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Optimization of Sorghum-Based Orodispersible Films Containing Cetirizine HCl Using PEG 400: a Central Composite Design Approach

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Abstract

Starch is one of the natural biopolymers that is commonly used as a film-forming agent. It can be enzymatically cleaved to form more soluble malt dextrin (MDX), which can be produced from sorghum. One of the film-forming plasticizers used for orodispersible films (ODFs) is PEG 400. The purpose of this study was to optimize the formulation of Cetirizine HCl ODFs using MDX-sorghum for the film-forming polymer and PEG 400 as the plasticizer through Response Surface Methodology (RSM). A Central Composite Design (CCD) was used to create 14 combinations of varying amounts of MDX-sorghum and PEG 400. The films were tested for disintegration time (DT), tensile strength (TS), and elongation (EL). The optimized formulation (4.34% MDX-sorghum, 10% PEG 400) demonstrated a DT of 99.2 s, TS of 1.26 MPa, and EL of 110.7%. Compared with previous MDX-sorghum ODFs plasticized with glycerol (DT 82.95 s, TS 1.50 MPa, EL 104.26%) and triethyl citrate (DT 75.67 s, TS 1.39 MPa, EL 108.85%), the PEG 400–based films exhibited comparable mechanical strength, higher flexibility, and suitable disintegration characteristics. This confirms the potential of PEG 400 as an effective plasticizer and highlights the novelty of employing MDX-sorghum as a sustainable biopolymer source for patient-friendly ODF formulations.

Keywords: orodispersible film; malt dextrin; sorghum starch; polyethylene glycol 400; central composite design.

1. Introduction

Sorghum (*Sorghum bicolor* L. Moench) is a member of the Gramineae family, comprised of approximately 70–80% starch, and thereby represents a promising alternative source of starch. Variation in the compositional profile—such as starch, protein, fat, and polyphenol content—occurs according to genotype and agronomic conditions. The comprehensive chemical profile of sorghum renders it advantageous for both dietary and pharmaceutical uses, as documented in recent studies[1]. However, the undisturbed amylopectin structure of native sorghum starch confers several functional limitations: the heat-induced gel formation necessitates prolonged time intervals, the resulting gels exhibit high firmness, visual clarity is subdued, adhesive behavior is pronounced, and retro gradation is aggravated at ambient temperatures. The cited phenomena can be ascribed to the amylose fraction, the geometric constitution of the granule exterior, and cooperative engagements with low-molecular-weight factors, including storage polypeptides and membrane lipids [2]. Conversion of the starch to malt dextrin (MDX) via controlled, enzyme-mediated hydrolysis is effectively undertaken to ameliorate these barriers. Outcome analyses demonstrate that the hydrolysate possesses higher aqueous solubility, expanded surface diffusivity during film drying, and better mechanical integrity, favorable traits for the rational design of orodispersible pharmaceutical films [3].

MDX generated through controlled partial depolymerization via either enzymatic or acid hydrolysis exhibits a manageable molecular weight coupled with only a mild propensity to absorb moisture. Consequently, it performs dual roles as both a plasticizer and a humectant, mitigating the embrittlement typically observed in starch-based matrical films and thereby elevating their mechanical pliability [4]. Hence, MDX-sorghum exhibits significant promise as a film-forming polysaccharide for the fabrication of orodispersible films (ODFs). These films are engineered to dissolve within seconds of salivary contact,

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facilitating the swift release of active pharmaceutical ingredients (APIs) and achieving rapid bioavailability without the consumption of water. Such a characteristic is paramount for pediatric and geriatric cohorts, as well as individuals afflicted with dysphagia, all of whom frequently encounter difficulties when ingesting standard solid oral dosage forms[5]. Furthermore, the ease of ODF administration promotes adherence to therapeutic regimens. The dosage form is placed directly onto the tongue, obviating the requirement for auxiliary apparatus and thereby providing a non-invasive option that is particularly beneficial for vulnerable subpopulations, including children and patients experiencing needle-related anxiety[6].

Despite the growing interest in starch-based and malt dextrin-based ODFs, systematic investigations into the use of sorghum-derived malt dextrin (MDX-sorghum) as a film-forming polymer remain limited. In particular, the effect of PEG 400 concentration on the mechanical and disintegration characteristics of MDX-sorghum ODFs has not yet been optimized using statistical design approaches.

Cetirizine hydrochloride (Cetirizine HCl) is a second-generation H1-receptor antagonist, characterized by a preferential activity on peripheral binding sites, modest blood-brain penetration, and consequently a limited sedative burden. It is routinely prescribed for the treatment of several immunological disorders, including allergic rhinitis, atopic dermatitis, and chronic urticaria. The clinical efficacy of the compound is primarily mediated by competitive inhibition of peripheral H1 receptors, resulting in a reduction of symptoms driven by histamine release and subsequent signaling pathways[7]. Additional modulatory activity observed in vitro and in animal models has demonstrated that the molecule also exhibits modest anti-inflammatory properties. Such properties are credited to a suppressive effect on pro-inflammatory cytokine synthesis, inhibition of late-phase eosinophilic infiltration, and down-regulation of intercellular adhesion molecule-1 (ICAM-1), thereby limiting both eosinophil transmigration and viral entry through epithelial barriers [8]. The Biopharmaceutics Classification System (BCS) categorizes Cetirizine hydrochloride as a class III compound, which is characterized by elevated solubility concomitant with diminished membrane permeability[9]. These physicochemical properties eventually contributed to the design of an ODF dosage form expected to enhance the therapeutic and adherence behavior of the drug in the intended population.

The incorporation of appropriate plasticizers is a requisite step in the formulation of ODFs to confer the necessary film flexibility and elongation. Among the available options, PEG 400 continues to be a preferred plasticizer, owing to its clear, completely water-soluble profile and its tendency to endow the films with tensile strengths that surpass those imparted by alternative plasticizers, such as glycerol [10,11]. Although the incorporation of PEG 400 substantially enhances the film's plastic deformability and lowers its tendency to fail in brittle fracture, progressive increments of plasticizer concentration yield a notable, reproducible reduction in tensile strength. This observation underscores the necessity of regulating the plasticizer content to optimize mechanical properties, ensuring that the anticipated gains in flexibility do not concurrently entail a deleterious compromise in the cohesive tensile integrity of the polymeric matrix [12]. Accordingly, the concurrent use of a film-forming copolymer composed of MDX-sorghum, in conjunction with an optimal level of PEG 400, is anticipated to arrive at a balanced configuration of mechanistic resilience and rapid disintegration, thereby rendering the formulation a sound candidate for the establishment of a novel pharmaceutical dosage form of Cetirizine HCl.

To date, there is no published literature documenting the co-application of sorghum-derived MDX and PEG 400 in the formulation of Cetirizine HCl ODFs, affirming the innovative character of the present investigation. This work, therefore, pursues the optimization of Cetirizine HCl ODFs through the dual incorporation of both excipients in accordance with the stipulated objectives. Optimization is conducted via Response Surface Methodology (RSM) predicated upon a Central Composite Design (CCD) model, the design facilitating the evaluation of independent variables—namely, the concentration of the film-forming polymer and the concentration of the plasticizer—against the predefined outcome measures of tensile strength, percentage elongation, and disintegration time of the ODFs[3]. This methodology is directed toward obtaining the optimal pharmaceutical formulation, thereby expediting the translational progress of orodispersible films derived from sorghum toward clinical use as a differentiated drug delivery platform.

2. Experimental (Materials and Methods)

2.1. Material

The study used Cetirizine HCl (Supriya Lifescience, India) procured from PT. Kimia Farma Indonesia, sorghum starch (Timurasa, Indonesia), PEG 400 (idCHEM, Korea), glucose (Merck, Germany), HPMC (Luxchem, Indonesia), α-amylase (Hench Biotech, China), citric acid and sucrose (HIMedia, India), hydrochloric acid and sodium hydroxide (ROFA Lab., Indonesia), calcium chloride anhydrous, Fehling's solutions A and B (Purnomo Putra Kimia, Indonesia), and distilled water.

2.2. Methods

2.2.1. Preparation of MDX-sorghum

Sorghum starch was suspended in distilled water to yield a 24% w/v aqueous dispersion, and the pH of this solution was adjusted to 6.0 by incremental addition with 0.1 N hydrochloric acid and 0.1 N sodium hydroxide. Subsequently, 100 µmol/L

anhydrous calcium chloride and 0.5 mg of α-amylase per gram of starch were introduced into the starch suspension. The dispersion was maintained under continuous stirring at 85 °C for 90 min in a thermostatically controlled water bath. Enzyme activity was subsequently terminated by the dropwise addition of 0.5 N hydrochloric acid until a final pH of approximately 4 was attained. The suspension was then cooled to 60 °C, neutralized to pH 7.0 with 0.1 N sodium hydroxide, and spread in a thin layer on a preheated, rectangular baking sheet. The thin layer was dried in a forced-air laboratory oven until a constant weight was reached. The dried gel was pulverized in a laboratory blender, and a fine fraction was isolated by sieving through a 0.5-mm aperture screen, collecting the powder for further analyses[3].

2.2.2. Characterization of MDX-Sorghum

The MDX-sorghum was characterized in terms of dextrose equivalent (DE), swelling power, and solubility, according to methods cited in Amalia et al. (2023) and Nining et al. (2024). DE analysis of MDX–sorghum dispersions was accomplished by titration to endpoint with added Fehling's solution; quantification was calibrated against an anhydrous d-glucose standard. Determinations of swelling power were executed by dispersing 0.1 g of the MDX–sorghum blend into 10 mL of deionized water, subjecting the mixture to 30 min of thermal agitation at 60 °C, followed by centrifugation at 2500 rpm for 15 min and gravimetric analysis of the sediment mass to derive swelling power. Solubility was assessed by collecting known aliquots of the supernatant, drying, and reweighing the dry residue to obtain mass recoveries[3,13].

2.2.3. Experimental Design

The experimental design was performed using RSM with a CCD. The independent variables were the concentration of MDX-sorghum (X_1) as the film-forming agent and PEG 400 (X_2) as the plasticizer, while the dependent variables (responses) included disintegration time (Y_1), elongation (Y_2), and tensile strength (Y_3). The factor levels and ranges are presented in **Table 1**. A total of 14 formulations were generated for response evaluation. The concentration ranges for both MDX-sorghum and PEG 400 were determined through preliminary film-forming trials. The selected ranges corresponded to formulations that produced uniform ODFs with good peel ability from the casting surface and without visible cracking or brittleness. Concentrations outside these limits led to films lacking structural integrity, while concentrations above resulted in excessively tacky films that were difficult to handle or remove cleanly. Formulations showing these deficiencies were excluded from the design space.

Table 1: Range and level of variable factor

Factor	Star point (-α)	Low (-1)	Center Level (0)	High (+1)	Star point (+α)
X_1: MDX-sorghum (% w/w)	2.0	2.59	4.0	5.41	6.0
X_2: PEG 400 (% w/w)	3.0	4.03	6.5	8.97	10.0

2.2.4. Preparation of ODF

ODFs were fabricated through a solvent-casting methodology. All components of the formulation were precisely measured prior to the initiation of the procedure. Citric acid (4% w/w) and sucrose (4% w/w) were co-dissolved in a predetermined volume of distilled water, generating Solution A. A blend of MDX-sorghum and the plasticizer PEG 400 was sequentially hydrated with distilled water to effect complete granule swelling, yielding Solution B. Hydroxypropyl methylcellulose (HPMC, 4% w/w) was suspended in pre-heated distilled water and agitated until complete film formation, producing Solution C. The composite mixture of Solutions B and C was then augmented with a supplementary portion of PEG 400; agitation persisted until a homogeneous dispersion was attained. Cetirizine HCl and the remaining distilled water were added to reach a final volume of 100 mL, and the mixture was stirred thoroughly. All steps involved steady stirring at 60°C.The resulting uniform solution was poured into a glass casting mold measuring 20 × 30 cm² and spread evenly. The mold was dried in an oven at 50°C for 24 hours to form films. After drying, the films were peeled off and sectioned into 2 × 2 cm² pieces, each containing 10 mg of cetirizine HCl. The whole mold produced 150 individual films containing a total drug mass of 1.5 g. This method provided ODFs with uniform thickness, consistent drug loading, and repeatable mechanical and disintegration properties[13,14].All film samples were stored in a desiccator prior to testing to minimize the influence of ambient humidity on their mechanical and disintegration properties.

2.2.5. Disintegration Time

Disintegration time was quantified by introducing 2 mL of distilled water into a petri dish containing a pre-cut segment of the film dosage form. Following the immersion of the film into the aqueous medium, the elapsed period required for complete dissolution of the polymeric structure was timed and subsequently documented as the effective disintegration time[15].

2.2.6. Elongation and Tensile Strength

Elongation was determined to quantify the capacity of the film to deform plastically and elastically. At the same time, tensile strength was obtained to characterize the maximum stress the film could sustain prior to rupture. Measurements were executed

on a universal testing machine (UTM, Strograph). A rectangular specimen of standard dimensions was secured centrally within the machine clamps and subjected to a uniaxial tensile force, the load and displacement simultaneously recorded until failure occurred, yielding both elongation data and peak tensile strength, as delineated in the referenced literature[16].

2.2.7. Data Analysis

The three responses obtained—disintegration time, elongation, and tensile strength—were further analyzed using RSM for optimal formulation determination. Regression models were created to define the relationship between the independent variables MDX-sorghum and PEG 400 concentrations [13].

2.2.8. Model Validation

The validation of predictive accuracy involved calculating the percentage error based on the difference between the observed responses from experiments and the values forecasted by the regression model. Low percentage error signified a dependable model for formulating the ODF optimization [17].

3. Results and discussion

3.1. Characterization of MDX-sorghum

MDX was produced by enzymatic hydrolysis of starch source using α-amylase with distilled water as the hydrolysis medium and calcium chloride as an enzyme stabilizer [14,18]. The DE value for MDX-sorghum was significantly elevated in comparison to native sorghum starch (6 vs 0.84), a finding that aligns with established behavior in enzymatic hydrolysis. In the experimental protocol, a suspension of starch was subjected to gelatinization at 85 °C, after which α-amylase catalyzed the hydrolysis of internal α-1,4 glycosidic bonds, leading to liquefaction of the gel. The enzymatic reaction yielded saccharides with reduced chain length, primarily oligosaccharides, maltose, and glucose. The release of these shorter oligosaccharides raises the concentration of reducing sugars in the supernatant, which in turn produces an increase in the measurable DE value. The elevated DE is a recognized correlate of enhanced film-forming capability, confirming the suitability of the hydrolyzed MDX-sorghum for film formulation [19].

The swelling power of MDX-sorghum starch increased modestly, shifting from 2.44 to 2.87, a change that correlates with the enzymatic derangement of the granular amylose network and the concomitant post-hydrolytic deterioration of crystalline domains. Such restructuring predisposes the starch to a greater molar ratio of disorder, thereby enhancing both hydration and potential enzymatic hydrolysis[1]. A concomitant rise in solubility was recorded, with MDX-sorghum solubilizing 52.9% of its mass—more than four times that of the untreated substrate (12.52%); this is rationalized by the progressive fragmentation of the parent granule into more reactive and spatially dispersed smaller lamellae, which promote hydrolytic release of more soluble oligosaccharide and malt oligosaccharide fragments [3].

The observed increases in DE, swelling power, and solubility for MDX-sorghum starch, when compared to the native polymer, provide unambiguous evidence that the enzymatic hydrolysis employed in the study effectively tailored the physicochemical properties of the sorghum starch. These modifications, taken together, significantly enhance the functional versatility of the modified polymer, positioning it as a promising film-forming excipient for integration within pharmaceutical dosage forms[3,13].

3.2. Optimization process

A CCD-RSM with two factors (MDX-sorghum X_1: 2.00–6.00% w/w; PEG 400 X_2: 3.00–10.00% w/w) was applied to optimize disintegration time (DT, Y_1), elongation (EL, Y_2), and tensile strength (TS, Y_3). Fourteen runs were evaluated (**Table 2**), and all formulations met general ODF acceptance criteria used in this study (DT<180s, EL >70%, TS within ranges 1.02–10.2 MPa)[3]. This indicates that the design space was appropriate for optimization.

Table 2: Experimental runs and observed responses for CCD-RSM optimization of MDX-sorghum and PEG 400

Run	X_1 (% w/w)	X_2 (% w/w)	Y_1 (seconds)	Y_2 (%)	Y_3 (MPa)
1	4.00	6.50	161	66.86	2.81
2	4.00	3.00	189	44.46	4.43
3	4.00	10.00	99	94.75	1.69
4	4.00	6.50	167	73.58	2.95
5	5.41	8.97	110	101.7	1.5
6	4.00	6.50	167	77.81	4.13
7	2.59	8.97	150	85.84	2.11
8	4.00	6.50	160	66.86	2.81
9	6.00	6.50	133	88.32	1.9

10	4.00	6.50	170	80.6	2.2
11	4.00	6.50	167	62.59	3.3
12	2.59	4.03	196	42.46	5.6
13	2.00	6.50	183	51.13	3.47
14	5.41	4.03	177	56.92	2.99

Analysis of the experimental data revealed notable trends. Films containing higher PEG 400 concentrations generally exhibited shorter DT and greater flexibility due to enhanced plasticization, while excessive PEG 400 reduced TS—consistent with previous reports showing that elevated plasticizer levels increase polymer chain mobility at the expense of mechanical resistance[20,21]. Conversely, higher MDX-sorghum concentrations improved film integrity and TS through matrix reinforcement but slightly prolonged DT because of a denser polymer network[22]. In contrast, a low polymer concentration can result in inadequate film-forming properties, causing reduced flexibility and prolonged DT[23].

The interaction between MDX-sorghum and PEG 400 further emphasized their complementary roles. At lower concentrations of both components, films tended to become rigid and brittle, whereas moderate MDX levels combined with higher PEG 400 contents produced uniform, flexible ODFs with rapid disintegration. These outcomes confirm that PEG 400 primarily influences disintegration and flexibility, while MDX-sorghum governs mechanical strength and film cohesion. The CCD-RSM approach effectively quantified these relationships, forming the basis for constructing response surface plots and identifying optimal formulation conditions in subsequent analyses.

3.3. Effect of variable response on disintegration time (DT, Y_1)

DT is a critical performance attribute of ODFs, as it determines patient compliance, onset of action, and overall acceptability of the dosage form [24]. Currently, no official DT limits are specified for ODFs in the European Pharmacopoeia or the US Pharmacopoeia. Therefore, most studies adopt the disintegration criteria for orally disintegrating tablets (ODTs)—≤180 seconds (Ph. Eur.) or ≤30 seconds (FDA Guidance for Industry)—as reference benchmarks for evaluating ODF performance [25].

The response was best fitted by a quadratic model (adjusted $R^2 = 0.9643$; predicted $R^2 = 0.8866$; adequate precision = 26.6371), confirming good model predictability and reliability. The fitted equation:

$$Y_1 = 165.33 - 16.21X_1 - 30.03X_2 - 5.25X_1X_2 - 1.85X_1^2 - 8.85X_2^2$$

Reveals that both MDX-sorghum (X_1) and PEG 400 (X_2) significantly reduce DT, as indicated by their negative coefficients. This relationship is further visualized in the contour and 3D response surface plots (**Figure 1**), which clearly illustrate the trend of shorter DT at higher concentrations of both variables.

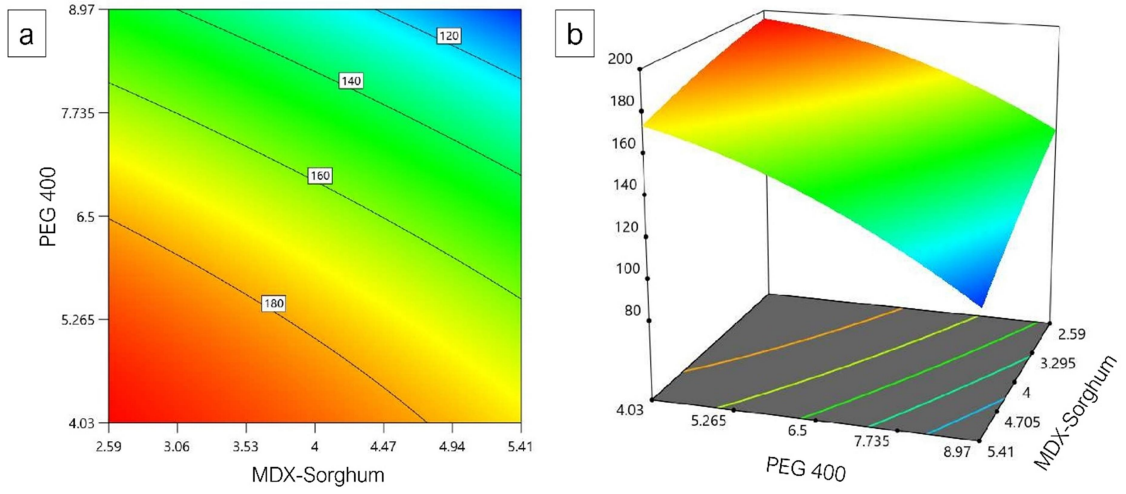

Figure 1: Contour plot (a) and 3D response surface (b) showing the effect of MDX-sorghum and PEG 400 on the disintegration time of ODFs.

Hydrophilic polysaccharides, enriched with abundant hydroxyl groups, readily interact with water through extensive hydrogen bonding. This interaction promotes significant hydration and swelling, which in turn increases the water content within the polymeric network. Such changes alter both the mechanical rigidity of the matrix and the hydration forces between

particles, ultimately inducing notable modifications in the rheological and mechanical properties that facilitate drug release.[23]. Coincidentally, the incorporation of PEG 400, a low-molecular-mass hydrophilic diluent, augments the effective pore volume of the polymeric matrix by the transient incorporation of water-miscible polymer domains. This increase in pore interconnectivity promotes the penetration of water, further accelerating the swelling dynamics and, ultimately, the disintegration of the dosage form [26].

The interaction term (X_1X_2) also bears a negative coefficient (–5.28), suggesting that combined increases of MDX and PEG 400 exert a synergistic effect on disintegration. However, the significant quadratic contributions (X_1^2 and X_2^2) highlight non-linear trends, implying that beyond a certain threshold, further addition of either component yields diminishing improvements or even counterproductive effects. Such non-linear behavior aligns with prior studies indicating that increasing plasticizer concentration reduces intermolecular forces within the polymer matrix, leading to decreased TS, increased flexibility, and enhanced water solubility of the film, which together influence its disintegration behavior [11,21].

Comparable findings have been reported in ODF systems incorporating starch derivatives, pullulan, or other polysaccharides, where the balance between hydrophilic polymer and plasticizer content governs rapid disintegration while maintaining mechanical robustness [15,27]. Notably, the current results demonstrate that MDX-sorghum, when combined with PEG 400, achieves comparable disintegration performance to previously reported starch-based ODFs, underscoring its potential as a sustainable and effective film-forming polymer for fast-dissolving formulations.

3.4. Effect of variable response on elongation (EL, Y_2)

EL is a key mechanical property of ODFs, reflecting the film's ability to withstand tensile stress before breaking. This attribute is critical for ensuring the film's flexibility, resistance to brittleness, and suitability for handling, packaging, and patient use [28]. In pediatric and geriatric formulations, sufficient extensibility prevents tearing during administration while maintaining patient compliance and dosage accuracy [15].

In this study, EL was best fitted by a linear model (adjusted $R^2 = 0.9035$; predicted $R^2 = 0.8804$; adequate precision = 22.9191), confirming the model's good predictability and robustness. The fitted equation was:

$$Y_2 = 70.99 + 10.36X_1 + 19.91X_2$$

The positive signs of the coefficients for both the MDX-sorghum variable (X_1) and the PEG 400 variable (X_2) confirm that increments in either input promote film elongation, with PEG 400 exerting the more pronounced influence. This trend is quantitatively corroborated by the contour and 3D surface plots (**Figure 2**), where EL consistently rises in concurrent elevations of both factors.

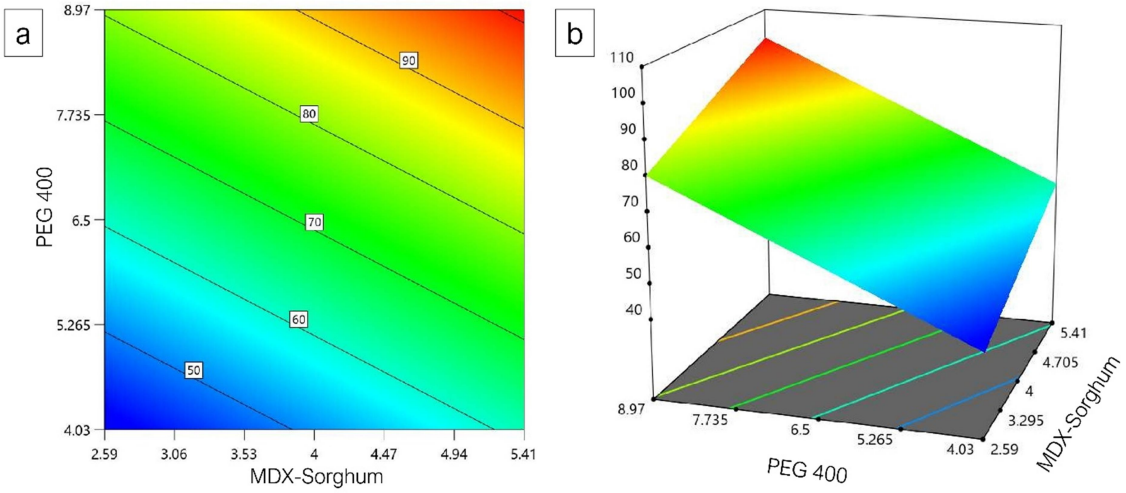

Figure 2: Contour plot (a) and 3D response surface (b) showing the effect of MDX-sorghum and PEG 400 on elongation of ODFs.

The underpinning mechanism is as follows: low-molecular-weight MDXs—like the MDX derived from sorghum-generate less cross-linked and thus more pliable polymer matrices compared with higher-molecular-weight analogues, permitting enhanced macromolecular mobility [3]. Concurrently, the PEG 400 acts as a classic low-temperature plasticizer, inserting itself into the amorphous interstitial zones of the polymer film, perturbing the native interchain hydrogen bonds and progressively lowering the overall glass transition temperature [10,27]. The resultant combined modification of both

configurational density and intrachain kinetic freedom is what ultimately yields the augmented extensibility observed in the ODF matrices.

This outcome aligns with prior reports showing that MDX enhances the flexibility of potato starch-based films by increasing EL at break and reducing stiffness but does not significantly improve TS, potentially decreasing film rigidity at higher concentrations [29]. The same thing also shows another study that higher amounts of plasticizer increase film flexibility but can sacrifice TS if used excessively [30]. Thus, optimizing EL requires balancing polymer–plasticizer ratios to achieve flexible films without sacrificing strength or integrity. Notably, the MDX-sorghum/PEG 400 system demonstrated elongation comparable to ODFs plasticized with triethyl citrate and slightly higher than those plasticized with glycerol, indicating a balanced mechanical performance and efficient film-forming capability.

3.5. Effect of variable response on tensile strength (TS, Y_3)

TS defines the uppermost stress that an ODF withstands before fracture, serving as an indispensable indicator of the film's mechanical reliability across the phases of fabrication, storage, and delivery [15,31]. A sufficiency of TS inhibits uncontrolled rupture during the manufacturing sequence, the packaging routine, and the operative moment of administration, thus safeguarding the film's structural uniformity and the concomitant stability of the dosage form [11,15,32].

In this study, TS was best fitted by a linear model (adjusted $R^2 = 0.7526$; predicted $R^2 = 0.6690$; adequate precision = 13.5443), confirming the model's suitability for predicting experimental outcomes. The fitted equation was:

$$Y_3 = 2.99 - 0.68X_1 - 1.11X_2$$

The negative coefficients for both MDX-sorghum (X_1) and PEG 400 (X_2) indicate that increasing either factor decreases TS. As shown in the contour and 3D response surface plots (**Figure 3**), higher concentrations of MDX-sorghum and PEG 400 resulted in lower TS values, reflecting reduced resistance of the film matrix to applied stress.

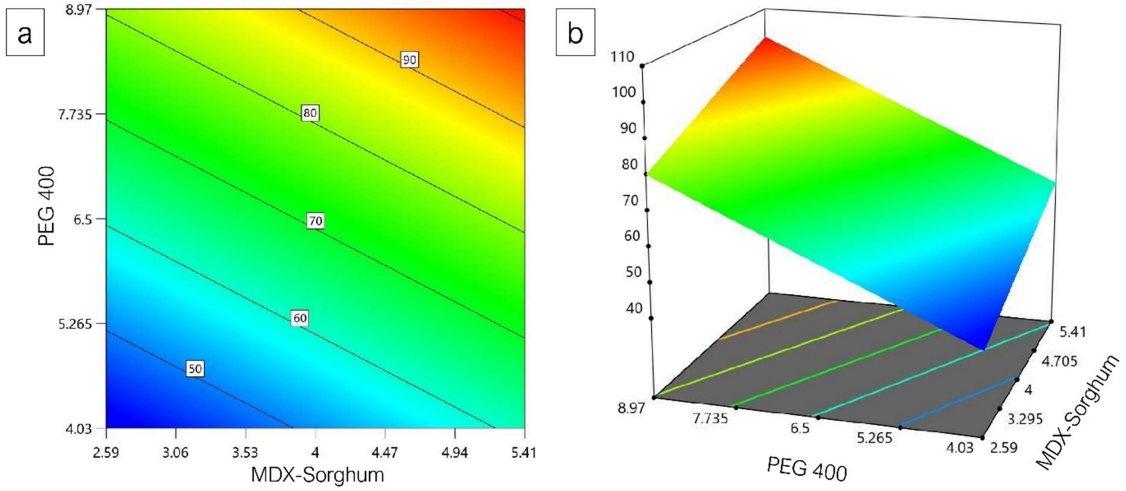

Figure 3: Contour plot (a) and 3D response surface (b) showing the effect of MDX-sorghum and PEG 400 on tensile strength of ODFs.

Mechanistically, low-molecular-weight MDXs form less entangled and less cohesive networks compared to high-Mw polysaccharides, thereby lowering film rigidity [11]. Similarly, plasticizers like PEG 400 intercalate between polymer chains, weakening intermolecular interactions and reducing cohesive energy density, all of which diminish TS[12,21].This outcome is consistent with previous reports showing that higher plasticizer or MDX content improves flexibility but compromises mechanical strength. Increasing PEG concentration as a plasticizer result in a decrease in the TS of the carrageenan film [33].Another study reported that an increase in the concentration of MDX generally decreases the TS of the films due to its plasticizing effect and its role as small molecular weight filler that disrupts polymer network strength. While TS remains relatively stable at MDX levels up to 40%, higher concentrations lead to significant reductions in mechanical strength as the continuous polymer networks are compromised [34].

Therefore, optimizing TS requires balancing polymer and plasticizer concentrations to ensure films remain both flexible and mechanically stable. Notably, the MDX-sorghum/PEG 400 system in this study maintained adequate tensile strength

while exhibiting comparable or slightly improved flexibility relative to other starch-based ODFs reported previously, highlighting its balanced mechanical properties and formulation efficiency

3.6. Optimization of ODF cetirizine HCl formulation

The optimized ODF formulation was selected using RSM with a desirability function approach, aiming to minimize DT (Y_1), maximize EL (Y_2), and maintain adequate TS (Y_3). These parameters are critical for ensuring rapid onset of action, patient compliance, and mechanical robustness during handling, packaging, and administration, particularly in pediatric and geriatric populations [24,27,31].

Numerical optimization predicted an optimal formulation containing 4.34% w/w MDX-sorghum and 10% w/w PEG 400, with an overall desirability of 0.67. The predicted responses were DT 99.20 s, EL 101.7%, and TS 1.26 MPa (**Table 3**).

Table 3: Comparison of predicted and experimental values for the optimized MDX-sorghum ODF formulation

Parameter	Y_1 (seconds)	Y_2 (%)	Y_3 (MPa)
Predicted	99.20	101.7	1.26
Experimental	99.7	101.67	1.28
Error (%)	0.50	0.03	1.59

The experimentally prepared film closely matched the predicted values, with percentage prediction errors below 5% for all responses, confirming the accuracy and reliability of the RSM model[3]. The optimized ODF displayed rapid disintegration, high extensibility, and adequate mechanical strength, which are key requirements for a patient-friendly oral dosage form [12,31].

The hydrophilic MDX facilitates fast water uptake and swelling due to abundant hydroxyl groups, promoting rapid disintegration [3,27]. In parallel, PEG 400, a hydrophilic plasticizer with low to moderate molecular weight, engages with the hydroxyl moieties of the polymer and subsequently lodges itself within the space among adjacent polymer chains. This intercalation effectively weakens the dense intra- and intermolecular hydrogen bonding, resulting in greater segmental freedom of the polymer backbone. As a direct consequence, the EL and TS are significantly elevated[35]. Another study reported that a similar plasticizing mechanism is operable within polylactic acid (PLA) as a polymer, where PEG 400 is shown to weaken hydrogen bonding between polymer chains [36]. This synergistic effect elucidates the high elongation value of 108.85%, suggesting that the film is flexible enough to withstand handling stresses without risk of tearing.

Hydration and plasticization increase flexibility and aid in disintegration, but they may compromise TS. In this case, a TS of 1.39 MPa indicates that the optimized polymer–plasticizer ratio sustains structural integrity while achieving acceptable flexibility. This balance is critical for the ODFs to withstand packaging, transport, and handling by the patient without distortion[12,28].The results presented confirm that the optimized formulation of MDX-sorghum/PEG 400 ODF exhibits a commendable triad of rapid disintegration, elevated extensibility, and sufficient mechanical strength. Such characteristics suggest that PEG 400 MDX-sorghum films may provide adequate fast delivery of cetirizine HCl. The study further illustrates the critical influence of finely tuned polymer-plasticizer ratios on both the technical performance of the dosage form and the practical usability for the patient [12,31].

MDX-sorghum demonstrates considerable potential as a multifunctional excipient applicable to diverse pharmaceutical formulations beyond ODFs. In general, maltodextrins from various starch sources are widely integrated into drug delivery systems as fillers, binders, stabilizers, and carriers, supporting both solid and liquid dosage forms such as rapidly dissolving tablets, encapsulation technologies, and macromolecule delivery platforms [4,11,37]. The ability to form films with excellent water solubility and fast disintegration makes MDX-based films an ideal platform for ODFs, with potential for controlled drug release and transdermal delivery[11,15,27].Furthermore, using sorghum-derived MDX provides a cost-effective and sustainable alternative to commercially available MDXs, aligning with the growing interest in renewable and locally sourced pharmaceutical excipients.

4. Conclusion

MDX-sorghum, obtained through enzymatic hydrolysis, exhibited improved solubility, moderate DE, and enhanced swelling capacity, making it suitable as a film-forming polymer for ODFs. RSM optimization revealed that PEG 400 primarily enhanced DT and EL, while MDX-sorghum contributed to the strengthening of TS. The optimized formulation (4.56% MDX-sorghum, 10% PEG 400) showed rapid DT (75.67 s), high EL (108.85%), and adequate TS (1.39 MPa), closely matching the predicted values. Mechanistically, the hydrophilic polymer and plasticizer synergistically promoted water uptake, swelling, and chain mobility, yielding films that are flexible yet mechanically robust. These results demonstrate that MDX-sorghum is a promising excipient for pediatric and geriatric ODFs. Furthermore, it shows potential as a versatile filler, binder, stabilizer, or

carrier in other dosage forms, offering a sustainable alternative to conventional MDXs. Future studies will focus on evaluating the drug content, in vitro release profile, and in vivo performance of the optimized Cetirizine HCl ODF formulation to confirm its pharmaceutical effectiveness and clinical applicability.

5. Conflicts of interest

The authors declare that there are no conflicts of interest associated with this manuscript.

6. Formatting of funding sources

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