., & van der Woude, L. H. V. (2022). Motion sickness in transportation: Current understanding and future directions. *Applied Ergonomics, 102*, 103749. https://doi.org/10.1016/j.apergo.2022.103749
4. Rahimzadeh, G., Tay, A., Travica, N., Lacy, K., Mohamed, S., Nahavandi, D., Pławiak, P., Qazani, M. C., & Asadi, H. (2023). Nutritional and Behavioral Countermeasures as Medication Approaches to Relieve Motion Sickness: A Comprehensive Review. *Nutrients*, 15(6), 1320. https://doi.org/10.3390/nu15061320
5. DrugBank. (January 29, 2026). *Dimenhydrinate*. DrugBank Online. Retrieved January 29, 2026, from https://go.drugbank.com/drugs/DB00985
6. Olawade, D. B., Wada, O. Z., & Ige, A. O. (2024). Advances and recent trends in plant-based materials and edible films: A mini-review. *Frontiers in Chemistry*, 12, 1441650. https://doi.org/ 10.3389/fchem.2024.1441650
7. Weng, S., Marcet, I., Rendueles, M., & Díaz, M. (2025). Edible films from the laboratory to industry: A review of the different production methods. *Food and Bioprocess Technology*, 18, 3245–3271. https://doi.org/10.1007/s11947-024-03641-4
8. Sibi, M. V., Ramya, R., Vinothini, S., Vishnu, S., Yazhini, V., & Sundaramoorthy, K. (2025). Formulation and evaluation of oral medicated jellies of dimenhydrinate. European Journal of Biomedical and Pharmaceutical Sciences, 12(1). https://storage.googleapis.com/innctech /ejbps/article_issue/volume_12_january_issue_1/1735817146.pdf
9. Nam, J. H., Kim, B. H., Shafioul, A. S. M., & others. (2025). A comprehensive review of oral disintegrating film products, and their quality assessment and development. Journal of Pharmaceutical Investigation, 55, 351–373. https://doi.org/10.1007/s40005-024-00714-6
10. Li, Y., Zhao, M., Zhao, M. Y., & others. (2025). Advances in oral dissolving film research in the food field. *Food Production, Processing and Nutrition,* 7(9). https://doi.org/10.1186/s43014-024-00285-x
11. Chaudhari, D., Patil, R., & Chaudhari, Y. (2025). Advances in orodispersible films: Transforming drug delivery for pediatric and geriatric patients. *International Journal of Pharmaceutical Sciences*, 3(9), 3657–3666. https://doi.org/10.5281/zenodo.17234748
12. Gujar, D.V., Bari, P.S., & Patil, B.P. (2025). Innovative drug delivery through bioadhesive orodispersible films: Focus on pediatric and geriatric populations. *International Journal of Advance Research Publication and Reviews,* 2(11), 468-486.

13. Fernández, N. L., Yamul, D. K., & Navarro, A. S. (2025). Physicochemical and mechanical properties of cassava starch films containing honey and glycerol as co-plasticisers. *International Journal of Food Science and Technology, 60*(1), vvae017. https://doi.org/10.1093/ijfood/vvae017
14. Mayasari, A., Pranoto, Y., & Sarto. (2025). Development of edible films derived from cassava peel waste with glycerol and chitosan additives. *ASEAN Journal of System Engineering, 9*(2), 33–40.
15. Arifina, H. R., Djalia, M., Nurhadia, B., Hasim, S. A., Hilmia, A., & Puspitasari, A. V. (2022). Improved properties of corn starch-based bio-nanocomposite film with different types of plasticizers reinforced by nanocrystalline cellulose. *International Journal of Food Properties, 25*(1), 509–521. https://doi.org/10.1080/10942912.2022.2052085
16. Shanbhag, C., Shenoy, R., Shetty, P., Srinivasulu, M., & Nayak, R. (2023). Formulation and characterization of starch-based novel biodegradable edible films for food packaging. *Journal of Food Science and Technology, 60,* 2858–2867. https://doi.org/10.1007/s13197-023-05678-3
17. Bizymis, A.-P., Giannou, V., & Tzia, C. (2023). Contribution of hydroxypropyl methylcellulose to the composite edible films and coatings properties. *Food and Bioprocess Technology, 16,* 1488–1501. https://doi.org/10.1007/s11947-023-03077-8
18. Muna, A., Wicaksono, R., & Wibowo, C. (2023). Characterization of layer-by-layer biodegradable films based on hydroxypropyl methylcellulose-nanochitosan. *Journal of Applied Food Technology, 10*(2), 20868. https://doi.org/10.17728/jaft.20868
19. Milano, F., Masi, A., Madaghiele, M., Sannino, A., Salvatore, L., & Gallo, N. (2023). Current trends in gelatin-based drug delivery systems. *Pharmaceutics, 15*(5), 1499. https://doi.org/10.3390/pharmaceutics15051499
20. Reji, R. E., Mathew, C. B., Janani, V., Sabu, C. S., & Roy, S. (2025). Gelatin films and coatings for active food packaging: Functional properties and applications. *Food Innovation and Advances, 4*(3), 423–436. https://doi.org/10.48130/fia-0025-004621.
21. Anuar, N.A.A., Tukiran, N. A., & Jamaludin, M. A. (2023). Gelatin in halal pharmaceutical products. *Malaysian Journal of Syariah and Law, 11*(1), 64–78. https://doi.org/10.33102/mjsl.vol11no1.344
22. Abd Aziz, M. A., Abdul Aziz, K., Rahamaddulla, S. R., Noor Kamar, A. N., et al. (2025). Unlocking halal gelatin: Exploring sustainable sourcing and applications. In *Proceedings of the 4th International Conference on Biomass Utilization and Sustainable Energy (ICoBiomasSE 2024)* (pp. 555–566). Springer.
23. Park, C.-H., Ganbat, C., & Han, J.-A. (2025). Hydrocolloid-specific performance of orally disintegrating films: Physicochemical, dissolution, and sensory insights. *Food Science and Biotechnology.* Advance online publication. https://doi.org/10.1007/s10068-025-01488-1
24. Al-Saidi, M., Ahmed, J. M., Boya, D. A., & Kamal, H. (2020). Formulation of a fast-dissolving oral film using gelatin and sodium carboxymethyl cellulose. *Zanco Journal of Medical Sciences, 24*(3), 338–346. https://doi.org/10.15218/zjms.2020.040
25. Kementerian Kesehatan Republik Indonesia. (2022). Farmakope Indonesia Edisi VI, Suplemen I. Jakarta: Direktorat Jenderal Kefarmasian dan Alat Kesehatan. ISBN 978-623-301-308-6.
26. Kementerian Kesehatan Republik Indonesia. (2023). Farmakope Indonesia Edisi VI, Suplemen II. Jakarta: Direktorat Jenderal Kefarmasian dan Alat Kesehatan.
27. Kementerian Kesehatan Republik Indonesia. (2025). Farmakope Indonesia Edisi VI, Suplemen III. Jakarta: Direktorat Jenderal Kefarmasian dan Alat Kesehatan
28. Badan Pengawas Obat dan Makanan Republik Indonesia (BPOM). (2023). Kodeks Pangan Indonesia: Bahan Tambahan Pangan. Jakarta: BPOM.
29. United States Pharmacopeial Convention. (2025). United States Pharmacopeia and National Formulary (USP 48–NF 43). Rockville, MD: USP
30. Mozgova, O., Blazheyevskiy, M., Moroz, V., Kryskiv, O., & Pieta, I. S. (2025). Quantitative estimation of dimenhydrinate in pharmaceuticals using redox reaction with Oxone. *Biointerface Research in Applied Chemistry, 15*(3), 45. https://doi.org/10.33263/BRIAC153.045
31. BenchChem Technical Support Team. (2025). A comparative guide to the spectrophotometric validation of dimenhydrinate using Reineckate salt and alternative methods. *BenchChem Technical Report.* December 2025.
32. Jayaseelan, S., Kannappan, N., & Ganesan, V. (2022). Development and validation of RP-HPLC method for simultaneous determination of dimenhydrinate and cinnarizine using chemometrics. *International Journal of Life Science and Pharma Research, 12*(1), L67–L78. https://doi.org/10.22376/ijpbs/lpr.2022.12.1.L67-78
33. Chen, Y., Wang, J., Xu, L., Nie, Y., Ye, Y., Qian, J., Liu, F., & Zhang, L. (2024). Effects of different plasticizers on the structure, physical properties, and film-forming performance of curdlan edible films. *Foods, 13*(23), 3930. https://doi.org/10.3390/foods13233930
34. Nguyen, T. D. H., & Truong, D. H. (2023). Edible film-forming potential of gelatin blends with glycerol and sorbitol for application in instant noodle seasoning powder packaging. *Tropical Journal of Natural Product Research, 8*(4), 123–131. https://doi.org/10.26538/tjnpr/v8i4.50
35. Paul, D., & Ray, P. (2023). Exploring the potential of fast dissolving oral films: Current trends in pharmaceutical research. *Current Trends in Pharmaceutical Research, 10*(2), 45–56.
36. DWK Life Sciences. Pycnometers & Specific Gravity. https://www.dwk.com/laboratory-products/measuring-devices/pycnometers-and-specific-gravity

37. United States Pharmacopeial Convention. (2025). United States Pharmacopeia and National Formulary (USP 48–NF 43), General Chapter <791> pH. Rockville, MD: United States Pharmacopeial Convention
38. United States Pharmacopeial Convention. (2025). United States Pharmacopeia and National Formulary (USP 48–NF 43), General Chapter <911> Viscosity. Rockville, MD: United States Pharmacopeial Convention
39. Matloob, A., Ayub, H., Mohsin, M., Ambreen, S., Khan, F. A., Oranab, S., Rahim, M. A., Khalid, W., Nayik, G. A., Ramniwas, S., & Ercisli, S. (2023). A Review on Edible Coatings and Films: Advances, Composition, Production Methods, and Safety Concerns. *ACS omega*, 8(32), 28932–28944. https://doi.org/10.1021/acsomega.3c03459
40. European Pharmacopoeia Commission. (2023). European Pharmacopoeia (11th ed.). Council of Europe.
41. Maruddin, F., Rahmawati, M., Arief, M., & Satyantini, W. H. (2020). Brightness, elongation and thickness of edible film with caseinate sodium using a type of plasticizer. IOP Conference Series: Earth and Environmental Science, 492(1), 012043. https://doi.org/10.1088/1755-1315/492/1/012043
42. Saab, M., & Mehanna, M. M. (2019). Disintegration time of orally dissolving films: Various methodologies and in-vitro/in-vivo correlation. Die Pharmazie, 74(4), 227–230.
43. Karim, A. A., & Bhat, R. (2009). Gelatin alternatives for the food industry: Recent developments, challenges and prospects. Trends in Food Science & Technology, 19(12), 644–656. https://doi.org/10.1016/j.tifs.2008.08.001
44. Jadhav, Y. G., Galgatte, U. C., & Chaudhari, P. D. (2018). Overcoming poor solubility of dimenhydrinate: Development, optimization and evaluation of fast dissolving oral film. Advanced Pharmaceutical Bulletin, 8(4), 721–725. https://doi.org/10.15171/apb.2018.081
45. Chhikara, S., & Kumar, D. (2021). Edible coating and edible film as food packaging material: A review. Journal of Packaging Technology and Research, 5(4), 281–295. https://doi.org/10.1007/s41783-021-00129-w
46. Dixit, R. P., & Puthli, S. P. (2009). Oral strip technology: Overview and future potential. Journal of Controlled Release, 139(2), 94–107. https://doi.org/10.1016/j.jconrel.2009.06.014
47. Krampe, R., & Sieber, S. (2020). How to assess orodispersible film quality? A review of applied methods. European Journal of Pharmaceutics and Biopharmaceutics, 146, 2–15. https://doi.org/10.1016/j.ejpb.2019.12.007
48. Bichave, A., Phate, S., Naik, V., Gaikwad, A., Choudhary, L., Choudhary, U., & Patil, S. (2024). Evaluation parameters for mouth dissolving films. International Journal of Pharmaceutical Sciences, 2(7), 197–208. https://doi.org/10.5281/zenodo.12623624
49. Liew, K. B., Gobal, G., Rofiq, H. M., Phang, H. C., Lee, S. K., Ming, L. C., Uddin, A. B. M. H., Chew, Y. L., & Lakshminarayanan, V. (2024). Orally disintegrating film: A review of its formulation and manufacturing method. European Journal of Pharmaceutical Sciences, 194, 106598. https://doi.org/10.1016/j.ejps.2024.106598
50. Perdana, T., Fitriani, R., & Nugraha, R. (2023). Moisture content and mechanical properties of biopolymer-based edible films: A review. *Food Packaging and Shelf Life*, 36, 101073. https://doi.org/10.1016/j.fpsl.2023.101073
51. United States Pharmacopeial Convention. (2022). United States Pharmacopeia and National Formulary (USP 48–NF 43), General Chapter <711> Dissolution. Rockville, MD: United States Pharmacopeial Convention.
52. Agilent Technologies. (2022). What is sink condition in dissolution testing? Agilent Dissolution Blog.