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Optimization of Hydrolyzed Pumpkin (*Cucurbita moschata*) Starch as Natural Superdisintegrant in Promethazine HCl Sublingual Tablets

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Abstract
Acid hydrolysis of pumpkin starch is a feasible strategy for developing novel pharmaceutical excipients, particularly natural superdisintegrants for sublingual and orally disintegrating tablet formulations. Given the requirement for extremely rapid tablet disintegration in sublingual dosage forms, selecting an efficient disintegrant is a critical formulation parameter. However, native pumpkin starch exhibits limited disintegration efficiency and generally requires high concentrations, which may adversely affect tablet hardness and friability. This study aimed to optimize the acid hydrolysis process of pumpkin starch and to evaluate the performance of the optimized hydrolyzed starch as a natural superdisintegrant in Promethazine HCl sublingual tablets. A factorial design was used to examine the impact of varying hydrolysis durations (3-9 days) and hydrochloric acid concentration (5-9%) on the physicochemical characteristics of the modified starch. The optimized hydrolyzed starch demonstrated a near-neutral pH (5.17 ± 0.03), acceptable moisture content (LOD 10.20 ± 0.44%), and excellent flow properties, as indicated by a low angle of repose (23.96°) and Carr's index (9.99%). Scanning electron microscopy revealed increased surface irregularity and porosity, while FTIR analysis indicated enhanced exposure of hydroxyl groups, consistent with partial depolymerization of the starch polymer. The amylose content increased to 35.17%, accompanied by improved water uptake and swelling capacity. The effective pore radius (25.03 ± 0.35 µm) and swelling index (70.25 ± 0.57) were markedly higher than those of native pumpkin starch (12.27 μm and 44.30 ± 0.85, respectively), although slightly lower than crospovidone (27.65 μm and 99.97 ± 0.13). Incorporation of the hydrolyzed starch into Promethazine HCl sublingual tablets resulted in formulations with adequate mechanical strength (hardness 3.35 ± 0.05 kg), low friability (0.53 ± 0.04%), rapid disintegration (49.18 ± 0.75 s), and high drug release (96.79 ± 0.13%). These performances were comparable to those of crospovidone and superior to formulations containing native pumpkin starch. The improved tablet characteristics were primarily attributed to enhanced porosity and swelling capacity induced by acid hydrolysis. Overall, optimized hydrolyzed pumpkin starch demonstrates considerable potential as a sustainable, biodegradable, and cost-effective natural superdisintegrant for fast-disintegrating pharmaceutical tablet formulations.

Keywords
Hydrolyzed Starch, Pumpkin Starch, Promethazine HCl, Tablet Formulation, Superdisintegrant

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1. INTRODUCTION

The growing demand for patient-friendly oral dosage forms has driven extensive development of orally disintegrating tablets (ODTs) and sublingual formulations. These dosage forms are designed to disintegrate rapidly upon contact with saliva, enabling fast drug release and absorption while improving patient convenience and compliance (Cantor et al., 2015). Rapid disintegration is particularly critical for enhancing the bioavailability of active pharmaceutical ingredients (APIs) and ensuring a rapid onset of therapeutic action, compared with conventional tablets that dissolve more slowly. As a result, ODTs and sublingual tablets rely heavily on specialized excipients, particularly superdisintegrants, which promote swift tablet fragmentation and accelerated dissolution (Gosavi and P., 2025).

Superdisintegrants are typically incorporated at relatively low concentrations (1-10% w/w) and function primarily by rapidly absorbing water and swelling upon exposure to moisture, leading to immediate tablet disintegration (Maheshwari et al., 2024). This rapid disintegration is significant for clini-

cal conditions requiring prompt pharmacological intervention. Although synthetic superdisintegrants such as crospovidone are widely used in commercial formulations, growing concerns about sustainability, environmental impact, and production costs have spurred the exploration of natural, plant-based alternatives. In this context, starches derived from renewable sources have gained increasing attention as environmentally sustainable and cost-effective pharmaceutical excipients.

Pumpkin (*Cucurbita moschata* Duch.), a member of the Cucurbitaceae family, is widely cultivated in Indonesia and is predominantly utilized as a food commodity. Despite its abundance, the pharmaceutical potential of pumpkin-derived materials remains underexplored. To date, research and industrial applications have primarily focused on its nutritional value, while its utilization as a source of natural pharmaceutical excipients has received limited scientific attention. Pumpkin starch constitutes a major structural component of the plant and contains approximately 8.76% amylose and 28.92% amylopectin (Khatib and Muhieddine, 2019). As a naturally occurring polysaccharide, starch is widely employed in pharmaceutical formulations due to its multifunctional roles, including use as a binder, disintegrant, and stabilizing agent in solid dosage forms (Kapoor et al., 2025).

However, native pumpkin starch exhibits several functional limitations when applied as a disintegrant. It's relatively poor disintegration performance often necessitates incorporation at higher concentrations to achieve acceptable tablet disintegration (Patomchaiviwat et al., 2011). Excessive starch content may adversely affect tablet mechanical properties, particularly hardness and friability, thereby limiting its practical application in fast-disintegrating dosage forms. These drawbacks highlight the need for modification strategies to improve the functional performance of pumpkin starch and enhance its suitability as a pharmaceutical superdisintegrant.

Starch modification, whether through chemical or physical approaches, has long been used to improve the functional properties of solid dosage forms. Among various modification techniques, acid hydrolysis has been recognized as a practical and effective method for enhancing starch disintegration. Acid hydrolysis involves controlled cleavage of glycosidic bonds using hydrochloric acid, resulting in reduced molecular weight, increased amylose content, and decreased amylopectin content (Wang and Copeland, 2015). The increase in amylose content enhances water uptake and swelling capacity, thereby facilitating faster tablet disintegration, while reduced amylopectin content minimizes gel formation that could otherwise hinder disintegration (Yu et al., 2016). Consequently, acid-hydrolyzed starch has emerged as a promising natural alternative to conventional synthetic superdisintegrants. Although this approach has been successfully applied to starches derived from corn (Zhu et al., 2017) and potato (Absar et al., 2009), studies focusing on acid-modified pumpkin starch remain scarce, particularly regarding its application in sublingual tablet formulations.

Sublingual dosage forms offer distinct advantages for drugs requiring a rapid onset of action, such as Promethazine HCl, an antiemetic commonly prescribed for the management of motion sickness, nausea, and vomiting (Alyami et al., 2021). Rapid drug absorption is essential to ensure therapeutic effectiveness and to reduce the likelihood of drug expulsion due to vomiting. Therefore, optimizing the disintegration behavior of sublingual tablets is of considerable clinical importance. The use of hydrolyzed pumpkin starch as a superdisintegrant in Promethazine HCl sublingual tablets represents a promising strategy to enhance drug bioavailability, improve patient adherence, and achieve favorable therapeutic outcomes, particularly in pediatric and geriatric populations who often experience difficulty swallowing conventional tablets (Latifani et al., 2024).

Accordingly, the present study was designed to address this research gap by investigating the acid hydrolysis of pumpkin starch as a strategy to develop an efficient natural superdisintegrant. The research systematically evaluated the effects of two critical process variables hydrochloric acid concentration and hydrolysis duration on the physicochemical and functional properties of the modified starch. Optimization of the hydrolysis process was carried out using a factorial design approach to assess both the main effects and interactions of the selected variables. Compared with custom design approaches, factorial designs offer greater optimization efficiency and better accommodate formulation variables (Kusuma, 2018). The resulting modified starches were characterized using key parameters relevant to superdisintegrant performance, including swelling capacity, water absorption, flow properties, and disintegration efficiency. The optimized hydrolyzed pumpkin starch was subsequently incorporated into Promethazine HCl sublingual tablet formulations, followed by a comprehensive evaluation of tablet characteristics. The disintegration performance and overall tablet properties of hydrolyzed starch were comparatively assessed with those of native pumpkin starch and crospovidone, a commercial superdisintegrant. Through this structured experimental approach, the study aims to identify optimal hydrolysis conditions that produce pumpkin starch with superior disintegration capability and to verify its effectiveness as a natural superdisintegrant in Promethazine HCl sublingual tablet formulations.

2. EXPERIMENTAL SECTION

2.1 Material

Fresh, immature yellow pumpkins with green skin were obtained from the Jember region, East Java, Indonesia. Botanical authentication was conducted by the Integrated Agricultural Development Unit (UPA), Jember State Polytechnic. Promethazine HCl was kindly supplied by PT Interbat. Pharmaceutical excipients used in tablet formulation including crospovidone, polyethylene glycol (PEG) 6000, magnesium stearate, Avicel® PH 102, talc, mannitol, and sucralose were procured from PT Brataco Chemical. All excipients were of pharmaceutical grade and were used as received without additional purification or modification.

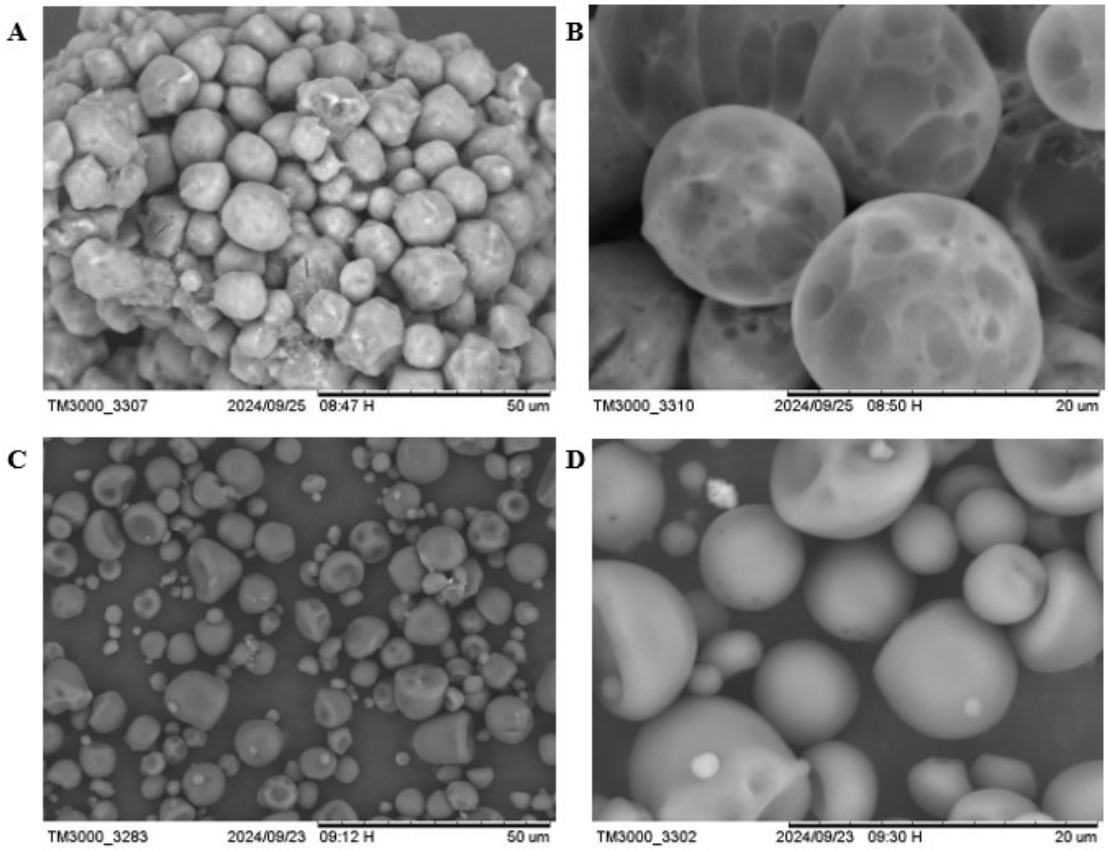

Figure 1. Electron Micrograph of Hydrolized Starch (A and B) and Native Starch (C and D). A and C: 1500× Magnification; B and D: 5000× Magnification

2.2 Instrumentation

The equipment employed in this study included an analytical balance (Adventurer, Ohaus), a pH meter (Denver Instruments, USA), and a drying oven (Memmert). Fourier-transform infrared (FTIR) spectra were obtained using an Alpha FTIR spectrometer (Bruker). The experimental design and statistical analysis were conducted using Design-Expert® software, version 13.0. Powder flow properties were assessed with a flowability tester (Pharmeq), while compressibility was evaluated with a tap density tester (Tap-25, Logan Instruments). Tablet compression was carried out using a single-punch tablet press (Minitab). Tablet hardness and friability were measured using a hardness tester (Erweka) and a friability tester (Hanyoung GX4), respectively. Disintegration time was determined using a disintegration tester (DT-2, TEQ-IND). Dissolution testing was carried out using a USP dissolution apparatus (UDT-804, Logan Instruments), and drug content analysis was conducted using a UV-Vis spectrophotometer (Genesys™10S, Thermo Scientific, USA).

2.3 Procedure of Starch Isolation and Hydrolysis

2.3.1 Isolation of Pumpkin Starch

Pumpkin starch was isolated using a modified procedure based on the method reported by Kovač et al. (2024). Fresh, immature pumpkins were washed, peeled, cut into small pieces, and blended with distilled water at a 2:1 (v/w) ratio. The resulting slurry was filtered through muslin cloth to separate fibrous material. The filtrate was allowed to stand undisturbed for 6-12 hours to enable starch sedimentation. The supernatant was carefully decanted, and the starch precipitate was repeatedly washed with distilled water until a clear supernatant was obtained. The purified starch was dried in an oven at 50 °C for 24 hours, then passed through a 100-mesh sieve to obtain a uniform particle size.

2.3.2 Preparation of Hydrolyzed Pumpkin Starch

Acid hydrolysis of pumpkin starch was optimized using a two-factor, two-level factorial design, with hydrochloric acid concentration (%) and hydrolysis duration (days) as independent variables. Four experimental formulations were generated: F1 (5%, 3 days), Fa (9%, 3 days), Fb (5%, 9 days), and Fab (9%, 9 days). Throughout the hydrolysis process, the following parameters were maintained constant: starch mass per batch, ambient hydrolysis temperature, and acid-to-starch volume ratio.

For each experimental run, 150 g of dried pumpkin starch was dispersed in 300 mL of hydrochloric acid solution at the designated concentration and hydrolyzed for the specified duration. Upon completion, the suspension was filtered to remove

the acidic medium, then neutralized with 5% (w/v) sodium hydroxide solution. The neutralized starch was allowed to rest for 1 hour, followed by refiltration and washing with distilled water five times to remove residual salts and impurities. The starch precipitate was then dried at 50 °C for 24 hours. The material was passed through a 100-mesh sieve to obtain a uniform particle size and stored in airtight containers for subsequent analysis (Zuhra et al., 2025).

2.4 Characterization of Hydrolyzed Pumpkin Starch

The hydrolyzed pumpkin starch was characterized through a series of physicochemical evaluations, including organoleptic properties, pH, loss on drying (LOD), flowability, angle of repose, powder compressibility, effective pore radius, swelling index, FTIR analysis, and determination of amylose and amylopectin contents. Organoleptic assessment was performed to evaluate physical appearance, including color, odor, texture, and overall morphology. The pH of starch dispersions was measured using a calibrated pH meter.

2.4.1 Loss on Drying (LOD)

Loss on drying was determined to quantify the moisture content of the starch powder. A pre-weighed sample (W_1) was placed in a drying oven and heated at 100 ± 5 °C for 2 hours. After drying, the sample was cooled in a desiccator to room temperature and reweighed (W_2). The percentage loss on drying, representing moisture and volatile content, was calculated using Equation 1 as described by Sulaiman et al. (2023).

$$\%\text{LOD} = \frac{W_1 - W_2}{W_1} \times 100 \tag{1}$$

2.4.2 Flow Time and Angle of Repose

A 50 g sample of starch powder was placed in a flow tester funnel, and the time required for the powder to flow completely was measured using a stopwatch. The flow time was then calculated using Equation 2:

$$\text{Flow time} = \frac{\text{Granule weight (grams)}}{\text{Flow time (seconds)}} \tag{2}$$

The angle of repose was calculated from the cone formed after the powder had fully flowed from the flow tester (Morin and Briens, 2013) using Equation 3.

$$\text{Angle of repose } (\Theta) = \tan^{-1}\left(\frac{2h}{D}\right) \tag{3}$$

2.4.3 Compressibility (Hausner Ratio and Carr's Index)

Compressibility testing was conducted in accordance with the standards outlined in the Indonesian Pharmacopoeia (Indonesian Ministry of Health, 2020). To evaluate powder compressibility, the Hausner ratio and Carr's index were determined. Both parameters were calculated from bulk density and tapped density measurements. Fifty grams of powder (M) were weighed and placed in a 250 mL measuring cylinder. The initial volume (Vo) was recorded to the nearest scale. Bulk density was calculated using Equation 4.

$$\text{BD} = \frac{\text{Weight}}{\text{Bulk volume}} \tag{4}$$

The tapped density was assessed by tapping the powder 10, 500, and 1250 times. If the difference in volume between the 500^{th} and 1250^{th} tap was ≤ 2 mL, the tapped volume after 1250 taps was recorded as the final value. However, if the volume difference exceeded 2 mL, the tapping procedure was repeated until the difference was ≤ 2 mL (Indonesian Ministry of Health, 2020). Tapped density was calculated using the formula in Equation 5, while Car's index and Hausner's ratio were calculated using Equations 6 and 7.

$$\text{TD} = \frac{\text{Weight}}{\text{Tapped volume}} \tag{5}$$

The Carr's index (CI) was calculated using the formula:

$$\text{CI} = \frac{\text{TD} - \text{BD}}{\text{TD}} \times 100\% \tag{6}$$

The Hausner's ratio (HR) was calculated using the formula:

$$\text{HR} = \frac{\text{TD}}{\text{BD}} \tag{7}$$

2.4.4 Effective Pore Radius (Reff.P)

The effective pore radius of the powder was determined using a method described by Chibowski and Perea-Carpio (2001). A 1 mL micropipette was filled with starch powder and weighed (W_i). Subsequently, n-hexane (surface tension, γ = 18.4 mN/m) was added dropwise to the top of the powder bed until it began to exit from the tip. The pipette was then reweighed (W_f), and the effective pore radius was calculated using Equation 8.

$$\text{Reff.P} = \frac{W_f - W_i}{2\pi\gamma} \times 100 \tag{8}$$

2.4.5 Swelling Index

The swelling index was determined using the methodology outlined: A 0.1 g sample of starch was initially dispersed in 10 mL of distilled water. This dispersion was then incubated for 30 minutes in a water bath under continuous agitation. The resulting slurry was subsequently centrifuged at 1600 rpm for 15 minutes to facilitate the separation of the supernatant from the sediment (Wijaya et al., 2019). The sediment was weighed, and the swelling index was calculated using Equation 9.

$$\text{Swelling Index} = \frac{W_1 - W_2}{W_2} \times 100 \tag{9}$$

Where W_1 is the weight of the sediment, and W_2 is the weight of the dry starch.

Table 1. Sublingual Promethazine HCl Tablet Formula

Ingredient	Function	F1 (%)	F2 (%)	F3 (%)
Promethazine HCl	API	8.3	8.3	8.3
Hydrolyzed Pumpkin Starch	Disintegrant	2.5	–	–
Native Pumpkin Starch	Disintegrant	–	2.5	–
Crospovidone	Disintegrant	–	–	2.5
PEG 6000	Binder	4	2	3
Mg Stearate	Lubricant	0.5	0.5	0.5
Talc	Glidant	1	1	1
Avicel PH 102	Filler	55	55	55
Mannitol	Filler	30	30	30
Sucralose	Sweetener	1	1	1
Total Weight		150	150	150

2.4.6 Fourier Transform Infrared Spectroscopy (ATR-FTIR)

Attenuated total reflectance-Fourier transform infrared (ATR-FTIR) spectroscopy was employed to examine potential alterations in the molecular organization of pumpkin starch induced by acid hydrolysis. Spectral measurements were obtained using an FT-IR spectrophotometer (Bruker Alpha II, Bruker Optics, Germany) equipped with an ATR module. The spectra were recorded over a wavenumber range of 4000-400 cm^{-1} with a resolution of 4 cm^{-1} under ambient conditions. The resulting spectra were evaluated by comparing the relative intensities and positions of characteristic absorption bands, which reflect changes in hydrogen bonding interactions and short-range molecular order rather than the formation of new functional groups.

2.4.7 Amylose and Amylopectin Content Test

Amylose content was determined using an iodine-binding colorimetric method. A standard amylose solution was prepared by dissolving 40 mg of pure amylose in 1 mL of 96% ethanol, then adding 9 mL of 1 N NaOH. The mixture was heated at 100 °C for 7 min with continuous stirring to ensure complete dissolution. After cooling to room temperature, the solution was diluted to a final volume of 100 mL with distilled water.

A calibration curve was constructed by transferring aliquots (0.2-1.0 mL) of the standard amylose solution into volumetric flasks, then adding 1.0 mL of acetic acid and 2.0 mL of iodine solution. The mixtures were diluted to volume with distilled water and allowed to stand for 20 min to ensure complete color development. Absorbance was measured at 625 nm using a UV-Vis spectrophotometer.

For sample analysis, 100 mg of starch was subjected to the same treatment and reacted with iodine under identical conditions. The absorbance was recorded at 625 nm, and the amylose content was calculated from the calibration curve. All measurements were conducted in triplicate (Indonesian Food and Drug Authority of the Republic of Indonesia, 2019). The amylopectin content was estimated indirectly by subtracting the amylose fraction from the total starch content, as expressed in Equation (10):

$$\text{Amylopectin content (\%)} = \text{starch content (\%)} - \text{amylose content} \quad (10)$$

2.4.8 Granule Morphology and Structure

The surface morphology and microstructural characteristics of native and acid-hydrolyzed starch samples were examined using a tabletop scanning electron microscope (SEM) (Hitachi TM100, Hitachi High-Technologies, Japan). Before analysis, dried samples were affixed onto aluminum stubs using double-sided carbon adhesive tape and observed without conductive coating. SEM imaging was performed under low-vacuum conditions at an accelerating voltage of 15 kV. Micrographs were captured at various magnifications to qualitatively assess morphological features, including granule integrity, surface texture, porosity, and fragmentation. Comparisons between native and modified starches were made to elucidate the structural impact of acid hydrolysis on granule size and shape.

2.5 Promethazine HCl Sublingual Tablet Preparation and Evaluation

Promethazine HCl sublingual tablets containing different types of disintegrants were formulated as summarized in Table 1. All tablet formulations were produced by direct compression and subsequently evaluated for their physicochemical properties.

2.5.1 Tablet Hardness

Tablet hardness was determined using a hardness tester, with 10 tablets randomly selected from each formulation. The breaking force was recorded in kilograms (kg). For sublingual dosage forms, a hardness range of 3-5 kg is generally considered appropriate to provide sufficient mechanical strength while maintaining rapid disintegration in the sublingual environment (Dalimunthe et al., 2022).

2.5.2 Tablet Friability

The friability test was performed according to United States Pharmacopeia (2023). For tablets weighing ≤ 650 mg, friability testing was performed using a friability tester operated at 25 rpm for 4 minutes. After the test, the tablets were removed, dedusted, and reweighed. The friability percentage was calculated

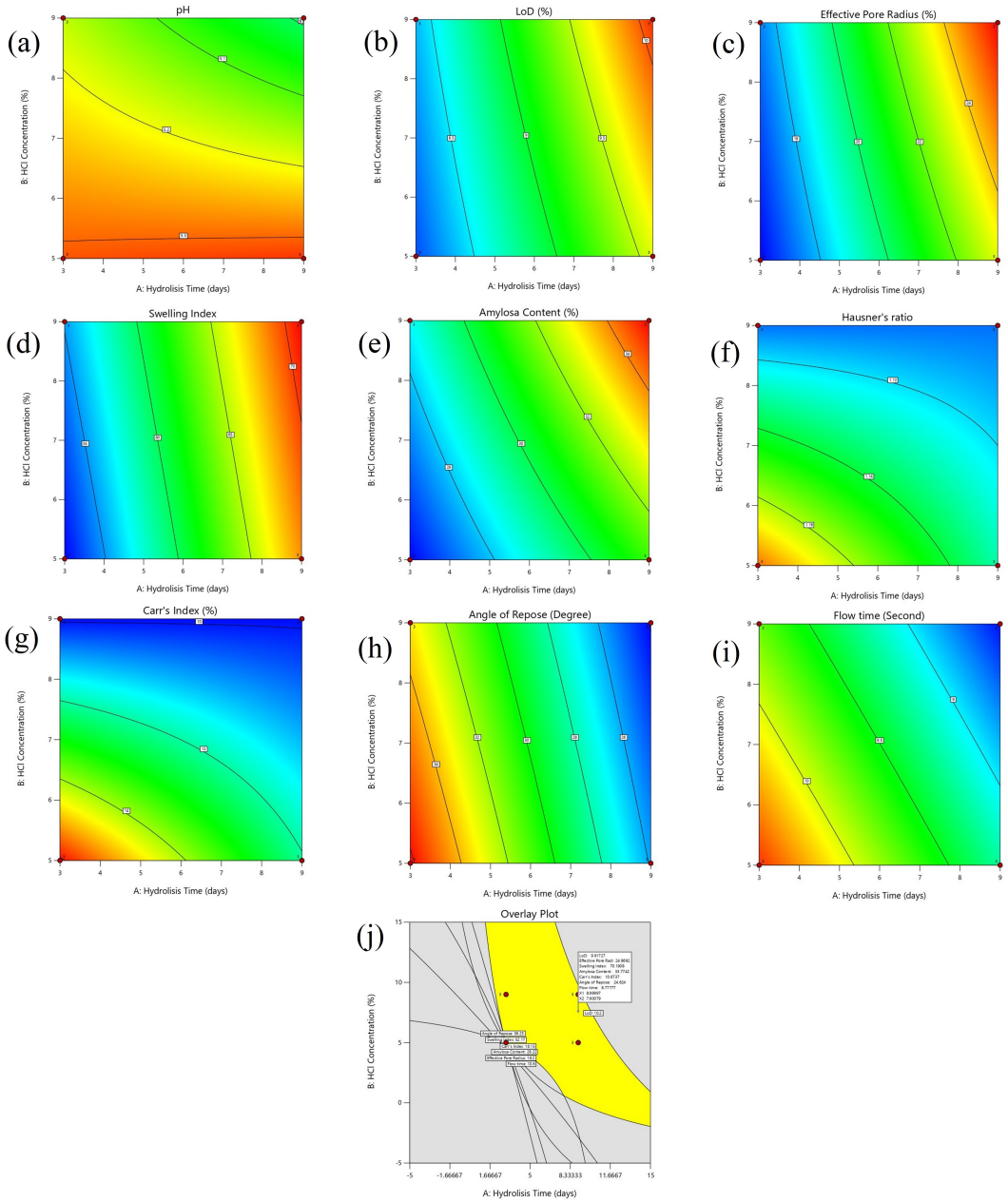

Figure 2. Contour Plot of Response: (A) pH, (B) LOD, (C) Effective Pore Radius, (D) Swelling Index, (E) Amylose Content, (F) Hausner's Ratio, (G) Car's Index, (H) Angle of Repose, (I) Flow Time, (J) an Overlay Plot of Responses Yielding the Optimum Hydrolysis Conditions

using the formula in Equation 11.

$$\%\text{Friability} = \frac{W_1 - W_2}{W_1} \times 100\% \quad (11)$$

2.5.3 Disintegration Time

Disintegration testing was conducted using six tablets placed in the basket of a disintegration tester, which was filled with distilled water maintained at 37 °C ± 0.5 °C. All six tablets were required to disintegrate completely. If one or two tablets failed to disintegrate, an additional 12 tablets were tested. The test was considered satisfactory if at least 16 out of 18 tablets disintegrated completely. The acceptable disintegration time for sublingual tablets is ≤ 2 minutes (Indonesian Ministry of Health, 2020).

2.5.4 Content Uniformity

Content uniformity testing was performed in accordance with the Indonesian Pharmacopoeia (Indonesian Ministry of Health,

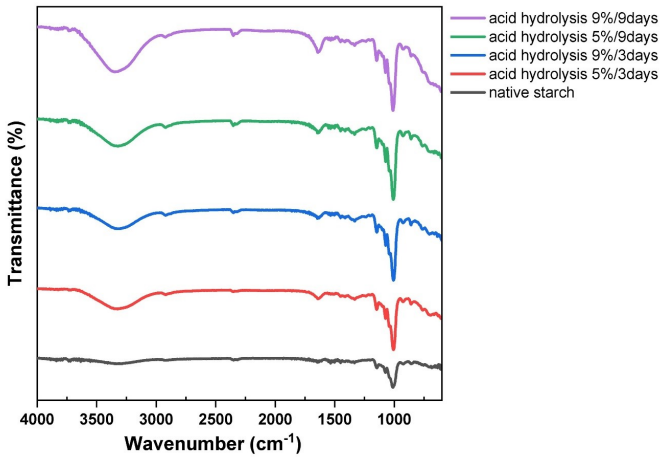

Figure 3. FTIR Spectra of Native Starch and Hydrolyzed Starch with Variations in Hydrolysis Time and HCl Concentration

2020). The assay was performed to verify the uniform distribution of the API within the sublingual tablets. Ten tablets were randomly selected from each batch of the formulation. Each tablet was weighed individually, finely ground, and dissolved in a suitable solvent. The resulting solution was appropriately diluted to the required concentration. The drug content was determined using a UV-Vis spectrophotometer at 249 nm (Alyami et al., 2021). The acceptance value (AV) was calculated using the formula in Equation 12.

$$AV = |M - \bar{X}| + kS \tag{12}$$

where: M = Label claim percentage; $\bar{X}$ = Mean of individual drug content percentages; k = Acceptance constant (depends on sample size, k = 2.4 for n = 10); S = Standard deviation of drug content percentages. The Acceptance Criteria were:

- If AV ≤ L1 (15.0%), the batch is considered acceptable.
- If AV > L1, 20 tablets were tested (totaling 30).
- If AV for 30 tablets ≤ L1 and no unit is outside the range [1 – (0.01 × L2)]M or [1 + (0.01 × L2)]M, the batch is acceptable.
- L1 = 15.0% and L2 = 25.0% per regulatory requirements (Indonesian Ministry of Health, 2020).

2.6 Dissolution Test

Dissolution testing was carried out using a USP Type II (paddle) apparatus containing 900 mL of phosphate buffer (pH 6.8 ± 0.05) maintained at 37 ± 0.5 °C and stirred at 50 rpm. Samples were withdrawn at predetermined time intervals of 2, 5, 10, 15, and 20 minutes, filtered, and analyzed using a UV-Vis spectrophotometer at 249 nm (Alyami et al., 2021). The dissolution of Promethazine HCl should be not less than 80% of the labeled amount within 20 minutes (Indonesian Ministry of Health, 2020).

2.7 Statistical Analysis

Analysis of the collected data used Design-Expert software to pinpoint the most effective hydrolysis conditions. Simultaneously, ANOVA (Analysis of Variance) was used to assess the resulting tablet characteristics and determine whether statistically significant differences existed between the formulations. The threshold for statistical significance was set at $p < 0.05$.

3. RESULT AND DISCUSSIONS

3.1 Hydrolized Starch Evaluation

3.1.1 Organoleptic Test

Starch, a polysaccharide synthesized by plants through photosynthesis, typically forms crystalline granules that are insoluble in water at room temperature (Apriyanto et al., 2022). The yellowish color of pumpkin starch is attributed to β-carotene, a carotenoid responsible for its characteristic pigmentation (Pereira and Del Pino Beleia, 2021). Following acid treatment, the hydrolyzed pumpkin starch exhibited organoleptic properties as a white-yellowish, odorless, tasteless powder. The neutralization step after acid hydrolysis plays a crucial role in modulating starch properties. The addition of excess NaOH may induce partial gelatinization, potentially altering the starch's physical characteristics, such as color changes under elevated pH conditions. These findings are consistent with previous studies Sumaiyah et al. (2018), which reported that neutralization at pH 7 yielded a white, powdery starch. Maintaining a neutral pH during hydrolysis indicates a successful neutralization process, ensuring the starch's suitability for pharmaceutical and food applications.

3.1.2 pH Test

The pH of modified starch falls within the standard range for native starch (Table 2), which typically ranges from 4.0 to 8.0 (Adewumi et al., 2020). The acid hydrolysis process, followed by neutralization with NaOH, ensures that the pH remains stable and close to neutral, as confirmed by this study. The outcomes of the factorial design analysis, illustrating the effects of hydrolysis time and HCl concentration on the pH of starch, are presented in Equation 13.

$$\begin{aligned} pH = {} & 5.32083 - 0.115833(HT) \\ & - 0.320833(HC) - 0.1075(HT \cdot HC) \end{aligned} \tag{13}$$

Equation 13, derived from the factorial analysis, indicates that both hydrolysis time and HCl concentration adversely affect the pH of the modified starch. During acid hydrolysis, glycosidic bonds are cleaved by the addition of water molecules, which may release acidic by-products into the reaction medium. This phenomenon contributes to a decrease in the overall pH of the starch suspension as the hydrolysis process progresses (Grace and Liew, 2016). Statistical analysis confirmed that hydrolysis time, HCl concentration, and their interaction had a significant effect on pH ($p < 0.05$).

The contour plot (Figure 2) represents responses on a two-dimensional plane using colors and contour lines. Color distri-

bution indicates the magnitude of the response variable. Different colors correspond to different response levels (blue indicates the lowest level and red the highest). This could allow rapid visual identification of optimal or critical regions. Contour lines connect points that have the same response value; straight or nearly parallel lines indicate a linear relationship between the independent variables and the response, suggesting minimal or no interaction. Curved or elliptical lines indicate a non-linear relationship and/or a significant interaction between variables (Micelle, 2023).

3.1.3 LOD Test

LOD serves as a critical parameter for assessing the stability and moisture content of starch. An LOD value of ≤10% is generally considered acceptable, indicating low moisture and solvent content, and confirming that the starch has undergone proper processing. In this study, the hydrolyzed pumpkin starch exhibited higher LOD values (Table 2), which may be attributed to the increased porosity of starch granules following acid hydrolysis. The formation of pores enhances water retention and facilitates greater evaporation during drying. These findings are consistent with those of Chen and Zhang (2012), who observed that the pore size of hydrolyzed corn starch granules increased progressively with increasing degree of hydrolysis, reflecting the structural breakdown of starch granules into smaller, more porous particles. The effects of hydrolysis duration and HCl concentration on the LOD were further analyzed using the factorial design model, as presented in Equation 14.

$$\begin{aligned}\mathbf{LOD} = {} & 9.12008 + 0.767583(\mathrm{HT}) \\ & + 0.176583(\mathrm{HC}) + 0.132417(\mathrm{HT}\cdot\mathrm{HC})\end{aligned} \tag{14}$$

Equation 14, derived from the factorial analysis, indicates that both hydrolysis time and HCl concentration positively influence the LOD of the modified starch. The result is also presented in the contour plot (Figure 2). Prolonged hydrolysis disrupts the intra- and intermolecular hydrogen bonds within the starch matrix, leading to structural loosening and increased granular porosity. This enhanced porosity facilitates greater water retention and evaporation during drying, thereby resulting in higher LOD values, as suggested by Chen and Zhang (2012).

3.1.4 SEM

SEM images of the hydrolyzed starch revealed a porous, irregular surface structure, consistent with the findings of da Silveira et al. (2019). The research showed that acid hydrolysis breaks down the crystalline domains within the starch granules. This process leads directly to a larger surface area and improved porosity. Similar structural alterations were observed in the SEM images of the hydrolyzed pumpkin starch in this study. The porous and irregular morphology reflects the partial breakdown of the starch's internal structure during hydrolysis, which produces rough and non-uniform granule surfaces compared to native starch.

3.1.5 Flow Time and Angle of Repose Test

Flow time serves as a key indicator of powder flowability, particularly in evaluating the suitability of starch powders for pharmaceutical applications. In this study, the acid-hydrolyzed pumpkin starch exhibited excellent flow characteristics (Table 2), with most samples having flow times of less than 10 seconds. The angle of repose also functions as a crucial supplemental measure for evaluating powder flow characteristics. The measured values in this investigation ranged from 'very good' to 'good' based on the individual hydrolysis parameters. Notably, the factorial analysis demonstrated that both the duration of hydrolysis and the concentration of HCl were strong determinants of the starch's flow properties. Notably, reductions in hydrolysis time and acid concentration were associated with increased angle of repose, indicating decreased flowability under milder hydrolysis conditions. This trend was also observed by Olorunsola and Mohammed (2012), who found that acid hydrolysis improved the flow properties of both Ipomoea batatas and Manihot esculenta starches. The Equations 15 and 16 for the effects of hydrolysis time and HCl concentration on flow time and angle of repose are as follows:

$$\begin{aligned}\mathrm{Flow\ \ Time} = {} & 9.55583 - 0.629167(\mathrm{HT}) \\ & + 0.0442(\mathrm{HC}) - 0.3742(\mathrm{HT}\cdot\mathrm{HC})\end{aligned} \tag{15}$$

$$\begin{aligned}\mathrm{Angle\ \ of\ \ Repose} = {} & 29.8892 - 0.245750(\mathrm{HT}) \\ & + 1.30167(\mathrm{HC}) - 0.199861(\mathrm{HT}\cdot\mathrm{HC})\end{aligned} \tag{16}$$

The relationships between flow time, angle of repose, and the hydrolysis parameters (hydrolysis time and HCl concentration) are shown in Equations 15 and 16, derived from the statistical analysis of this study. These equations indicate that optimized acid hydrolysis conditions enhance the flow properties of starch by depolymerizing starch macromolecules into smaller, more uniform, and free-flowing particles. The negative coefficients for hydrolysis time and its interaction with HCl concentration suggest that prolonged hydrolysis significantly decreases both flow time and angle of repose, likely due to the increased granular flexibility, surface smoothness, and water absorption capacity resulting from structural modifications, as shown in Figure 2. In contrast, a higher acid concentration alone tended to increase these parameters, implying a potential trade-off between reaction intensity and structural integrity during optimization. Among the two factors, hydrolysis time exerted a more substantial influence. The ANOVA results further confirmed that hydrolysis duration had a statistically significant effect ($p < 0.0001$) in reducing both flow time and angle of repose. In contrast, HCl concentration and its interaction with time were not statistically significant ($p = 0.0592$ and $p = 0.1392$, respectively). These findings highlight the crucial role of hydrolysis time in determining the flow characteristics of hydrolyzed pumpkin starch, rather than acid strength.

3.1.6 Compressibility Testing

The compressibility index serves as a valuable indicator of a powder's flow characteristics and its propensity to consolidate

Table 2. Hydrolyzed Starch Characteristics

Characterization	9 Days 9%	9 Days 5%	3 Days 9%	3 Days 5%
pH	4.99 ± 0.24	5.35 ± 0.08	5.17 ± 0.03	5.31 ± 0.05
LOD (%)	10.20 ± 0.44	9.58 ± 0.60	8.40 ± 0.65	7.98 ± 0.59
Flow time (s)	8.60 ± 0.29	9.26 ± 0.07	9.77 ± 0.12	10.60 ± 0.09
Angle of repose	23.96 ± 0.38	25.95 ± 0.44	33.42 ± 0.65	36.23 ± 1.42
Carr's Index (%)	9.99 ± 0.008	12.00 ± 0.000	9.99 ± 0.006	16.00 ± 0.006
Hausner ratio	1.11 ± 0.001	1.14 ± 0.000	1.11 ± 0.000	1.19 ± 0.003
Swelling index	71.14 ± 0.24	68.55 ± 1.27	55.14 ± 0.50	52.17 ± 0.93
Effective Pore Radius (Reff.P)	25.93 ± 0.14	23.25 ± 0.15	23.25 ± 0.15	16.25 ± 0.22
Amylose content (%)	35.17 ± 0.11	31.21 ± 0.02	28.52 ± 0.19	26.28 ± 0.05
Amylopectin content (%)	64.83 ± 0.04	68.79 ± 0.03	71.48 ± 0.06	73.72 ± 0.07

under mechanical stress. A lower compressibility value, reflected by a Carr's Index below 10% and a low Hausner ratio, denotes superior flowability and minimal interparticle friction (Table 2). These parameters are essential for predicting the performance of powders during tablet compression and die-filling processes. The mathematical models derived from the factorial design are presented in Equations 17 and 18, which illustrate the quantitative relationship between hydrolysis conditions (time and HCl concentration) and the compressibility behavior of hydrolyzed pumpkin starch.

$$\text{Hausner Ratio} = 1.15125 - 0.03375(\text{HT}) - 0.02125(\text{HC}) + 0.00875(\text{HT} \cdot \text{HC}) \quad (17)$$

$$\text{Carr's Index} = 11.9992 - 0.999067(\text{HT}) - 2.00117(\text{HC}) + 0.9981(\text{HT} \cdot \text{HC}) \quad (18)$$

Both hydrolysis time and HCl concentration negatively affect the Hausner ratio and Carr's index, thereby enhancing flowability (Equations 17 and 18). The slight positive effect from their interaction suggests that at certain combined levels, some compromise may occur. The result is also presented in the contour plot of Figure 2. It corroborates earlier work by Olorunsola and Mohammed (2012), who also observed that acid treatment improves the flow properties of starch by modifying its particle size and morphology, thereby reducing particle cohesion.

3.1.7 Effective Pore Radius (Reff.p) and Swelling Index

A higher effective pore radius indicates increased porosity, improving water penetration (wicking) and subsequent swelling (Table 2). The regression model is shown in Equation 19.

$$\text{Reff.p} = 16.3563 + 3.72125(\text{Hydrolysis Time}) + 0.57625(\text{HCl Concentration}) + 0.40625(\text{Hydrolysis Time} \cdot \text{HCl Concentration}) \quad (19)$$

Both hydrolysis time and HCl concentration increase the effective pore radius, as shown in Equation 19 and Figure 2. Acid hydrolysis disrupts the starch granule structure, facilitating water ingress (Rashwan et al., 2024). The significant p-value for hydrolysis time ($p < 0.0001$) further supports the notion that prolonged treatment substantially enhances porosity.

3.1.8 Swelling Index

Swelling behavior is critical for disintegration, especially in tablet formulations. The highest swelling index was observed in the modified starch treated with 9% HCl for 9 days (Table 2). This can be attributed to the altered amylose-to-amylopectin ratio resulting from the modification process. The increase in amylose content occurs because strong acid hydrolysis breaks down glycosidic bonds, resulting in shorter amylopectin chains. A high swelling index facilitates starch disintegration, suggesting that this parameter can be considered when using the modified starch as a superdisintegrant. The model derived is shown in Equation 20.

$$\text{Swelling Index} = 60.1769 + 8.96063(\text{Hydrolysis Time}) + 1.59813(\text{HCl Concentration}) - 0.395625(\text{Hydrolysis Time} \cdot \text{HCl Concentration}) \quad (20)$$

An increased swelling index is desirable for faster disintegration. The positive effects of hydrolysis time and HCl concentration are evident, as shown in Equation 20 and Figure 2. The trend here aligns with that of Kibar et al. (2010), who noted that higher amylose content resulting from acid hydrolysis improves water uptake and swelling, which are crucial for rapid disintegration in tablet formulations. The significant effect of hydrolysis time ($p = 0.0019$) is again highlighted, reinforcing its critical role in starch modification.

3.1.9 FTIR Analysis

The FTIR spectra in Figure 3 show a comparison between native starch (A) and acid-hydrolyzed starch with variations in acid concentration (5% and 9%) and hydrolysis time (3 and 9 days) [(B)-(E)]. In general, all spectra show the characteristic absorption bands of polysaccharides, indicating that the basic starch structure remains intact after hydrolysis, although the bands' intensities and sharpness change (Yunita et al., 2022). Overall, the FTIR results confirm that acid hydrolysis alters

the physical and chemical structure of starch without altering its basic functional groups. This modification is characterized by a decrease in the intensity of the –OH band, changes in the characteristic C–O–C band, and a reduction in the regularity of the starch structure, indicating the success of the acid hydrolysis process in modifying the starch.

A broad absorption band in the range of 3600-3200 cm^{-1} was observed in all samples and is related to the stretching of hydroxyl groups (–OH) from glucose units and water bound within the starch structure. In hydrolyzed starch, this band appeared more intense and broader compared to native starch, especially in samples with higher acid concentrations and longer hydrolysis times. This indicates an increase in the number of free -OH groups due to the cleavage of glycosidic bonds and an increase in inter-chain hydrogen interactions in starch (Silverstein and Webster, 1996; Tester et al., 2004).

Absorption bands in the 2800-3000 cm^{-1} region, attributed to aliphatic C–H stretching vibrations of glucose units, were detected with relatively low intensity and showed no significant differences between samples, indicating that the starch carbon backbone remained intact despite acid hydrolysis (Silverstein and Webster, 1996). Absorption in the 1600-1650 cm^{-1} region is associated with the H–O–H bending vibrations of water molecules bound within the starch granules. The decrease in the intensity of this band in hydrolyzed starch indicates a reduced ability of the starch to bind water, which is related to changes in the amorphous fraction and the degradation of the granular structure due to acid hydrolysis (Asrofi et al., 2018; Šárka et al., 2023).

The fingerprint region (1000-1150 cm^{-1}) shows strong and characteristic absorption bands for starch, which are associated with C–O–C and C–O bond stretching vibrations from α-1,4 glycosidic bonds and the glucopyranose ring structure. In hydrolyzed starch, the bands in this region appear sharper and slightly shifted, indicating partial cleavage of glycosidic bonds and the formation of shorter polysaccharide chains such as dextrins or oligosaccharides (Cai et al., 2015). Additionally, the change in intensity in the 800-950 cm^{-1} region, which is related to the vibration of α-glycosidic bonds, indicates partial damage to the crystalline structure of starch. This effect becomes more pronounced in samples with higher acid concentrations and longer hydrolysis times, indicating that these conditions accelerate the starch degradation process (Zhang et al., 2013).

3.1.10 Amylose & Amylopectin Content

Starch is composed of two main polysaccharides: amylose and amylopectin. A low amylose concentration directly correlates with reduced swelling capacity and weaker gel strength in the starch. Conversely, a high proportion of amylopectin, particularly when it possesses short lateral chains, facilitates hydration through hydrogen bonding, leading to gel formation (Cornejo-Ramírez et al., 2018). The amylose content is measured by UV-Vis spectrophotometry at 625 nm. The test results (Table 2) show that modified starch has a higher amylose content than natural starch (25,16 ± 0.02%), with the modified starch after 9 days of treatment with 9% HCl having the highest amylose content (35.17 ± 0.11%). This increase in amylose is attributed to acid hydrolysis, which breaks the chains in the amorphous regions, thereby increasing the linear amylose fraction and decreasing the amylopectin content (Gonzalez and Wang, 2023). The results of the factorial design analysis yield the following equation (Equation 21).

$$\text{Amylose Content} = 30.0825 + 2.945(\text{A}) + 0.4375(\text{B}) + 1.465(\text{AB}) \quad (21)$$

Factor analysis shows that hydrolysis time and HCl concentration positively affect amylose content (p-value < 0.0001). The result is also shown in Figure 2. The increase in amylose content enhances the disintegration properties of the starch. The observed trend supports previous findings by Gonzalez and Wang (2023), which showed that acid hydrolysis preferentially breaks down the amorphous regions of starch, thereby increasing the linear amylose fraction.

3.2 Determination of the Optimal Formula

Using an overlay plot from Design Expert software, the optimal conditions for hydrolyzed pumpkin starch were determined to be 7.60% HCl for 9 days, yielding a desirability of 0.721 (Figure 2). This optimization process aligns with modern formulation strategies that balance multiple response variables, as supported by design-of-experiment literature.

3.3 Comparative Analysis with Crospovidone

A comparison was made between the optimized hydrolyzed pumpkin starch, native starch, and crospovidone, a widely used superdisintegrant. The key parameters compared were the effective pore radius and swelling index (Table 3). The optimized hydrolyzed starch's effective pore radius and swelling index are significantly higher than those of native starch (p < 0.05, Tukey HSD), indicating enhanced water absorption and disintegration properties. While crospovidone still exhibits a higher swelling index, the modified pumpkin starch shows competitive porosity and good swelling behavior, although Tukey HSD analysis revealed a significant difference (p < 0.05). This comparison suggests hydrolyzed pumpkin starch could be a promising alternative to commercial superdisintegrants. The findings align with earlier studies, which also support the use of modified starches in pharmaceutical preparations (Olorunsola and Mohammed, 2012).

3.4 Tablet Characterization

The tablet containing hydrolyzed starch was compared with native starch and crosspovidone, showing similar performance to crosspovidone (Table 3) but superior to native starch, which failed to meet the disintegration requirement (exceeding 2 minutes). The incorporation of hydrolyzed starch as a disintegrant demonstrated promising performance, comparable to that of native starch and the synthetic superdisintegrant

Table 3. Comparison of the Starch Characteristics and Tablet Characteristics Containing Optimum Hydrolyzed Starch, Native Starch, and Crospovidone as Disintegrant

Responses	Optimum Hydrolyzed Starch	Native Starch	Crospovidone
Starch Characteristics			
Effective Pore Radius (μm)	25.03 ± 0.35	12.27 ± 0.35	27.65 ± 1.40
Swelling Index	70.25 ± 0.57	44.30 ± 0.85	99.97 ± 0.13
Tablet Characteristics			
Hardness (Kg)	3.35 ± 0.05	3.30 ± 0.03	2.76 ± 0.06
Friability (%)	0.53 ± 0.04	0.55 ± 0.07	1.05 ± 0.09
Disintegration time (seconds)	49.18 ± 0.75	246.00 ± 0.11	36.00 ± 0.04
Drug content (%)	96.90 ± 0.20	93.70 ± 0.12	103.83 ± 0.22
L value (acceptance criteria)	3.99	5.68	14.78
% Drug released	96.79 ± 0.13	89.28 ± 0.46	97.06 ± 6.14

crospovidone. Tablets containing hydrolyzed starch exhibited adequate mechanical strength (Table 3), with a hardness value of 3.35 ± 0.05 kg, comparable to native starch (3.30 ± 0.03 kg) (p >0.05; on post hoc test tukey HSD) and higher than crospovidone (2.76 ± 0.06 kg) (p <0.05; on post hoc test tukey HSD). The higher hardness of hydrolyzed starch tablets suggests that hydrolysis improved the starch's compressibility by reducing crystallinity and increasing plastic deformation during compression (Olorunsola and Mohammed, 2012). This modification allows starch granules to deform and interlock more effectively, thereby strengthening interparticulate bonding.

Regarding friability, all formulations met the pharmacopeial acceptance criterion of less than 1% (Table 3). Notably, tablets containing hydrolyzed starch showed lower friability (0.53 ± 0.04%) than native starch (p >0.05; on post hoc test Tukey HSD), indicating good mechanical resistance and compressibility, likely due to the presence of both amorphous and crystalline regions that enable balanced elasticity and strength (Kouka et al., 2025). In contrast, crospovidone-containing tablets exhibited the highest friability (1.05 ± 0.09%), likely due to the high porosity and brittle nature of superdisintegrants (p < 0.05).

In contrast, tablets containing crospovidone exhibited the lowest hardness and higher friability (1.05 ± 0.09%) compared to starch-based formulations (p <0.05) (Table 3). Crospovidone is a highly porous, crosslinked polymer that lacks plastic deformation capacity; it primarily fractures in a brittle manner during compression (Brady et al., 2017). Consequently, fewer solid bridges form between particles, leading to reduced mechanical strength and a greater tendency to chip or abrade under stress (Ramírez and Robles, 2015).

The disintegration time results (Table 3) revealed that hydrolyzed starch (49.18 ± 0.75 s) exhibited significantly (p < 0.05) faster disintegration than native starch (246.00 ± 0.11 s) and slightly slower than crospovidone (36.00 ± 0.04 s) (p < 0.05). The improved performance compared to native starch can be attributed to increased water absorption and swelling capacity following hydrolysis, thereby promoting faster tablet breakup. The improved disintegration performance can be attributed to the increased effective pore radius and swelling index observed in the hydrolyzed starch, which enhances water penetration and capillary action within the tablet matrix. Meanwhile, crospovidone acts primarily through wicking and capillary mechanisms, rather than swelling, resulting in extremely rapid disintegration (Brady et al., 2017). Regarding drug content uniformity, all formulations complied with pharmacopeial standards (<15% variation), indicating homogeneous distribution of the API (active pharmaceutical ingredient) (Table 3). The hydrolyzed starch tablets showed consistent drug content (96.90 ± 0.20%), comparable to crospovidone (103.83 ± 0.22%) and superior to native starch (93.70 ± 0.12%).

In terms of dissolution behaviour (Table 3), tablets containing hydrolyzed starch released 96.79 ± 0.13% of the drug within 20 minutes, outperforming those formulated with native starch (89.28 ± 0.46%) (p < 0.05) and showing a release profile similar to crospovidone (97.06 ± 6.14%) (p > 0.05). The enhanced dissolution with hydrolyzed starch can be attributed to its increased hydrophilicity, improved porosity, and rapid disintegration, collectively enhancing surface wetting and drug (Pereira and Del Pino Beleia, 2021; Ulbrich et al., 2016).

These findings indicate that hydrolyzed starch exhibits physicochemical and functional properties comparable to those of crospovidone, with a balanced hardness, low friability, rapid disintegration, and high dissolution efficiency. The findings conclude that hydrolyzed starch presents a highly promising, natural, biodegradable, and economical substitute for synthetic disintegrants. This outcome reinforces the accelerating trend toward the use of environmentally conscious excipients in the development of pharmaceutical tablets.

4. CONCLUSIONS

Optimizing pumpkin starch acid hydrolysis yielded a modified starch with enhanced physicochemical and functional properties compared with native starch. The optimized hydrolyzed starch demonstrated improved flowability, porosity, swelling capacity, and amylose content. When incorporated into Promethazine HCl sublingual tablets, the hydrolyzed starch produced formulations with adequate hardness, low friability, rapid disintegration, and high drug release. Tablet dissolution perfor-

mance was comparable to crospovidone ($p > 0.05$), while mechanical strength was significantly improved ($p < 0.05$). These results indicate that optimized hydrolyzed pumpkin starch functions effectively as a natural superdisintegrant, offering a viable alternative to native starch in fast-disintegrating tablet formulations.

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