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Influence of Native and Acid-Modified Ofada Rice (*Oryza glaberrima*) Starches on the Mechanical and Release Properties of Folic Acid Gummies

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ABSTRACT

Background: Folic acid deficiency is a major cause of anaemia in children; formulating it as medicated gummies may improve therapeutic outcomes through enhanced palatability and patient compliance.

Objectives: This study evaluated effects of native Ofada rice (NOS) and acid-modified Ofada rice starches (AOS) co-gelling agents on properties of folic acid gummies.

Methods: NOS was acid-hydrolysed and characterized by scanning electron microscopy (SEM) and Fourier transform infrared (FTIR) spectroscopy. Full factorial design-based desirability function approach evaluated the effects of gelling agent type (X_1) and percentage (X_2) on crushing strength and dissolution time (t_{50}) folic acid gummies prepared using gelatin alone and 1:1 gelatin-starch blends (5.0, 7.5, and 10.0 %w/w).

Results: Starch-containing gummies had acceptable organoleptic properties. Crushing strength ranked Gelatin > AOS > NOS, while AOS gave the fastest drug release (t_{50} = 8.50 ± 0.63 - 15.00 ± 1.00 min, p = 0.019). Factorial analysis identified X_1 as the major determinant of crushing strength (p = 0.000), whereas X_2 had a smaller but significant effect (p = 0.002). Optimized formulation achieved a composite desirability of 0.9988, with a crushing strength of 30 N and dissolution time of 15 min.

Conclusion: Folic acid gummies can be formulated using native and acid-modified Ofada rice starches as co-gelling agents.

Keywords: Acid modification, Anaemia, Folic acid gummies, Factorial design, Ofada rice starch

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Influence des amidons de riz Ofada (*Oryza glaberrima*) natifs et modifiés par acidification sur les propriétés mécaniques et de libération des gommes à l'acide folique

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RÉSUMÉ

Contexte : La carence en acide folique est une cause majeure d'anémie chez l'enfant ; sa formulation sous forme de gommes médicamenteuses pourrait améliorer les résultats thérapeutiques grâce à une meilleure acceptabilité gustative et une meilleure observance du traitement par le patient.

Objectifs : Cette étude a évalué les effets des agents co-gélifiants d'amidon natif de riz Ofada (NOS) et d'amidon de riz Ofada modifié à l'acide (AOS) sur les propriétés des gommes à l'acide folique.

Méthodes : Le riz natif Ofada (NOS) a été hydrolysé en milieu acide et caractérisé par microscopie électronique à balayage (MEB) et spectroscopie infrarouge à transformée de Fourier (IRTF). Une approche factorielle complète basée sur la fonction de désirabilité a permis d'évaluer les effets du type (X_1) et du pourcentage (X_2) d'agent gélifiant sur la résistance à la compression et le temps de dissolution (t_{50}) de gommes à l'acide folique préparées avec de la gélatine seule et des mélanges gélatine -amidon 1:1 (5,0 ; 7,5 et 10,0 % p/p).

Résultats : Les gommes à base d'amidon présentaient des propriétés organoleptiques acceptables. Le classement de la résistance à la compression était la suivante : Gélatine > AOS > NOS, tandis que l'AOS permettait la libération du principe actif la plus rapide (t_{50} = 8,50 ± 0,63 à 15,00 ± 1,00 min, p = 0,019). L'analyse factorielle a identifié X_1 comme le principal déterminant de la résistance à la compression (p = 0,000), tandis que X_2 avait un effet plus faible mais significatif (p = 0,002). La formulation optimisée a atteint un score de désirabilité composite de 0,9988, avec une résistance à la compression de 30 N et un temps de dissolution de 15 min.

Conclusion : Il est possible de formuler des gommes à l'acide folique en utilisant des amidons de riz Ofada natifs et modifiés par l'acide comme agents co-gélifiants.

Mots-clés : Modification à l'acide, anémie, gommes à l'acide folique, plan factoriel, amidon de riz Ofada

INTRODUCTION

Anaemia, defined as a low blood haemoglobin level or red blood cell mass that is insufficient to meet the oxygen demands of peripheral tissues and organs, is one of the most common hematologic disorders in children.[1] Approximately 39.8 % of children aged 6 to 59 months are reported to be anaemic, with Africa having the highest (60.2 %) prevalence.[2] Causes of anaemia include iron and folic acid deficiencies, chronic infections and hereditary hemoglobinopathies.[3] Folic acid supplementation is important in the production of red blood cells and prevention of neural tube defects, thereby improving overall health. However, there is the need for age-appropriate medications to treat paediatric patients who may often face challenges in adhering to conventional folic acid formulations (such as tablets, capsules or liquid dosage forms) due to difficulty in swallowing and/or taste aversion.[4]

An alternative delivery system to overcome some of these challenges is medicated gummies. Medicated gummies are edible, chewable dosage forms that contain one or more active ingredients for therapeutic or supplemental use.[5] Gummies effectively mask unpleasant tastes, a common barrier to medication adherence, making them appealing to paediatric patients. In addition, unlike many solid dosage forms, gummies do not require water and can be taken anywhere and at any time, making them ideal for modern lifestyles. Furthermore, mastication can result in partial buccal absorption and increased bioavailability.[6] Flexibility of medicated gummies has allowed for the inclusion of a wide range of APIs, such as vitamins, minerals, and other therapeutic agents, allowing them to be used for both preventive and curative purposes.

Although gelatin is an essential gelling ingredient in the preparation of gummy formulations, consumers are beginning to demand non-animal products.[7] Other hydrocolloid agents such as starch, gums, pectin, and carrageenan can be utilized for a range of different textures that cater to the preferences of the modern market.[8] Starch functions as a versatile gelling agent capable of improving the texture and stability of gummies.[9] Incorporating locally sourced starch, known for their low allergenic potential, could provide a sustainable, biocompatible, and cost-effective alternative to imported gelatin.[7,10] Ofada rice, *Oryza glaberrima* Steud (Family Poaceae), has been reported to have high starch content with functional properties suitable for pharmaceutical applications.[11,12] Acid modification alters the molecular structure of starch by partially hydrolysing its polymer chains, resulting in enhanced water solubility and improved gel firmness and mechanical strength, making acid-modified starch a suitable excipient for gummy formulations.[13]

Thus, the aim of this study is to formulate medicated gummies of folic acid using native and acid-modified Ofada rice (*Oryza glaberrima*) starches, each as co-gelling agents, in comparison to gelatin alone. A 3^2 factorial design was employed to evaluate the effects of the type of gelling agent and their percentage content on the mechanical strength, and drug release behaviour of the gummy formulations. Formulation requirements were optimized by maximizing mechanical strength and minimizing drug release through the desirability function approach.

MATERIALS AND METHODS

Materials

Ofada rice was purchased from a local market in Ibadan, Oyo State. Folic acid was from Hebei Jiheng, Pharmaceutical Shengzhou Co. Ltd, China. Gelatin was purchased from Shandong Deshang Chemical Co. Ltd., Shadong, China. Hydrochloric acid was from ACS Chemicals, Ahmedabad, India.

Methods

Extraction of starch

The grains of Ofada rice were washed and soaked in distilled water and blended to obtain a slurry that was strained through a screen. The slurry was suspended in distilled water and the supernatant was decanted at 12-hour interval, after which the sediment was re-suspended in distilled water and the process repeated for 72 h. The starch cake obtained was dried in a hot air oven at 50 ^{O}C for 48 h. The dried mass was pulverised and then screened through a sieve of size 250 µm.[14]

Acid modification of starch

Starch (300 g) was hydrolysed using 600 mL of 6 % v/v hydrochloric acid solution at 25 ± 1 ^{O}C for 192 h without stirring. Following hydrolysis, the suspension was neutralized with 250 mL of 10 % w/v sodium hydroxide solution, after which the starch slurry was washed five times with distilled water. The washed slurry was then dried in a hot-air oven at 40 ^{O}C for 24 hours. The dried starch was milled using a laboratory grinder and subsequently sieved through a 125 µm mesh sieve.[15]

Characterization of native and acid-modified Ofada rice starches

Morphology

The size and shape of the starch was determined using a scanning electron microscope (Phenom-ProX desktop SEM, Phenom-World, Eindhoven, Netherlands) at an accelerating potential of 5.0 kV. All samples were spur-coated with Au/Pd prior to examination.

Fourier Transform Infrared analysis

FTIR spectra of the native and modified starches were recorded with a FTIR spectrum BX II by Perkin Elmer, USA, in transmission mode. The absorbance spectra were computed between 4000 and 400 cm^{-1} at 8 cm^{-1} resolution. Symmetrical interferograms on 64 scans were added for each spectrum. The mean of four spectra of the same sample from different pellets was then calculated.

Formulation of medicated gummies

Gelatin with a bloom strength of 250 was dissolved in 35 mL of distilled water in a 250-mL beaker and allowed to stand for 10 min to bloom, forming a swollen gel. Starch was separately dispersed in 15 mL of distilled water and gently heated in a water bath to form a gel. In another 250-mL beaker, granulated sugar (40 g) was combined with 15 mL of water, stirred, and heated to 120 ^{O}C. Corn syrup (50 g) was then added with continuous stirring. The gel base, consisting of gelatin alone or a 1:1 blend of gelatin with NOS or AOS, was incorporated into the sugar-corn syrup mixture and stirred continuously. Citric acid (2.5 g) was added, and stirring was continued for 10 min until a clear mixture was obtained. The froth formed on the surface was carefully removed. Folic acid powder (0.20 g), flavouring and colouring agents, were added and mixed thoroughly to the cooled gel until homogenous. The gummy mixture was poured into silicone molds previously lubricated with coconut oil and then refrigerated at 4 ^{O}C for 24 h to allow for setting. After solidification, the gummies were carefully de-molded, lightly dusted with corn starch to prevent sticking, and packaged in moisture-resistant bags and stored under refrigerated conditions until further evaluation. The composition of the various formulations is presented in Table 1.

Evaluation of medicated gummies

Organoleptic properties, weight and thickness

The gummies were visually examined to assess their general appearance, shape and size. Organoleptic properties such as colour, odour and texture were evaluated. Twenty gummies were randomly selected from the batch and individually weighed (g). The total weight of the 20 gummies was then determined, and the mean weight was calculated. The percentage deviation of each gummy from the mean weight was subsequently calculated. The thickness of the medicated gummies was measured using a micrometer screw gauge and expressed in mm.

Compression test

The crushing strength of six gummies was measured at room temperature by diametrical compression using a tablet hardness tester (MHT - 100, Model P&M 01, Pharma Alliance Group, Indonesia).

In-vitro dissolution

The dissolution studies were carried out by the basket method (USP Apparatus I) using 900 mL of distilled water as dissolution medium. The apparatus was operated at 75 rpm and maintained at 37 ± 2 ºC. The amount of drug released was evaluated at wavelength 283 nm using a UV/Visible Spectrophotometer (Spectrumlab 752S, China). All determinations were performed in triplicate, and the results were expressed as the mean ± standard deviation.

Experiment design

A 3^2 full factorial design was employed to systematically optimize the gummy formulations.[16] The design consist of two independent variables, type of gelling agent (X_1) and percentage content of gelling agent (X_2), each evaluated at three levels (low, medium, and high), resulting in nine experimental runs representing all possible combinations of the factors. The crushing strength (N) and dissolution time, t_{50}, (min) were selected as the dependent response variables. The experimental design, statistical analysis, and optimization were performed using MINITAB Version 19 software (Pennsylvania, U.S.A.) to evaluate the individual and interactive effects of the formulation variables on the selected responses. The results obtained were then subjected to regression analysis. One-way analysis of variance (ANOVA) was used to conduct statistical comparisons and p-values were deemed statistically significant if they were less than 0.05. Surface plots and contour plots were developed. After fitting the mathematical model, the optimization process was carried out using the desirability function approach. The desirability function combines all responses into a single variable to predict the optimal values of the independent variables. A desirability value of 0 indicates the least desirable response, whereas a value of 1 represents the most desirable response.[17]

Table 1: Formulation composition for folic acid gummies

Formulation code	Gelatin (g)	NOS (g)	AOS (g)	Folic acid (g)	Granulated sugar (g)	Corn syrup (g)	Citric acid (g)	Flavour (mL)	Colourant (mL)	Water to (mL)
F1	7.50	-	-	0. 20	40	50	2.5	0.5	0.5	100.0
F2	12.50	-	-	0. 20	40	50	2.5	0.5	0.5	100.0
F3	15.00	-	-	0. 20	40	50	2.5	0.5	0.5	100.0
F4	3.75	3.75	-	0. 20	40	50	2.5	0.5	0.5	100.0
F5	6.25	6.25	-	0. 20	40	50	2.5	0.5	0.5	100.0
F6	7.50	7.50	-	0. 20	40	50	2.5	0.5	0.5	100.0
F7	3.75	-	3.75	0. 20	40	50	2.5	0.5	0.5	100.0
F8	6.25	-	6.25	0. 20	40	50	2.5	0.5	0.5	100.0
F9	7.50		7.50	0. 20	40	50	2.5	0.5	0.5	100.0

RESULTS

The Scanning electron micrographs (SEM) images of NOS and AOS are presented in Figure 1. The Ofada rice starch in their native form showed polyhedral granules with an average particle size of 58.93 ± 25.29 µm. Acid hydrolysis resulted in the formation of smaller granules with irregular structure and size of 13.14 ± 6.85 µm.[13] The FTIR spectra of NOS and AOS are presented in Figure 2. The FTIR spectra of the native starch showed the fingerprint region had characteristic starch bands at positions 1148.71, 1078.87, and 996.36 cm^{-1}, corresponding to C-O stretching and C-O-C glycosidic vibrations of the polysaccharide backbone. Similar absorption bands at 3282.64 cm^{-1} and 2928.87 cm^{-1} were observed in the spectra of the acid modified starch which identified the presence of hydroxyl and aliphatic groups. The peak at 3282 cm^{-1} was however sharper, indicating weaker hydrogen bonding. The 1634.91 cm^{-1} band remained, and the fingerprint region showed peaks at 1148.93, 1076.90 and 996.98 cm^{-1}, indicating the glycosidic structure remained intact but with minor variations and relative alterations in intensity.

The images of the gummy formulations are presented in Figure 3. Gummy formulations containing gelatin alone (F1-F3) and those containing the blends of gelatin with NOS and AOS (F3 - F6, and F7 - F9, respectively) had attractive colour with smooth surfaces and well-defined edges. There was no mottling in colour but the gummies containing NOS appeared opaque and less transluscent than the others. All gummies had an acceptable odour of the flavouring agent. Gummies containing native starch were coarser with slightly stickier texture than those with modified starch. The values of average weight, thickness, crushing strength and dissolution time (t_{50}) are presented in Table 2. All batches met the specifications for weight variation (≤ 7.50 % of mean weight) and complied with USP standards for chewable gel dosage form.[18] Reduction in gummy thickness was observed with increasing starch content. Figure 4 shows the dissolution plots of the gummies from which the values of t_{50} (time for 50 % drug release) were determined. The t_{50} values are also presented in Table 2.

A full factorial design was employed to comprehensively assess the two independent variables: type of gelling agent (X_1) and percentage content of gelling agent (X_2). The real and coded values of the independent variables and the responses are presented in Table 2. Data from the experimental runs were subjected to regression and graphical analysis, which produced the equations with F ratios that were statistically significant ($p < 0.05$) and Adj-R^2 values in the range of 0.8 - 0.99. The significance of the effects on crushing strength and dissolution time (t_{50}) were established using ANOVA and the linear regression equations fit to the data were:

Crushing strength =

$$32.901 + 8.306\,X1_1 - 9.954\,X1_2 + 1.649\,X1_3 - 3.781\,X2_1 + 0.019\,X2_2 + 3.762\,X2_3 \quad (1)$$

$$t50 = 16.28 - 3.94\,X1_1 + 9.06\,X1_2 - 5.11\,X1_3 - 5.78\,X2_1 + 0.39\,X2_2 + 5.39\,X2_3 \quad (2)$$

The results of the statistical analysis are presented in Table 3. Overall, the models suggests that type of gelling agent is the dominant determinant of crushing strength (maximum coefficient magnitude = 9.954, p = 0.000), while percentage content provides additional but less pronounced modification of the gel strength (p = 0.002). On the other hand, X_{12} has the greatest positive effect, markedly increasing t_{50} and therefore slowing drug release. The model revealed that manipulating the type and percentage content of gelling agents can be used to tailor the mechanical strength and drug release rate by influencing crushing strength and dissolution time of the gummies, t_{50}. X_{13} produced the greatest reductions in t_{50}, implying faster release was achieved from the blend was with AOS and percentage content increased from 7.50 to 10 % w/w (p = 0.019).

The 3-D surface and contour plots are graphical illustrations of how the two independent variables, X_1 and X_2, either individually or in combination, influence the measured responses, crushing strength and t_{50}, and these are presented in Figure 5. The plots can be used to visualize the direction and magnitude of the effects of the variables and to identify regions where the desired response is achieved. The desirability function was then used to combine all responses into a single variable to predict the optimal value of the independent variables and is presented in Figure 6. The desirability function was used to select the optimized batch. The responses were assigned a value between 0 to 1 depending upon the desirability: 0 for the least expected value and 1 for the most desirable ones. The factors obtained at the maximum points of Y_1 and Y_2 (target: 30 N and 15 min, respectively) were calculated as X_1 = AOS: gelatin X_2 = 7.537 %), known as the estimated condition. Validation experiments were applied at the estimated condition. The predicted and verified values are presented in Table 4. The experimental results were observed to be close to the estimated results.

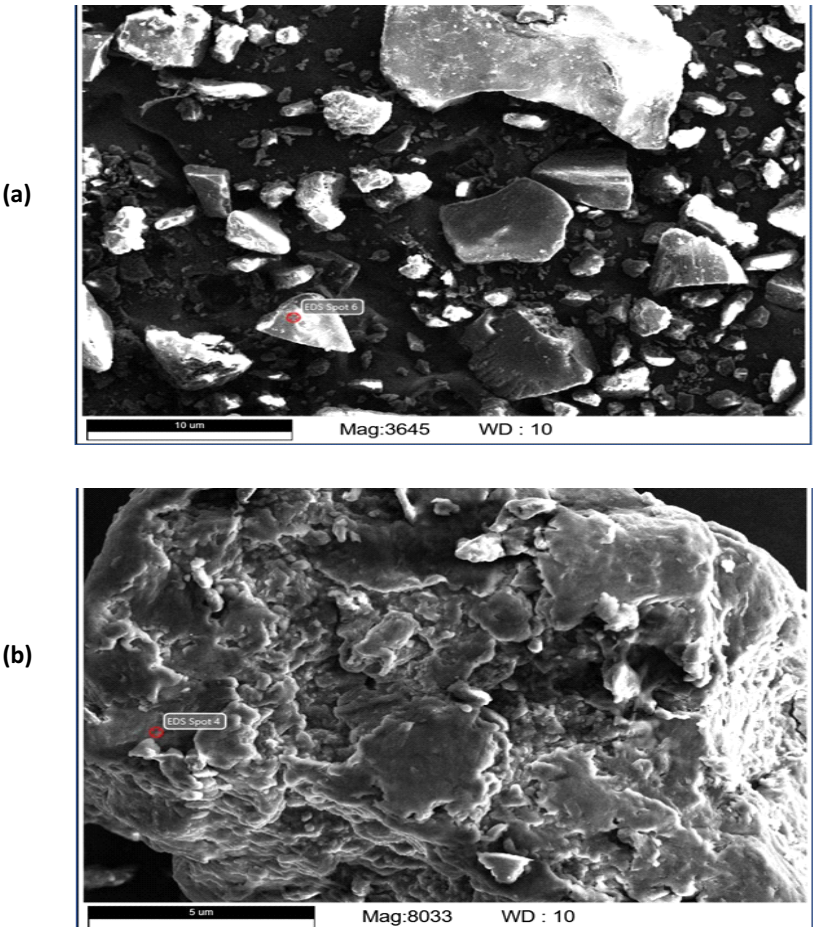


Figure 1: SEM images of (a) native Ofada rice starch and (b) acid modified Ofada rice starch

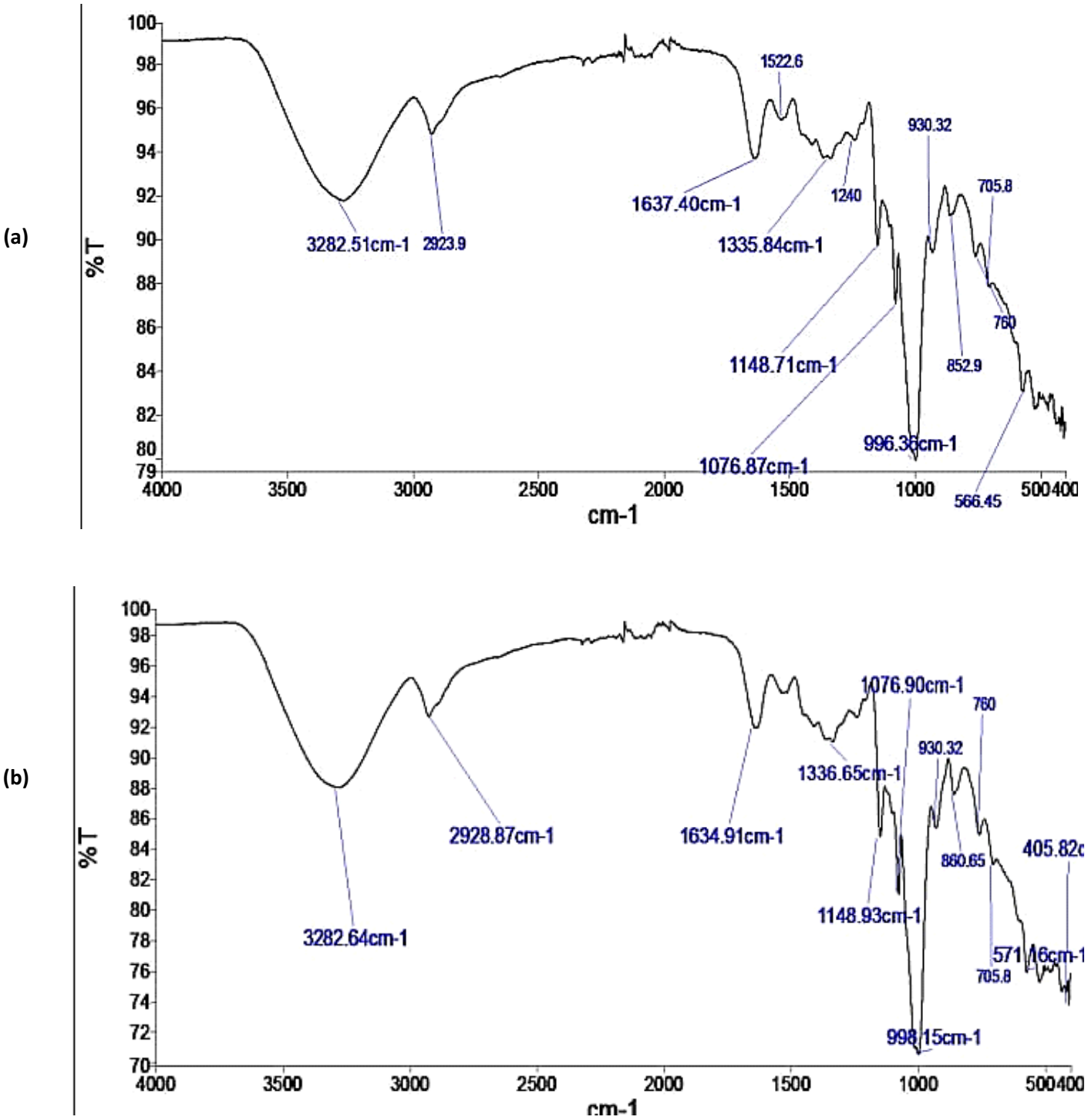


Figure 2: FTIR spectra of (a) native Ofada rice starch and (b) acid - modified Ofada rice starch



Figure 3: Images of medicated gummies of folic acid containing: (a) gelatin alone, (b) blend of gelatin: native Ofada starch (1:1) (c) blend of gelatin: acid-modified Ofada starch (1:1)

Table 2: 3^2 factorial design with independent variables and all responses of the medicated gummies of folic acid (mean ± standard deviation)

	Gelatin g	NOS g	AOS g	Gelling agent type (gelatin: starch)	Gelling agent percentage %w/w	Average weight g	Thickness mm	Crushing strength N	t_{50} min
F1	7.50	-	-	1:0 (-1)	5.0 (-1)	2.04 ± 0.10	12.50 ± 0.15	38.18 ± 1.73	7.00 ± 0.73
F2	12.50	-	-	1:0 (-)	7.5 (0)	2.05 ± 0.26	12.22± 0.14	40.48 ± 1.28	10.00 ± 1.10
F3	15.00	-	-	1:0 (-1)	10.0 (+1)	2.14 ± 0.18	13.75 ± 0.23	44.96 ± 3.93	20.00 ± 3.03
F4	3.75	3.75	-	1:1 (0)	5.0 (-1)	2.07 ± 0.05	14.31 ± 0.10	18.28 ± 2.97	16.00 ± 1.65
F5	6.25	6.25	-	1:1 (0)	7.5 (0)	2.27 ± 0.17	17.31 ± 0.10	24.28 ± 2.97	27.50 ± 2.50
F6	7.50	7.50	-	1:1 (0)	10.0 (+1)	2.08 ± 0.10	18.31 ± 0.10	26.28 ± 2.97	30.00 ± 2.99
F7	3.75	-	3.75	1:1 (+1)	5.0 (-1)	2.30 ± 0.09	11.70 ± 0.19	30.90 ± 2.09	8.50 ± 0.63
F8	6.25	-	6.25	1:1 (+1)	7.5 (0)	2.31 ± 0.11	11.85 ± 0.19	34.00 ± 2.09	10.00 ± 1.30
F9	7.50	-	7.50	1:1 (+1)	10.0 (+1)	2.04 ± 0.20	11.99 ± 0.19	38.75 ± 4.00	15.00 ± 1.00

* -1 low level; 0 medium level; +1 high level

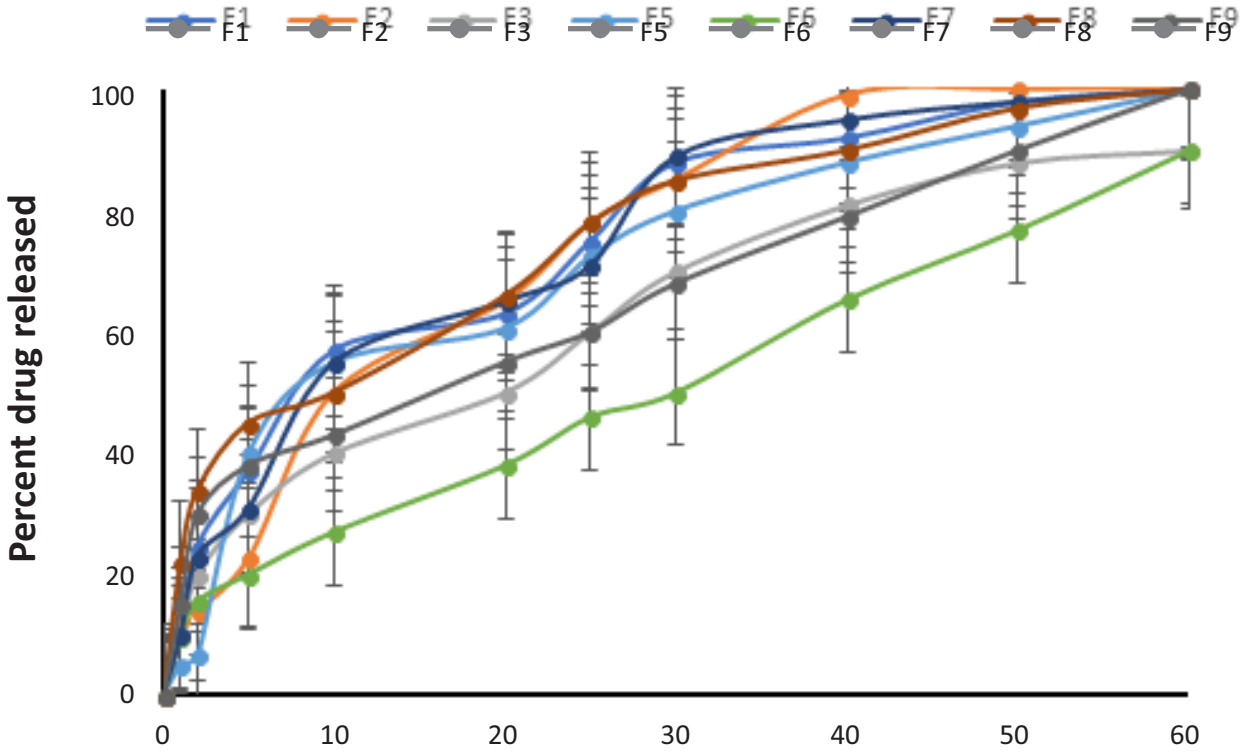


Figure 4: Dissolution profile of medicated gummies of folic acid

Table 3: Results of statistical analysis of the 3^2 full factorial design

Response	Source			
	Model p value	R^2	Adjusted R^2	Predicted R^2
Crushing strength	0.000	0.9928	0.9855	0.9634
Dissolution time t_{50}	0.000	0.9048	0.8096	0.5182

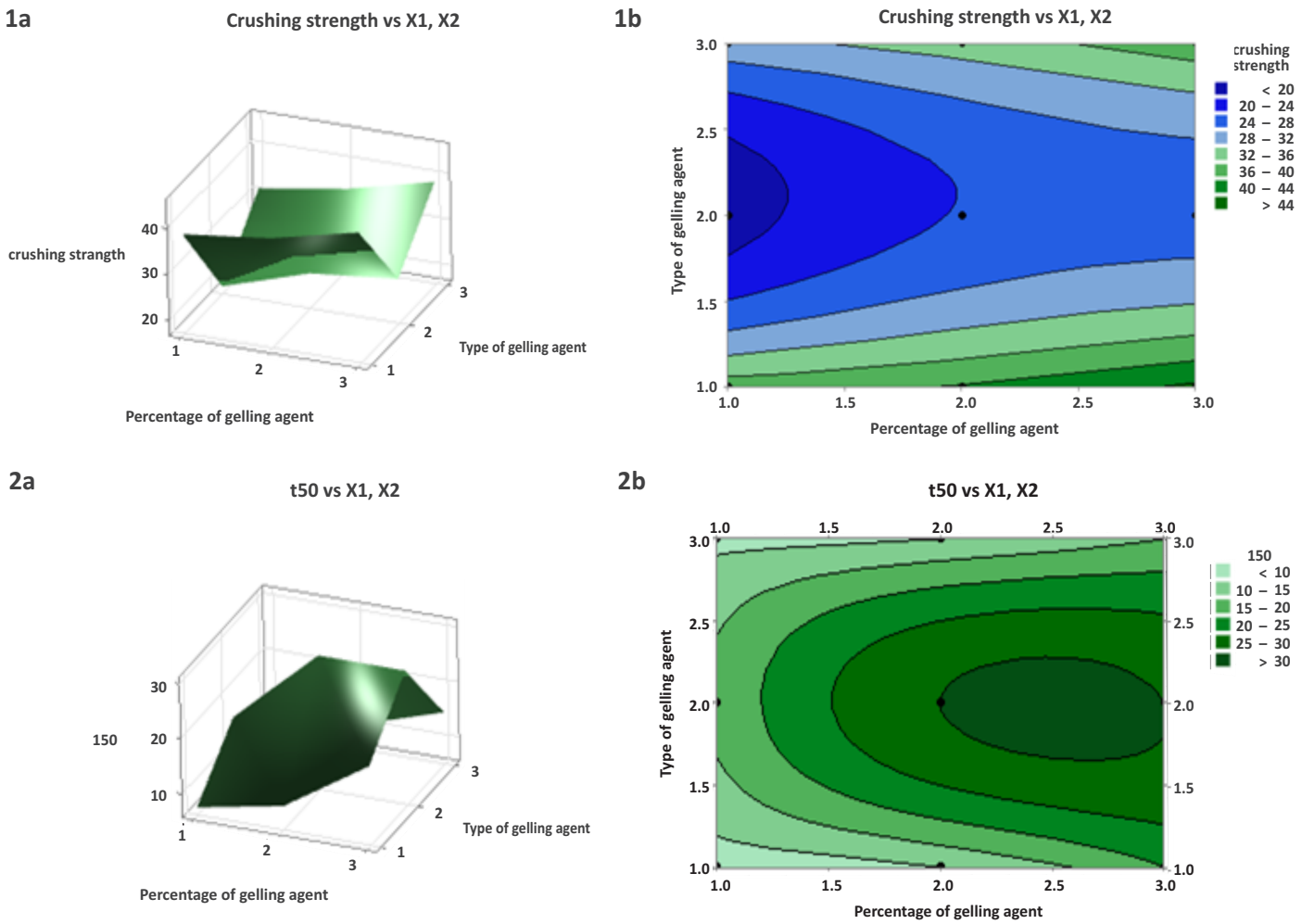


Figure 5: (a) 3D surface and (b) contour plots for (1) crushing strength vs X_1, X_2 and (2) t50 vs X_1, X_2

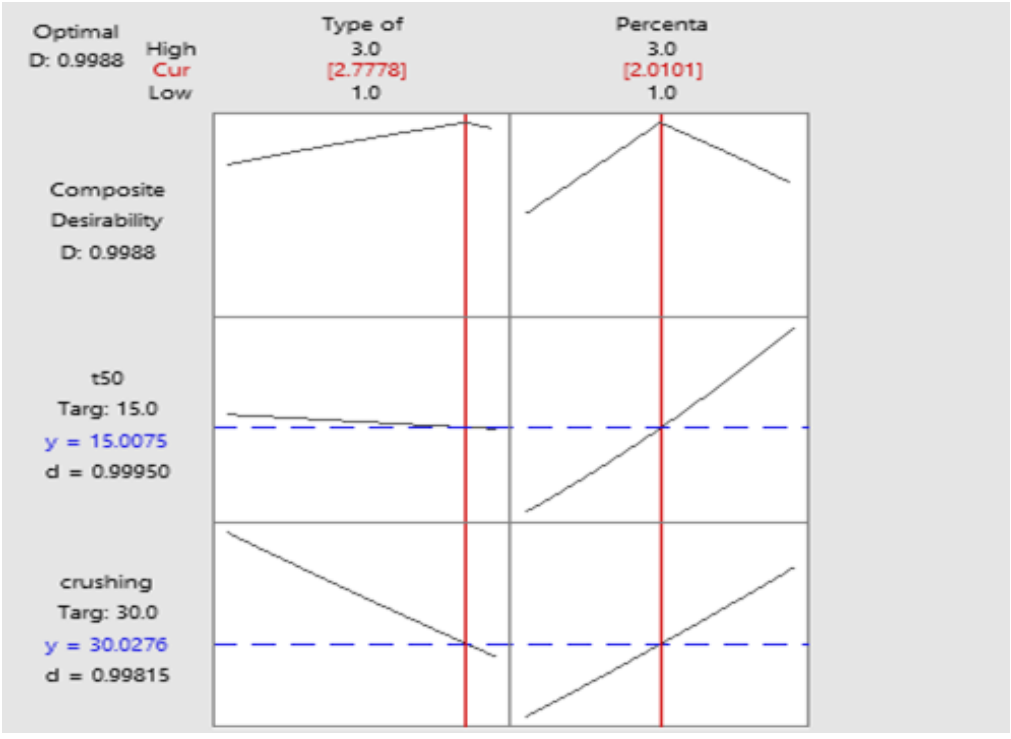


Figure 6: Optimization plot

DISCUSSION

Characterization of native and acid modified Ofada rice starch

Evaluating starches from different botanical sources enables the selection of starches that naturally or can be easily modified to achieve, the desired properties. In this study, indigenous Ofada rice starch (NOS) was modified by acid-hydrolysis to obtain acid-modified starch (AOS). The Scanning electron micrographs (SEM) images confirmed morphological changes had occurred with starch granules of AOS becoming aggregated. FTIR is an important analytical tool in starch characterization to identify functional groups, confirm chemical modifications, determine molecular order, and distinguish between physical and chemical changes.[19] FTIR was used to identify the functional groups and the spectra confirmed modification of the starch had occurred.

Organoleptic properties of gummies

The folic acid gummies formulated offer the benefits of attractiveness and easy consumption for children in the treatment of anaemia. Generally, gummy formulations with starch content were softer, implying they may be easier to chew, and may be beneficial in paediatric applications where ease of chewing and pleasant taste are desirable characteristics that increase compliance.[20]

Weight and thickness

All batches met the specifications for weight.[18] This indicates good consistency of mold filling and batch uniformity.[21] The reduction in gummy thickness with increasing starch content may be attributed to interactions between starch and gelatin; during cooling. The higher starch concentrations promoted retrogradation, resulting in the formation of a denser polymer network. This denser structure facilitated greater water expulsion (syneresis), leading to the reduction observed in gummy thickness.[22]

Factorial design

In addition to the organoleptic properties, mechanical strength and drug release behaviour of medicated gummies are critical quality attributes because they directly influence product stability, patient acceptability, and therapeutic performance.[23] Adequate mechanical strength ensures the gummies maintain their shape and are less likely to lose fragments, safeguarding accurate dosing. Gummies should be firm enough to handle easily yet soft enough to chew comfortably, particularly for paediatric patients. Efficient drug release ensures that the drug becomes available for absorption, leading to the desired pharmacological effect.[24] Furthermore, drug release studies help assess the influence of excipients such as gelling agents and processing conditions on product performance. Therefore, optimizing these two attributes is essential to produce gummies with sufficient structural stability, consistent dosing, and reproducible drug release characteristics, ensuring both product quality and clinical effectiveness. A full factorial design was employed to comprehensively assess the variables.

The regression model of crushing strength in Equation 1 demonstrates that crushing strength is highly dependent on the levels of the formulation variables. The positive coefficients associated with X_{11} and X_{13} indicate that using the gelling agent gelatin and AOS enhanced the mechanical integrity of the gummy matrix, by promoting stronger intermolecular interactions and a more cohesive gel network. Conversely, the negative coefficients for X_{12} suggest that changing gelling agent from gelatin to native Ofada produced softer gummies with reduced resistance to compressive force. The negligible coefficient for X_{12} indicates that the change in percentage content from 5.0 to 7.5% had little or no measurable effect on crushing strength. On the other hand, the positive coefficients of X_{23} suggest increase from 7.50 to 10.0 % enhanced crushing strength. Overall, the model suggests that type of gelling agent is the dominant determinant of crushing strength (maximum coefficient magnitude = 9.954, p = 0.000), while percentage content provides additional but less pronounced modification of the gel strength (p = 0.002).

The regression model for t_{50} shows that both formulation factors significantly influence the time required for 50 % drug release. Among the levels X_{12} has the greatest positive effect, markedly increasing t_{50} and therefore slowing drug release. While gelatin hydrates rapidly in aqueous media, its matrix swells and gradually dissolves, allowing drug molecules to diffuse out easily. Blending gelatin with NOS modified the gelatin matrix by increasing structural rigidity and reducing matrix solubility, resulting in slower and more prolonged drug release than gelatin alone. Conversely, X_{13} produced the greatest reductions in t_{50}, implying faster release was achieved from the blend that has AOS as co-gelling agent and the percentage content increased from 7.50 to 10 %w/w. Acid modification changed starch functionality and the improved solubility and hydration resulted in the formation of a more uniform polymer network with gelatin, producing a shorter dissolution time and faster drug release than gelatin-NOS blend or gelatin alone. The

coefficient for X_{22} is close to zero, suggesting that percentage content of gelling agent at 7.5 % had minimal influence on the response (p = 0.057). Overall, the model indicates that manipulating the type and percentage content of gelling agents can be used to tailor the drug release rate by influencing dissolution time of the gummies, t_{50}.

Surface plot was used to provide a three-dimensional graphical representation of the relationship between the two independent variables and a dependent response. The two variables are represented on the X- and Y-axes, while the response is represented on the Z-axis. The plots help to visualize the direction and magnitude of the effects of the variables and to identify regions where the desired response is achieved. Contour plots were also generated to present the same relationship in a two-dimensional format using lines or regions of equal response values. The plot allows the effects of the two independent variables and their interaction on the response to be easily visualized. Regions with similar response values are represented by similar contour levels, making it useful for identifying the optimum combination of the formulation variables.

The overall desirability D and predicted value were calculated and the factors obtained at the maximum points of Y_1 and Y_2 (target: 30 N and 15 min, respectively) were calculated as X_1 = Gelatin: AOS (1:1) and X_2 = 7.537 % which are known as the estimated condition.

Verification of optimal parameters

Validation experiments were applied at the estimated condition. The results illustrate that the experimental results are close to the estimated results. Here, the % biased between predicted values from the equation and practical measured values was less than 5 %, which proved the validity of the estimated model.[25]

The above study compared native and acid-modified Ofada starches as co-gelling agents with gelatin for formulating folic acid gummies, but was limited to controlled laboratory settings. Key operational factors such as scale-up, sensory testing, and economic viability are beyond the scope of this study. Future research will address commercial and regulatory readiness, including pharmacopeia compliance.

CONCLUSION

Medicated gummies of folic acid were successfully formulated using the native and acid-modified Ofada rice starch as co-gelling agent in combination with gelatin. The resulting formulations showed desirable organoleptic qualities for paediatric administration. Gelatin: Acid-modified Ofada starch blend (1:1, ≤ 7.50 %w/w) was found to enhance mechanical strength and produce fast drug release in optimized formulations of folic acid gummies. Ofada rice starch showed potential as suitable and cheaper co-gelling agent with gelatin in medicated gummies of folic acid.

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