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Optimized Extraction, Characterization, and Cytotoxicity Assessment of Biodegradable *Nopalea cochenillifera* Salm-Dyck Mucilage

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ABSTRACT

Mucilage is a plant-derived polysaccharide-rich complex with valuable physicochemical properties for food, cosmetic, and pharmaceutical applications. This study optimized the extraction of biodegradable mucilage from *Nopalea cochenillifera* Salm-Dyck and evaluated its physicochemical, thermal, technological, and cytotoxic characteristics. A Box-Behnken design was employed using water ratio (1:2, 1:6, and 1:10), temperature (50, 70, and 90°C), solvent (ethanol, isopropanol, and acetone), and solvent ratio (1:2, 1:6, and 1:10) as independent variables. The extracts were characterized using UV-Vis, Fourier Transform Infrared Spectroscopy (FTIR), Thermogravimetric Analysis (TGA), and differential scanning calorimetry (DSC), as well as molecular size and weight, X-ray diffraction (XRD), and rheology analyses. Cell viability was assessed using RAW 264.7 and HEK 293 cell lines. Optimization increased mucilage yield by 14.6%, with higher levels of soluble carbohydrates and reducing sugars, and reduced protein content. The mucilage remained stable at high temperatures, exhibited an amorphous structure, and was chemically rich in carbohydrates, displaying pseudoplastic behavior. Additionally, high cell viability (>100 µg/mL) was observed for both cell lines. In conclusion, the mucilage from *Nopalea cochenillifera* Salm-Dyck represents a promising material for applications across various industries as a substitute for non-biodegradable polymers.

Keywords: Cactaceae; Carbohydrates; Mucilage; *Nopalea cochenillifera* Salm-Dyck, biodegradable polymer.

1. INTRODUCTION

Cacti are considered the family with the largest number of genera, comprising approximately 127 species, found in a wide range of habitats (Horibe, 2021). These plants are abundantly distributed across the American continent and are often used as ornamental plants; however, their flowers, fruits, and stems are also used for human and animal consumption (Horibe, 2021). Due to their unique physiology, resulting from adaptations to survive water stress, these plants are predominantly found in arid and dry regions, as they can store water in their tissues to prevent dehydration (Breslin et al., 2021).

Opuntia ficus-indica L. Miller, a species native to Mexico and widely distributed in countries like Brazil, is known for its highly nutritious and antioxidant-rich cladodes due to the presence of polyphenols, flavonoids, and tannins (Tosif et al., 2021). One of its most valuable components for the food and pharmaceutical industries is mucilage, a polysaccharide-rich complex with high water retention capacity (Tosif et al., 2021). Rodríguez-González et al., (2021) report the presence of β -D-xylopyranosyl, β -L-rhamnopyranosyl, β -D-galactopyranosyl, α -D-galactopyranosyluronic acid, and other linked sugar residues.

Mucilage has recently been used in various industrial sectors as a potential substitute for synthetic polymers (Tosif et al., 2021) due to its physicochemical properties. It can serve as a gelling agent, thickener, stabilizer, and emulsifier (Kamel et al., 2020). To the best of our knowledge, no comprehensive reports exist on its structural or functional properties, physiological roles, or prior extraction and characterization methods of the mucilage of organisms such as *Nopalea cochenillifera* Salm-Dyck, a cactus widely cultivated for animal nutrition and rich in mucilage with a carbohydrate composition that remains unexplored (Bezerra et al., 2023).

This gap in the literature reinforces the novelty and relevance of our study, which aims to contribute to fundamental knowledge about this little-explored plant species, especially in the molecular context. This organism is known to be resistant to the Indian mealybug (*Dactylopius opuntiae*) and, due to its xerophytic habit and crassulacean acid metabolism (Saraiva et al., 2021), may become important for purposes other than agricultural use. When fully characterized in terms of their physical, chemical, and technological properties, mucilage carbohydrates may present promising structures for the manufacture of food products such as baked goods, meat emulsions, fermented dairy products, among many others (Goksen et al., 2023). The use of these biomolecules as primary materials for various

products has gained increasing attention in recent decades due to their low cost, flexibility, availability, biodegradability, and, in most cases, low toxicity (Ansari et al., 2020)

In this manuscript, we hypothesize that the optimized extraction and characterization of mucilage from *Nopalea cochenillifera* Salm-Dyck will reveal significant physicochemical and biological properties that support its potential as a sustainable alternative to synthetic polymers in food, cosmetic, and pharmaceutical applications. Thus, in this study, we aimed to optimize the extraction of mucilage from *Nopalea cochenillifera* Salm-Dyck and conduct a comprehensive characterization of its physicochemical, thermal, technological, and cytotoxic properties.

To this end, we adapted and modified the extraction protocols previously applied to other cactus species. Key modifications included adjustments in water volume and homogenization temperature to enhance carbohydrate solubilization, followed by precipitation using different solvents and concentrations. A statistical design was employed to evaluate the influence and significance of the extraction variables on carbohydrate yield. The extracted mucilage was thoroughly characterized and assessed for biological safety using HEK-293 (human embryonic kidney) and RAW 264.7 (murine macrophage) cell lines. Optimization was essential to establish a reproducible and efficient extraction protocol, forming the foundation for future investigations into the structural and functional potential of *N. cochenillifera* mucilage for various biotechnological applications.

2. MATERIAL AND METHODS

2.1 Material

Ethanol (96%) and isopropanol (99%) were obtained from CRQ Química (São Paulo, Brazil). Acetone (99.5%), Trolox (98%), quercetin (99%), and copper sulfate (99%) were supplied by ACS Científica (São Paulo, Brazil). Sulfuric acid (96%), gallic acid (99%), Ascorbic acid (99%), Triton X-100, 3,5-Dinitrosalicylic acid (98%), 2,2-diphenyl-1-picrylhydrazyl (DPPH, 99%), Dulbecco's Modified Eagle Medium (DMEM), bovine serum albumin (BSA, 98%), 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT, 99%), and Folin–Ciocalteu reagent were obtained from Sigma-Aldrich (St. Louis, Missouri, USA). Sodium-potassium tartrate (99%), sucrose (99%), glucose (99%), and dimethyl sulfoxide (DMSO, 99%) were provided by Synth (São Paulo, Brazil). ABTS (2,2'-Azino-Bis(3-Ethylbenzothiazoline-6-Sulfonic Acid, 98%) was purchased from Biosynth (Zurich,

Switzerland). Ammonium persulfate (98%), Sodium carbonate (99%) and sodium hydroxide (98%) were obtained from Dinâmica Química (Indaiatuba, SP, Brazil). Ultra purified water was produced using a Milli Q system (Rahway, NJ, USA).

2.2 Collection and Preparation of the Plant Material Pulp

The cladodes of the cactus pear (*Nopalea cochenillifera* Salm-Dyck) were cultivated on March 4, 2021, under drip irrigation conditions at the experimental unit of the Federal University of Paraíba (UFPB), located in the municipality of São João do Cariri-PB, Brazil (7° 23' 27" S, 36° 32' 2" W). Harvesting was carried out on May 28, 2022, between 8:00 AM and 12:00 PM, and is deposited in the herbarium HEPH under number 00005361. The plant material was thoroughly sanitized in a 2% sodium hypochlorite solution for 10 minutes, rinsed abundantly with distilled water, and dried. Finally, the epidermis of the cladodes was removed, the internal pulp was ground, and the processed material was stored in a freezer (-20°C).

2.3 Mucilage Extraction

The mucilage extraction was carried out using three different methodologies (Dick et al. (2019); Monrroy et al. (2017), and Gheribi et al. (2018), adapted from literature descriptions for other types of cactus extracts. For the extraction method based on Dick et al. (2019), with modifications, the pulp was mixed with deionized water at a 1:2 ratio (pulp: water, w/v) and homogenized using a food processor. The mixture was then heated to 80°C for 30 minutes in a water bath (Buchi-Heating Bath, Flawil, Switzerland), with mechanical stirring every 5 minutes. Subsequently, the paste was vacuum-filtered using qualitative filter paper (80g) to remove fibrous fragments and centrifuged (Eppendorf-5430, Hamburg, Germany) at 11,180 g for 20 minutes at 24°C. The supernatant was precipitated with 96% ethanol (PA grade) at a 1:3 ratio (supernatant: ethanol, v/v) and left undisturbed for 12 hours at 4°C. The resulting white precipitate (mucilage) was vacuum filtered using a Büchner funnel and qualitative filter paper (80g). The material retained on the filter paper was dried in the oven (Tecnal-TE-39413, São Paulo, Brazil) with air circulation at 55°C for 24 hours.

The mucilage extraction using the methodology of Monrroy et al. (2017) with modifications involved homogenizing the pulp in a food processor with deionized water at a 1:2 ratio (pulp: water, w/v). The mixture was then heated in a water bath (Buchi-Heating Bath, Flawil, Switzerland) at 80°C for 30 minutes with mechanical stirring every 5 minutes

using a glass rod. Subsequently, 96% ethanol (PA grade) was added at a 1:3 ratio (pulp: ethanol). The precipitate was collected and dried in an oven with air circulation (Tecnal-TE-39413, São Paulo, Brazil) at 55°C for 24 hours.

The third extraction followed the methodology of Gheribi et al. (2018), which involved homogenizing the pulp in a food processor with distilled water at a 1:2 ratio, followed by direct precipitation with 96% ethanol at a 2:3 ratio in the food processor. Afterward, the precipitate was collected through filtration and washed with 96% ethanol (PA grade) until it appeared white. Finally, it was dried in an oven with air circulation (Tecnal-TE-39413, São Paulo, Brazil) at 55°C for 24 hours.

2.4 Optimization of the Extraction Method

Extraction optimization was carried out by assessing key variables influencing mucilage solubilization and precipitation, including water-to-pulp ratio (1:2, 1:6, and 1:10), homogenization temperature (50, 70, and 90 °C), solvent type (96% ethanol, 99% isopropyl alcohol, and 99.5% acetone — all analytical grade), and solvent-to-extract ratio (1:2, 1:6, and 1:10), as detailed in Table 1. For this purpose, the same amount of fresh cladode without epidermis (10 g) used in the previous analyses was used in the analysis. A randomized optimization strategy was employed to enhance both the yield and total carbohydrate content during mucilage extraction.

Further modifications included the use of an Ultra-Turrax homogenizer (IKA-T18, Staufen im Breisgau, Germany) operating at 25,155 g for 1 minute during the pulp homogenization step with water. Ten grams of pulp were used and solubilized according to the water concentration determined by the statistical design (Table 1). Centrifugation during the pulp–water separation step was reduced to 5,478 g for 10 minutes. The mucilage was subsequently precipitated by adding different solvents (ethanol, acetone, or isopropanol) in concentrations defined by the experimental design, followed by centrifugation at 2,795 g for 10 minutes to recover the precipitate.

Table 1. Experimental Design Matrix for the optimization of the extraction method.

Sample	Water ratio	Temperature (°C)	Solvent type	Solvent Ratio
1	1:6	70	Acetone	1:6
2	1:2	50	Isopropyl	1:2
3	1:6	70	Acetone	1:6
4	1:2	90	Isopropyl	1:10

5	1:10	50	Ethanol	1:2
6	1:2	50	Ethanol	1:2
7	1:10	90	Isopropyl	1:10
8	1:6	70	Acetone	1:6
9	1:10	50	Ethanol	1:10
10	1:10	90	Ethanol	1:10
11	1:10	90	Isopropyl	1:2
12	1:10	50	Isopropyl	1:2
13	1:2	90	Isopropyl	1:2
14	1:10	50	Isopropyl	1:10
15	1:2	50	Ethanol	1:10
16	1:2	50	Isopropyl	1:10
17	1:10	90	Ethanol	1:2
18	1:2	90	Ethanol	1:2
19	1:2	90	Ethanol	1:10

2.5 Characterization of Mucilage

2.5.1 Yield

The yield calculation was determined by gravimetry using the following mathematical equation (Eq1), which correlates the dry weight of mucilage with the fresh weight of the cladode without the epidermis.

$$\text{Extraction yield(\%)} = \frac{\text{Weight of mucilage(g)}}{\text{Weight of raw material(g)}} \times 100 \quad (\text{Eq1})$$

2.5.2 Biochemical Analyses

2.5.1.1. Total Carbohydrate Content

To evaluate the total soluble carbohydrate content, the method of Schaubroeck et al., 2022 with some modifications was used. 50 µL of phenol (5%) was added to 50 µL of the sample diluted in deionized water (1 mg/mL) for 10 minutes. Subsequently, 150 µL of concentrated sulfuric acid (98% PA) was added and incubated for 15 minutes. The samples were analyzed at 490 nm using a plate reader (Biotek-Synergy HT, Winooski, Vermont, USA) with a calibration curve produced with a sucrose solution (50 to 500 µg/mL).

2.5.1.2. Reducing Sugar Assay

For the analysis of reducing sugars, 25 μL of the samples diluted in deionized water (1 mg/mL) were added to microtubes, followed by 25 μL of DNS reagent (1% 3,5-dinitrosalicylic acid and 30% sodium potassium tartrate in 0.4 mol/L NaOH). The microtubes were then heated at 90°C for 5 minutes in a water bath, followed by cooling in an ice bath and then adding 330 μL of distilled water to the reaction mixture (Lam et al., 2021). The readings were performed at 490 nm using a plate reader (Biotek-Synergy HT, Winooski, Vermont, USA), and the concentration was calculated using a glucose standard solution (50 to 500 $\mu\text{g/mL}$).

2.5.1.3 Protein Content Analysis

For the total protein analysis, the Bradford reagent was first prepared by diluting 1.5 g of copper sulfate and 0.6 g of sodium potassium tartrate in 500 mL of distilled water. After homogenizing the solution, 300 mL of 10% (w/v) sodium hydroxide was added, and filtration was performed. Then, 50 μL of the sample diluted in deionized water (1 mg/mL) was placed into a 96-well plate (flat-bottom TPP), and 200 μL of Bradford reagent was added. After 5 minutes, analyses were performed at 595 nm using a plate reader (Biotek-Synergy HT, Winooski, Vermont, USA), and the standard curve was created with a bovine serum albumin solution (10 to 100 $\mu\text{g/mL}$).

2.5.3 Determination of Total Polyphenols and Flavonoids

To evaluate the total polyphenol content, 120 μL of the sample diluted in deionized water (1 mg/mL) was transferred to a tube, and 900 μL of distilled water was added. After homogenizing, 500 μL of 10% Folin-Ciocalteu reagent was added, and the mixture was left to rest for 8 minutes. Subsequently, 400 μL of 7.5% sodium carbonate was added, and after 120 minutes, 200 μL of the solution was transferred to a 96-well plate (flat-bottom TPP). Analyses were performed at 765 nm using a plate reader (Biotek-Synergy HT). The calibration curve was created using a standard solution of gallic acid with concentrations ranging from 25 to 150 $\mu\text{g/mL}$.

For the determination of total flavonoid content, 100 μL of the sample diluted in deionized water (1 mg/mL) was added to a 96-well plate (flat-bottom TPP), followed by 100 μL of a solution of aluminum chloride in methanol (2% w/v). After 30 minutes, the absorbance was measured at 410 nm using a plate reader (Biotek-Synergy HT). The standard curve was generated using a quercetin solution (5 to 200 $\mu\text{g/mL}$).

2.5.4 Hydrodynamic Radius and Average Molecular Weight

For the analysis of the hydrodynamic radius and average molecular weight, the mucilage powder was solubilized in deionized water (1 mg/mL), filtered and diluted within the range of 0.2-1.0 mg/mL. The measurements were performed using a dynamic light scattering device (Zetasizer, Malvern, United Kingdom) with a fixed angle of 90° at 25 °C and a dn/dc value of 0.160.

2.5.5 X-Ray Diffraction (XRD)

The X-ray diffraction (XRD) analysis of the mucilage was performed using a Shimadzu-XRD-600 (Kyoto, Japan) at 25°C, with the voltage and current maintained at 30 kV for 30 minutes, at a 2 θ angle with a scan time of 10.33 seconds within the range of 0.2°.

2.5.6 Thermal Analyses

The thermogravimetric analysis (TGA) was conducted using a STA 409 PC (Mettler Toledo, Zurich, Switzerland), under a nitrogen atmosphere with a heating scan range from 30 to 600°C at a heating rate of 10°C/min. In the Differential Scanning Calorimetry (DSC) analysis, the sample was sealed in an aluminum crucible and analyzed from 0°C to 300°C. The atmosphere was synthetic air at a flow rate of 300 mL/min, with a heating rate of 10°C/min.

2.5.7 Fourier Transform Infrared (FTIR) Spectroscopy

For this analysis, a Fourier transform infrared (FTIR) spectrophotometer (Agilent-Cary-630, Santa Clara, California) was used. The spectra were acquired in the range of 4000–600 cm⁻¹, with a resolution of 2 cm⁻¹ and 128 scans. Measurements were taken directly from the dry mucilage powder.

2.5.8 Scanning Electron Microscopy (SEM)

For SEM analysis, the samples were placed on aluminum stubs with double-faced carbon tape and subjected to compressed air to remove any surplus sample that did not adhere to the tape. The samples were then examined under a scanning electron microscope (Thermo Scientific Phenom ProX G6 Desktop SEM model) to observe the morphology of the powder.

2.5.9 Rheological Properties

All rheological measurements were performed using a Fann 35A viscometer. The mucilage solutions were characterized for their constant shear viscosity function, using a unidirectional steady shear flow, with shear rates varying from 0.3 to 300 s⁻¹. The viscous properties, storage modulus (G') and loss modulus (G'') were determined through small amplitude oscillatory shear flows at frequencies ranging from 1 to 50 rad/s. Before any dynamic experiment, a strain sweep test at a constant frequency of 1.0 rad/s under stress conditions from 0.01 to 10 Pa at 30 °C was performed to determine the upper limit of the linear viscoelastic zone, with a strain value of 0.30. However, based on the experimental conditions, the region up to 0.10 was defined as the reliability limit.

2.6.0 Evaluation of Antioxidant Activity

The antioxidant activity was evaluated using the DPPH (1,1-diphenyl-2-picrylhydrazyl) method according to Kalkan and Maskan (2023), with modifications. In this procedure, 100 µL of DPPH (0.3 mM) was added to 100 µL of mucilage at different concentrations (800, 1000, 1200, 1400, and 1600 µg/mL). As a standard antioxidant substance, ascorbic acid was used. Additionally, a negative control was prepared consisting of 100 µL of DPPH solution and 100 µL of methanol. The samples were incubated in the absence of light for 30 minutes at room temperature. Absorbance was then measured at 517 nm using a BioTek® Synergy HT Multimode Reader (Santa Clara, USA). The experiment was performed in triplicate, and the results were calculated according to equation (2).

$$\%AS = \frac{ABS \text{ negative control} - ABS \text{ sample}}{ABS \text{ negative control}} \times 100 \quad (\text{Eq. 2})$$

The ABTS (2,2'-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid)) radical assay was conducted according to the methodology described by Cano et al. (2023), with modifications. The ABTS radical was prepared by mixing 7 mM ABTS and 245 mM Ammonium Persulfate (APS) and incubating for 16 hours. As the standard substance, Trolox was used at a concentration of 2 mM, dissolved in methanol. 10 µL of mucilage solutions (800, 1000, 1200, 1400, and 1600 µg/mL) were added to a 96-well plate along with 190 µL of the ABTS radical. The samples were analyzed using a spectrophotometer at a wavelength of 734 nm, and the results were calculated based on the percentage reduction of the radical (equation 3).

$$\% \text{ ABTS decolorization} = \frac{\text{ABS negative control} - \text{ABS sample}}{\text{ABS negative control}} \times 100 \quad (\text{Eq. 3})$$

2.7 Cellular Viability Assay

For the cellular viability test, cells from distinct lineages were used: HEK-293 and Raw-264.7. Cells were seeded in 96-well plates and maintained for 24 hours in a 5% CO₂ incubator under standard conditions, with 100 µL of Modified Eagle's Medium (DMEM) with high glucose content, at a density of 1x10⁵ cells per well. After 24 hours, the initial medium was removed, and a culture medium containing mucilage at different concentrations (10 and 100 µg/mL) was added. As a positive control, 1% Triton X-100 was used for HEK-293 cells, and dimethyl sulfoxide (DMSO) was used for Raw-264.7 cells. The negative control was the culture medium itself. After 24 hours, the supernatant was removed, and 200 µL of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) at a concentration of 0,5 mg/mL was added. The plate was then incubated for 4 hours in the absence of light. Afterward, the MTT was removed, and 100 µL of DMSO was added to solubilize the formazan crystals. Finally, the plate was analyzed in a plate spectrophotometer (ELISA reader) at an absorbance of 570 nm.

2.8 Statistical Analysis

All tests were performed in triplicate, and results are expressed as mean ± standard deviation. Statistical analyses were performed using Statistica 10 software (StatSoft, Inc., USA), where the means of two groups were compared using the unpaired Student's t-test and one-way analysis of variance (ANOVA) with Tukey's multiple comparison test for comparing multiple groups. Statistical significance was considered when $p < 0.05$.

3.0 RESULTS AND DISCUSSION

3.1. Extraction of mucilage

The highest mucilage extraction yield obtained was through the method described by Gheribi et al. (2018), with a yield of 1.45%. However, despite the high yield, fibers were observed in the mucilage, similar to the method by Monrroy et al. (2017) that obtained 0.46%. Both methods are characterized by the direct precipitation of the material after the pulp is solubilized in water, without the presence of a filtration process. In the parenchyma of Cactaceae and throughout the cladode region, a variety of structures are found, such as

calcium oxalate crystals, cellulose, and lignins (Maceda et al., 2021), among other chemical components that directly influence the material's purity. Without an appropriate separation process, these components may limit the material's applicability in certain areas.

There are still a few studies in the literature reporting the yield of mucilage from *Nopalea cochenillifera* Salm-Dyck. However, Ferreira et al. (2022) evaluated the yield of mucilage from *Opuntia ficus-indica*, collected during the rainy and dry seasons, using the extraction method described by Gheribi et al. (2018). They obtained a lower yield in the rainy season (1.13%) and a higher yield during the dry season (6.77%). This result is expected, as the yield is a ratio between the fresh mass of the cladodes and the dry mucilage extracted. Therefore, if the plant has greater water availability, it will present a higher fresh mass (Ferreira et al., 2022).

The method described by Dick et al. (2019) yielded the lowest results among the methodologies tested, with approximately 0.38%, which is even lower than the yield found in the literature of 0.69% for *Opuntia milpa alta* using the same method (Cai et al. 2008). The mucilage yield can be influenced by chemical factors, such as the choice of extraction method, or biological factors, such as harvest time, management practices, the species used, water availability, and nutrient input, among others.

In the determination of total soluble carbohydrates (Figure 1-A), the method described by Dick et al. (2019) stood out compared to those of Monrroy et al. (2017) (63.78 µg/mg) and Gheribi et al. (2018) (57.84 µg/mg), with a soluble carbohydrate content of 383.2 µg/mg of mucilage. This justifies its selection for optimization, primarily due to its higher yield. This result is explained by the selectivity of the methodology, where the precipitation of the material occurs only in the soluble fraction, due to filtration and centrifugation processes that prioritize the presence of soluble components. In contrast, the other extraction methods utilize the entire internal part of the cladode, which may lead to the presence of insoluble components such as cellulose, potentially interfering with the results.

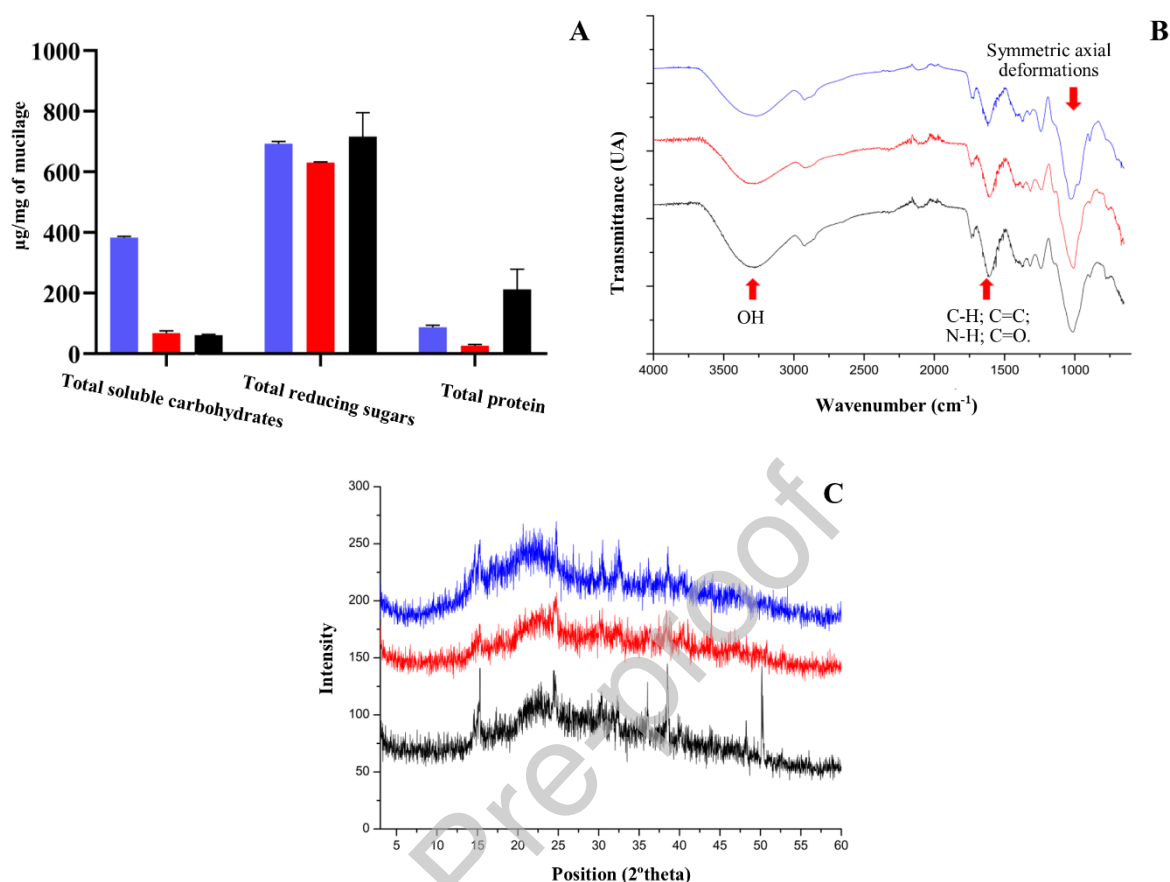


Figure 1. Characterization of *Nopalea cochenillifera* Salm-Dyck at different extraction methods. **A-** Evaluation of total soluble carbohydrate contents, reducing sugars, and total soluble proteins. **B-** Infrared spectrum of extracted mucilage. **C-** X-ray diffraction spectrum of mucilage. Across all graphs, the blue colors denote the extraction method of Dick et al. (2019), red corresponds to Monrroy et al. (2017), and black represents the approach by Gheribi et al. (2018).

The content of reducing sugars was high in all extractions, being highest in the method of Gheribi et al. (2018) with 716.3 µg/mg, followed by Dick et al. (2019) with 693.3 µg/mg and Monrroy et al. (2017) with 630.3 µg/mg. Although reducing sugars are formed from soluble carbohydrates, steps in their analysis involve homogenizing the sample with DNS at 90°C, which promotes solubility and results in greater method sensitivity (Lam et al., 2021).

In the total soluble protein content, the methodology of Gheribi et al. (2018) achieved the highest yield of 211.81 µg/mg, followed by Dick et al. (2019) with 87.27 µg/mg

and Monrroy et al. (2017) with 25.90 $\mu\text{g}/\text{mg}$. Due to the high nutritional value of proteins, these biomolecules are primarily used in the food industry for the manufacture of products and formulations. In the pharmaceutical industry, they are utilized in the production of nanofibers (Yildiz; Kara; Acartürk, 2020), delivery systems via transfer RNA (O'flaherty et al., 2020), and recombinant systems (Pham; Meng, 2020), among others. Despite their numerous advantages, depending on the product, proteins can be considered interfering agents, as is the case in the production of carbohydrate-based polymeric nanocarriers.

In the determination of total polyphenols and flavonoids, no significant amounts of these molecular groups were found in the mucilage. This result can be understood through the specific characteristics of plant secondary metabolites, which can vary among plant species depending on genetic or environmental factors (LI et al., 2020). Therefore, such quantifications were not performed in the extractions of the experimental design.

The infrared analysis was performed to verify the spectral pattern of the extractions and to observe whether the changes in the variables were modifying the chemical pattern of the material (Figure 1-B). It is possible to observe the presence of characteristic bands for functional groups in all spectra, which are characteristic of carbohydrates: at 3500 cm^{-1} for O-H bonds related to polymeric association, as well as amines and carboxyl groups. The intensity of this peak in the extraction method of Dick et al. (2019) may indicate a higher presence of free O-H groups. Another band around 1600 cm^{-1} - 1800 cm^{-1} , characteristic of C-H and C=C stretching, N-H and C=O, shows lower intensity in the method of Monrroy et al. (2017). The peak with the highest intensity in the extractions appears at 1000 cm^{-1} , corresponding to symmetrical axial deformations. In other cactus species such as *Opuntia ficus-indica*, the presence of polymeric O-H groups and signals of amines and carboxyl's was found, characterized by the broad peak around 3500 cm^{-1} (Quintero-García et al., 2021).

X-ray diffraction is useful for verifying the arrangement of atoms and molecules in the studied material. When there is the presence of an ordered arrangement at an approximate and repeated distance with a magnitude like the wavelength of the light used, information about the polymer's geometry can be generated through the interference pattern (Deore & Mahajan, 2021). In all extractions, there was no arrangement ordered, demonstrating that the material is amorphous (Figure 1-C), as shown in the micrographs. This amorphous pattern is also found in the mucilage of cladodes of *Opuntia ficus-indica* by García-Barradas et al. (2022). Some crystalline structures were found, especially in the method of Gheribi et al. (2018), characterized by calcium oxalate and mineral salts, as identified in the study

conducted Gómez-Castaño (2023), such as sodium nitrate (NaNO_3), calcium carbonate (CaCO_3), sin-nitromagnetite ($(\text{Mg}(\text{H}_2\text{O})_6)(\text{NO}_3)_2$), weddellite ($\text{Ca}(\text{C}_2\text{O}_4)(\text{H}_2\text{O})_{2.35}$), sin-weddellite ($\text{C}_2\text{CaO}_4 \cdot 2\text{H}_2\text{O}$), sin quartz (SiO_2), and potassium aluminum phosphate ($\text{AlK}(\text{P}_2\text{O}_7)$) in the mucilage of *Selenicereus megalanthus* fruits. This occurs due to the chemical composition of these materials, which are rich in macro and micronutrients, particularly calcium.

The study evaluated the average molecular weight of the mucilage and the hydrodynamic radius of the particles. Among the methods described in the literature, the one that yielded the lowest molecular weight was that of Gheribi et al. (2018), with 314 KDa, while the smallest hydrodynamic radius was obtained by Dick et al. (2019), with 480.8 nm. This also corresponds to a relatively low average molecular weight for the extractions, which is promising because smaller matrices are crucial for the development of formulations, as they are effective in interacting with cells and membranes. The hydrodynamic radius of the methods by Monrroy et al. (2017) (1584,0 nm) and Gheribi et al. (2018) (1912,0 nm) was similar to the value found by Amiri et al. (2021) in the mucilage of Hollyhock roots, which was 2021.0 nm, with the molecular weight of the complex being larger at 2.275×10^6 kDa. In scanning electron microscopy (Figure 2), a greater presence of smaller particles in the methodology of Gheribi et al. (2018) (Figure 2-C) is observed, as well as larger structures in the Dick et al. (2019) method (Figure 2-A), results that are consistent with the analysis. Since Gheribi et al, (2018) obtained a value of 314.0 KDa, Monrroy et al, (2017) 974.0 KDa, and Dick et al, (2019) 409.0 KDa.

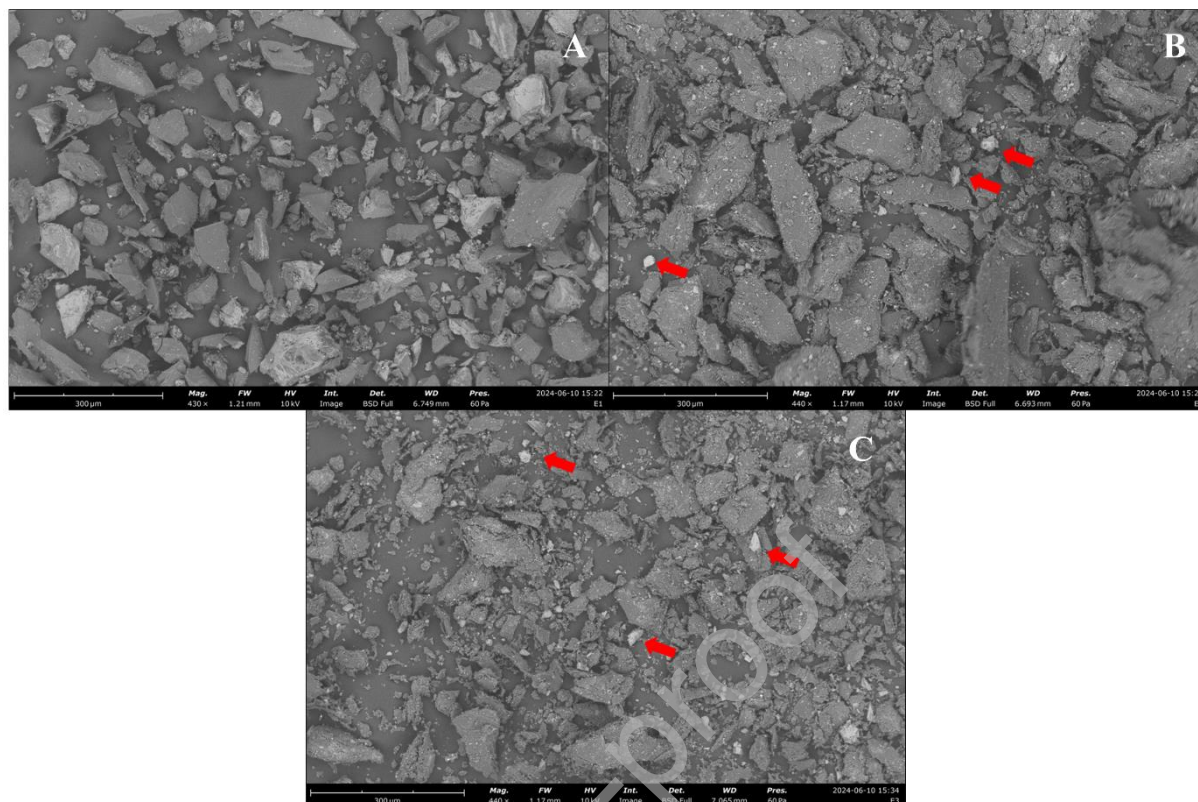


Figure 2. Scanning electron microscopy of mucilage from *Nopalea cochenillifera* Salm-Dyck using different methods: **A-** Dick et al. (2019), **B-** Monrroy et al. (2017), **C-** Gheribi et al. (2018). Red arrows indicate the presence of insoluble whitish structures. Scale bar = 300 µm

Figure 2 shows the surface of the material after maceration. In all samples, the mucilage exhibited an irregular morphology, along with a diverse distribution of particles, which can be explained in this type of compound by the aggregation of smaller chemical complexes due to the electrostatic charge of the particles. The methodologies of Monrroy et al. (2017) and Gheribi et al. (2018) presented small whitish structures, which were insoluble in deionized water when the mucilage was resuspended, possibly indicating the presence of insoluble molecules contained in the parenchyma of the cladode.

The polysaccharide composition of the mucilage can directly influence the morphology and surface characteristics of the particles, as evident when analyzing the micrograph of the methodology by Dick et al. (2019). Due to modifications in the precipitation of the material, it appeared more uniform with smaller particles, which may directly influence solubilization through kinetics due to greater surface contact.

3.2. Optimization of Mucilage Extraction

The methodology selected for optimization through experimental design was that of Dick et al. (2019), due to the direct relationship between yield and total soluble carbohydrate content. Despite a low yield, this method stood out in this quantification, in addition to presenting a small hydrodynamic radius and molecular weight. Therefore, the optimization was performed aiming to obtain high yield and total carbohydrate in the mucilage extraction.

It is observed that an extraction protocol, such as that realized in experiment 19 (1.45%), performed better than the others, with a yield close to that of Gheribi et al. (2018), as well as better homogeneity in water (Figure 3-A), characteristic of the methodology by Dick et al. (2019). In this extraction, ethanol is used in a 1:10 ratio. The use of ethanol, isopropyl alcohol, and other components with oxygenated groups, such as the carbonyl group in acetone, is commonly used in polysaccharide extractions due to their greater affinity for the sugars in carbohydrates compared to water (Ai et al., 2020). The temperature used was 90°C, which favored the homogenization of the components. This variable directly affects the solubility coefficient of a solvent, either promoting or hindering dissolution (Schick et al., 2023). The extractions with the lowest yields were 5, 9, and 12, with 0.007%, 0.019%, and 0.028%, respectively (Figure 3-A). The similarities between these extractions were the precipitation agent, which was isopropyl alcohol, and the solubilization temperature, which occurred at 50°C.

The extractions performed using the experimental design yielded total soluble carbohydrate content ranging from 64.51 to 252.16 µg/mg of mucilage (Figure 3B). Extractions 4 and 16 stood out compared to the others, with 252.16 and 234.78 µg/mg of mucilage, respectively. These extractions are similar to each other, except for the temperature used during sample solubilization. Regarding the determination of total proteins, only traces of these biomolecules were found in almost all extractions, with quantification being possible only in extraction 15, which yielded 6.07 µg/mg of mucilage. All extractions exhibited high levels of reducing sugars.

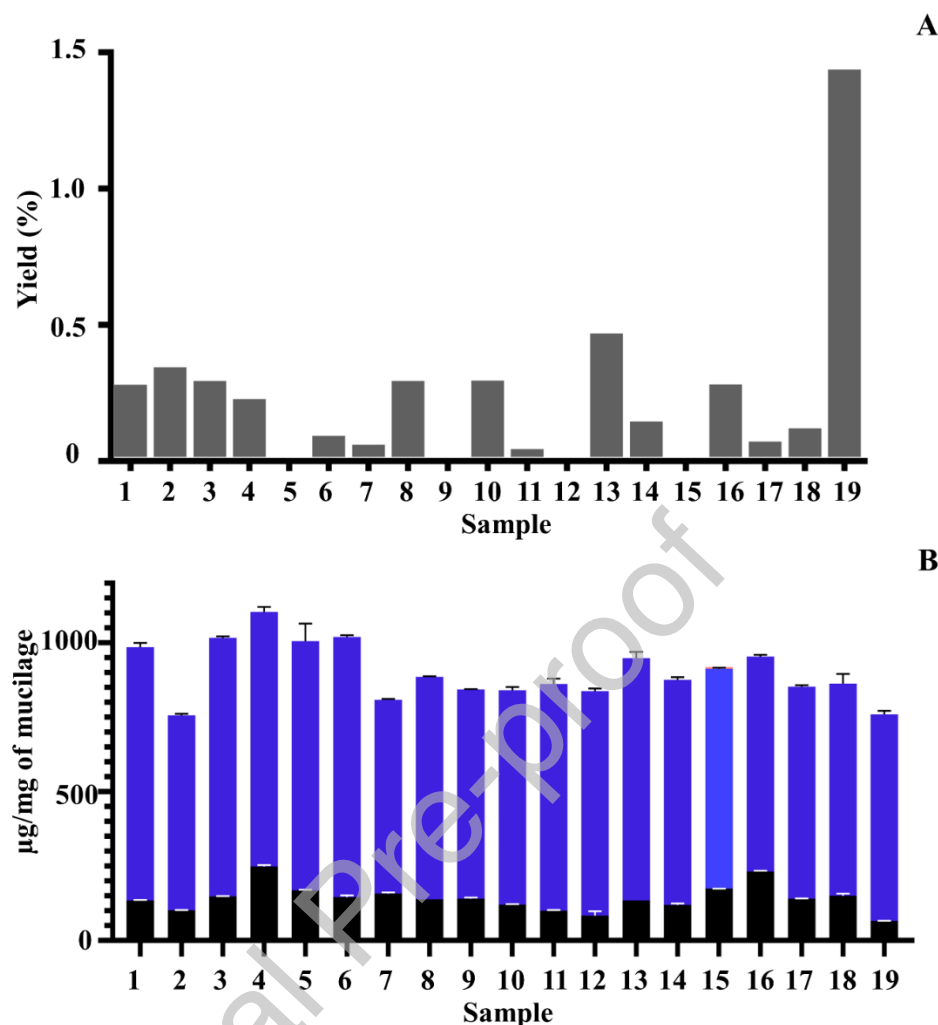


Figure 3. A- Yield of the mucilaginous fraction of *Nopalea cochenillifera* Salm-Dyck from the experimental design. B- Total soluble carbohydrates (indicated in black), reducing sugars (in blue), and total protein (in red) were quantified; notably, total protein was detected in only a small amount in sample fifteen.

In the infrared analysis (Figure 1S, supplementary material), the extractions exhibited a spectral pattern similar to the methodologies selected from the literature, with characteristic peaks corresponding to functional groups present in carbohydrates, such as 3500 cm^{-1} for O-H bonds from the polymeric association, as well as amines and carboxyls. Bands around 1600 to 1800 cm^{-1} were attributed to C-H and C=C stretching, N-H, and C=O, while an intense peak at 1000 cm^{-1} corresponded to symmetric axial deformations. This was consistent with the infrared spectrum obtained in the methodology of Dick et al. (2019), indicating that physical alterations did not modify the molecules present in the material but only their concentration, as evidenced by the intensity of bands primarily related to carbohydrates, such as at 3500 cm^{-1} .

A wide range of hydrodynamic radius and average molecular weight for different extractions was obtained (Table 2). Given that this type of equipment measures the overall average of particles in suspension, it was only possible to assess, in general terms, which extractions yielded particles with a smaller molecular weight and hydrodynamic radius. Extractions 18 and 14 stood out, with 0.7 and 33.4 kDa, respectively. The best hydrodynamic radius was observed in extraction 16, measuring 468 nm.

Table 2. Average molecular weight and hydrodynamic radius of extractions performed in the experimental design

Sample	Molecular weight (KDa)	Hydrodynamic Radius (nm)
1	5×10^6	609.7
2	389.5	340.6
3	196.6	511.2
4	486.7	735.0
5	179.9	1670.0
6	4.1×10^3	615.0
7	187.6	976.7
8	718.6	576.7
9	108.8	1034.0
10	56.7	462.9
11	52.7	922.3
12	9.5×10^4	1308
13	133.3	711.3
14	33.4	381.7
15	78.3	614.2
16	51.5	468.0
17	630.1	623.4
18	0.7	1574.0
19	1.600	499.8

Thus, considering the two main dependent variables selected in this study, it was confirmed that all independent variables had significant effects ($p < 0.05$) on the yield (Figures 4-A and B) and total carbohydrate (Figures 4-C and D) (Figure 2S, supplementary material).

Analysis of variance (ANOVA) was employed to assess the significance of the independent variables and their interactions. The model's goodness of fit was evaluated using the coefficient of determination (R^2), which indicates the proportion of variability in the response variable explained by the model. The experimental matrix showed a strong linear relationship with an R^2 value of 0.9409 and 0.9644 for yield and total carbohydrate, respectively. Furthermore, the adjusted R^2 ($\text{Adj}R^2 = 0.734$ and 0.786 for yield and total carbohydrate, respectively) reinforced the statistical relevance and robustness of the model. These results confirm that the experimental matrix provided a satisfactory fit of the polynomial model to the observed data.

By applying multiple regression analysis on the design matrix and analyzing the responses given in the experiments, the polynomial equation was established to yield (Eq 4) and total carbohydrate (Eq 5):

$$Y_1 = 0.2 - 0.15X_1 + 0.12X_2 - 0.03X_3 + 0.08X_4 - 0.08X_1X_2 + 0.01X_1X_3 - 0.03X_1X_4 - 0.11X_2X_3 + 0.08X_2X_4 - 0.10X_3X_4 + 0.06X_1X_2X_3 - 0.07X_1X_2X_4 + 0.09X_1X_3X_4 - 0.12X_2X_3X_4 \quad (\text{Eq 4})$$

$$Y_2 = 28.74 - 17.25X_1 + 9.85X_2 + 5.83X_3 + 8.36X_4 - 4.76X_1X_2 - 7.30X_1X_3 - 2.15X_1X_4 - 7.98X_2X_3 + 3.86X_2X_4 - 2.16X_3X_4 + 2.06X_1X_2X_3 - 2.50X_1X_2X_4 + 1.92X_1X_3X_4 - 9.74X_2X_3X_4 \quad (\text{Eq 5})$$

Where Y_1 denotes the dependent variable representing yield (%), Y_2 corresponds to the total carbohydrate content, X_1 represents the water ratio, X_2 the temperature, X_3 the type of solvent, and X_4 the solvent ratio.

The higher the water ratio, the lower the yield, which can be justified by the effective solvating action of water on sugars and carbohydrates (Chaubey et al., 2021), hindering the interaction of polysaccharides with the precipitating solvent. The same occurred with the type of solvent used, with ethyl alcohol performing better compared to the other solvents. Both temperature and solvent ratios yielded positive results for the yield, which is expected since temperature can enhance the solubility of the material. Similarly, a higher solvent concentration in the reaction medium results in more effective interaction with the component of interest.

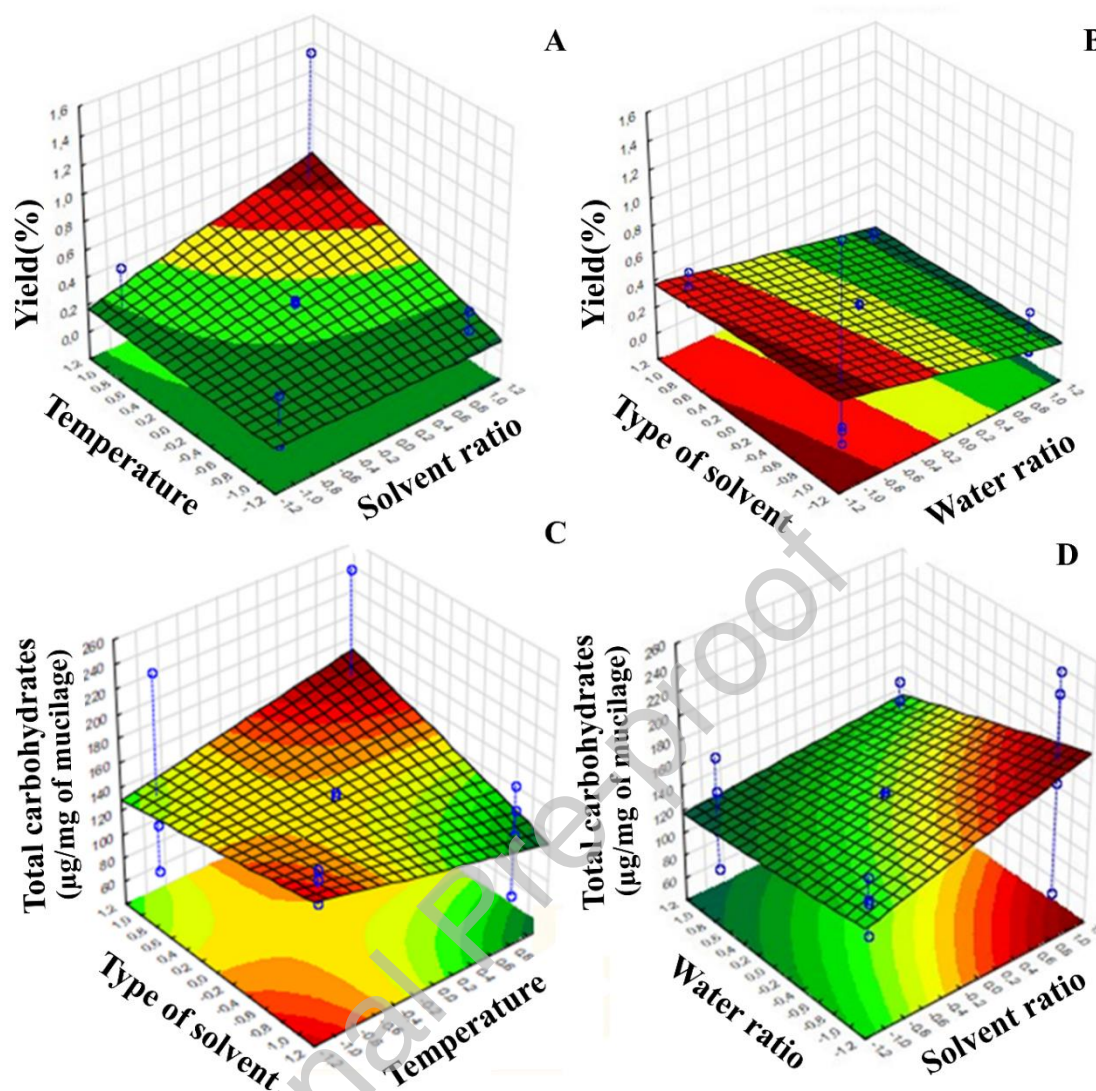


Figure 4. Response surface plots showing the effects of extraction variables on the yield and total soluble carbohydrate content of *Nopalea cochenillifera* Salm-Dyck mucilage. **A** – Effect of solvent ratio and temperature on extraction yield; **B** – Effect of solvent type and water ratio on extraction yield; **C** – Interaction between solvent type and temperature on total soluble carbohydrate content; **D** – Interaction between water ratio and solvent ratio on total soluble carbohydrate content.

Reducing sugars are generated through the cleavage of glycosidic bonds, a process that can occur via enzymatic, physical, or chemical mechanisms. In our extraction procedures, temperatures ranged from 50 °C to 90 °C, conditions that favor the formation of reducing sugars. This is because elevated temperatures promote the hydrolytic cleavage of carbohydrate glycosidic bonds, yielding free sugars that may subsequently undergo further reduction reactions (Deshavath et al., 2020). In the experimental design, all variables

significantly affected the total soluble carbohydrate content (Figure 4-C and 4-D). The water ratio was the variable that most negatively affected the total soluble carbohydrate concentration (Figure 4-D). The type of solvent, solvent ratio, and temperature positively influenced the carbohydrate concentration (Figures 4-C and 4-D), with ethyl alcohol showing the best performance at high temperature.

However, extractions with a lower water ratio and higher temperature favor yield, as do the type of solvent and solvent ratio, though they may affect the molecular weight and size of the polysaccharides. The total soluble carbohydrate content is directly influenced by the type of solvent, solvent ratio, and temperature. Therefore, the result of the optimization study following the experimental design approach allowed to identification of the optimal conditions for mucilage extraction that have both high yield and total carbohydrate. The optimal characteristics of the mucilage extraction were 1:3 water ratio, with a solubilization temperature of 90°C using ethanol at solvent ratio of 1:10. The samples prepared under these conditions showed a significant improvement in the mucilage yield, with a percentage increase of 14.62% from 0.38% to $0.43 \pm 0.03\%$ compared to the initial methodology Dick et al. (2019). The total soluble carbohydrate content was similar from 383.2 µg/mg to 382.43 ± 6.31 µg/mg, while the reducing sugars showed a slight increase of 2.81%, with 693.3 µg/mg in the methodology Dick et al. (2019) to 712.80 ± 16.26 µg/mg. No protein was detected with the applied method, and the hydrodynamic size was similar (497.8 nm), although the molecular weight showed a slight increase from 480.8 nm to 483.3 KDa.

3.3. Characterization of optimized mucilage from *Nopalea cochenillifera* Salm-Dyck

The morphological aspects of cactus mucilage *Nopalea cochenillifera* Salm-Dyck were observed using scanning electron microscopy (SEM), which is represented in Figure 5-A. The mucilage images demonstrated a material with an amorphous aspect, composed of fibrous nature particles that form aggregates with irregular shapes and dimensions, compatible with data presented in other studies reported in the literature for other cactus species (Deore & Mahajan, 2021). These morphological aspects influence the obtention and production of biofilms by cactus mucilage, so it's important to evaluate the structural information of the samples by SEM (Pinheiro et al., 2024), and this aspect can influence the extraction and purification method of mucilage, furthermore aspects such as genotype, cladode harvest time, which can also influence the properties of the compound (Mannai et al., 2023).

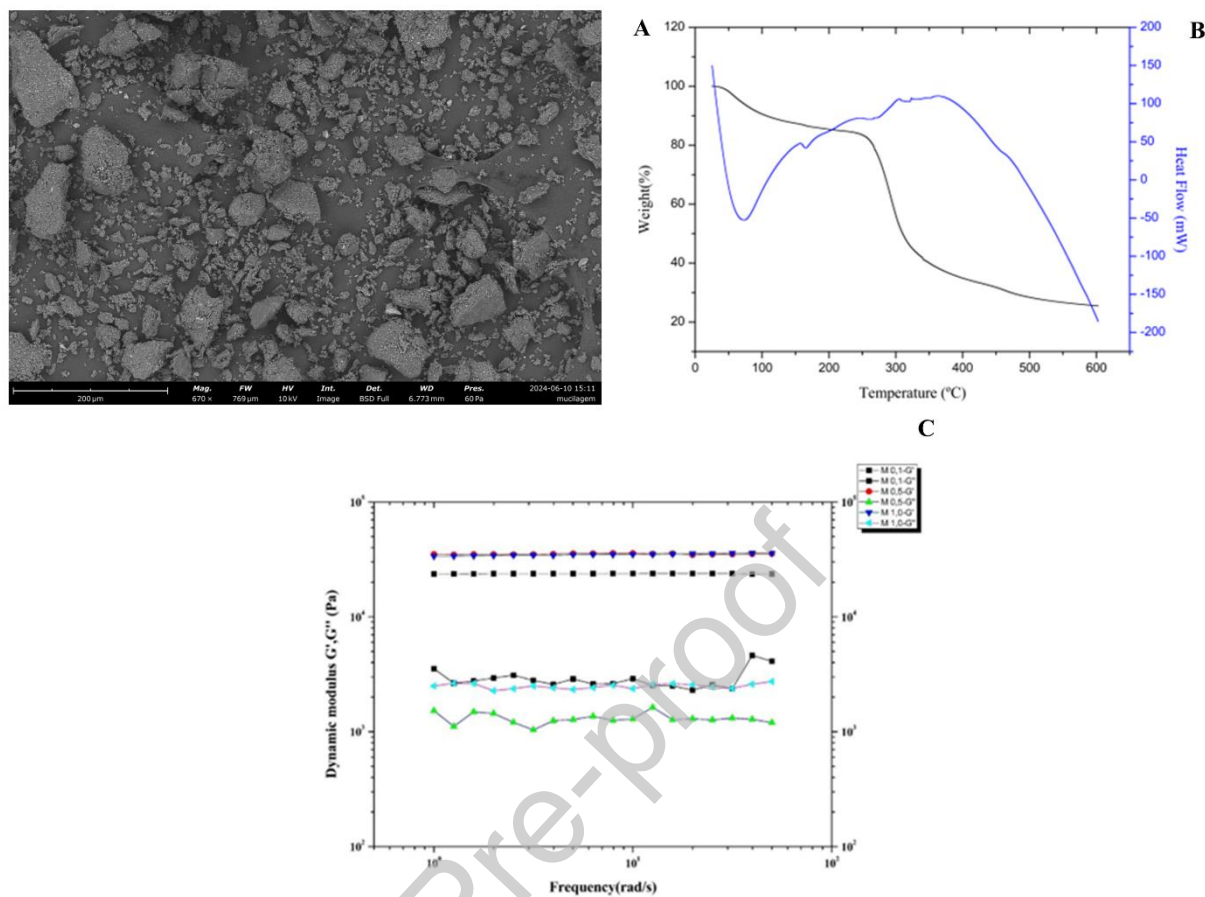


Figure 5. Characterization of mucilage after experimental design. **A**-Scanning electron microscopy of the mucilage 200 μm . **B**- Spectra of thermogravimetric analysis and differential scanning calorimetry of mucilage. Where: black is TGA and blue is DSC. **C**- Apparent viscosities at concentrations of 0.1, 0.5, and 1% according to the dynamic storage moduli (G') and viscous modulus (G'') correlated to the frequency dependence parameter in rad/s.

The material in Figure 5-B exhibited good thermal stability, showing no significant weight loss before reaching 100 $^{\circ}\text{C}$. This stability was maintained up to 300 $^{\circ}\text{C}$, with a 20% loss of initial weight. After this temperature, the mucilage showed significant weight losses, which can be confirmed by the integral, indicating a greater physical change in the mucilage at 300 $^{\circ}\text{C}$. The cactus mucilage showed greater thermal stability than the okra mucilage, which showed significant losses at 240 $^{\circ}\text{C}$ (Glaue et al., 2023).

The Differential Scanning Calorimetry (DSC) indicates a phase change (fusion) occurring at 50 $^{\circ}\text{C}$, which happens due to the presence of impurities in the material or its amorphous characteristic, as it remained relatively constant until 250 $^{\circ}\text{C}$. However, a loss of

intensity was observed at 400°C, attributed to the crystallization of the solid material (Deore & Mahajan, 2021), suggesting that the material remained stable even at high temperatures.

As shown in Figure 5-C, the typical oscillatory curves as a function of mucilage concentration, both in the dynamic storage modulus G' (Pa) and the loss modulus G'' (Pa), can be observed and correlated to a frequency (rad/s) dependence. In this regard, at low concentrations, G'' tends to be greater than G' . That is, in a product with low mucilage concentrations, it will tend to be more viscous and less prone to gel formation. However, as the concentration increases, G' will become greater than G'' , promoting the formation of greater system elasticity. As demonstrated in its pseudoplastic nature and conformational aspects, Van Rooyen et al. (2024) state that the increase in the viscosity of the sample in aqueous solution may be correlated with the nature of the polymer.

3.4. Antioxidant Activity

It was observed that at the maximum dilution concentration of 1600 µg/ml, the mucilage reduced to 29.4% of the DPPH radical and 13.2% of ABTS, showing no significant antioxidant activity. This contrasts with the results found by Fabela-Illescas et al. (2022), whose activity was 15.28 mmol and 51.31 mmol, respectively. Magaña-Cerino et al. (2022) also observed that this species reduced DPPH by 95.6%, however, they obtained similar results to the present study with a reduction of ABTS by 16.8%.

The antioxidant activity of these methodologies is a result of the substances in the mucilage capable of donating hydrogen to reduce the oxidized radical (Theofanous et al., 2022). However, as there were low concentrations of polyphenols, this activity is consequently reduced. Furthermore, the reduction in antioxidant capacity when comparing the methods can be justified by the reaction time employed, since some antioxidants require a longer incubation time to complete the reaction.

The low levels of phenolics and other antioxidants can be explained by the purification methods applied to the mucilage, ensuring that the polysaccharides are isolated from other constituents obtained during extraction. Thus, there is a greater guarantee of its application in the food industry and the development of polysaccharide-coated nanoparticles (Cruz-Rubio et al., 2023).

3.5. Cell Viability Study

The *in vitro* cytotoxicity evaluation of *Nopalea cochenillifera* Salm Dyck mucilage was conducted using HEK-293 and Raw-264.7 cell lines. The investigation was performed using the MTT assay, which is a cell viability indicator based on the reducing properties of MTT to stain insoluble formazan crystals synthesized by viable mitochondrial cells (Khan et al., 2022). Figure 6 shows this cell viability test using HEK-293 and Raw-264.7 cell lines treated with the mucilage at concentrations of 10 and 100 $\mu\text{g/mL}$. Regarding the HEK-293 cell line (Figure 6-A), a significant difference was observed between the mucilage concentrations used and the positive control, but no difference was observed between the mucilage concentrations concerning cell viability. Therefore, this suggests that cytotoxic effects on normal cells are not concentration-dependent, and that the mucilage did not alter the cell viability for this cell type.

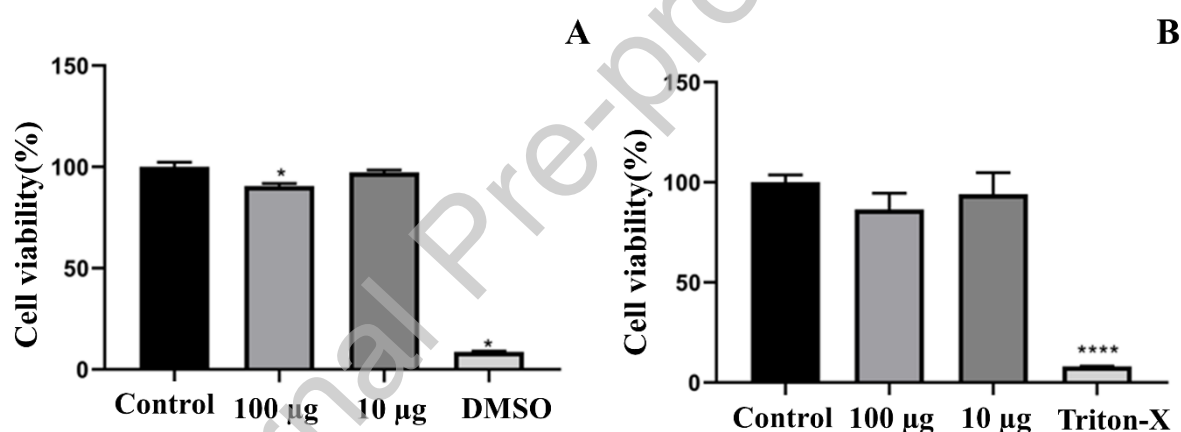


Figure 6. Cell viability test performed on *Nopalea cochenillifera* Salm-Dyck mucilage at 10 and 100 $\mu\text{g/mL}$ concentrations in non-tumor cell lines (A-HEK-293, B-Raw-264.7).

For the Raw-264.7 macrophage cells (Figure 6-B), a significant difference was observed between the mucilage concentrations used and the positive control. This suggests that the cytotoxic effects on murine macrophage tumor cells are concentration-dependent. However, regardless of this, cell viability remained satisfactory, indicating that the raw material does not present toxic effects.

Thus, cell viability was significantly elevated for both cell lines treated with the mucilage at concentrations of 10 and 100 $\mu\text{g/mL}$, indicating that the mucilage did not exert significant cytotoxicity on the evaluated cells and showed good biocompatibility. This makes

it promising as a raw material for the production of pharmaceutical systems intended for human use. However, further studies are needed to confirm its low toxicity.

In summary, despite the limited characterization of the plant species under investigation and the scarcity of comparable studies, our work provides novel insights into the biochemical profile of its mucilage, particularly with respect to its carbohydrate content. By optimizing the extraction protocol, we aimed to maximize both purity and yield, parameters that are critical for the intended application of this material as a polymeric matrix in the industry. While residual biomolecules such as proteins and fibers may act as functional additives in some contexts, they represent undesirable interferents in our formulation strategy. Furthermore, the inherently low mucilage yield poses a challenge to scalability and economic feasibility, reinforcing the need for improved extraction efficiency. These findings emphasize the importance of aligning extraction methodologies with application-specific requirements and highlight the translational potential of this biopolymer in biomedical applications.

4. CONCLUSION

Mucilage is a complex material that alters its chemical composition and yield depending on the selected organism, harvest time, methodology, and plant organ, which should be selected based on the researcher's interests. Changes in physical variables have been observed to influence the composition and yield of the material and may reduce the presence of some groups of biomolecules, such as proteins. Statistical planning has proven to be a promising tool for understanding the variables in extraction yield. FTIR spectroscopy revealed characteristic absorption bands associated with carbohydrate functional groups, indicative of polysaccharide structures. Plant-derived carbohydrates demonstrated high thermal stability by thermogravimetric analysis, exhibiting mass losses of approximately 20% at temperatures approaching 300 °C. The extracted mucilage displayed low molecular weights and small hydrodynamic radii, attributes advantageous for applications in the food and pharmaceutical sectors, particularly in the design of delivery systems for active compounds, whether for targeted drug delivery or for encapsulating bioactive molecules to enhance the shelf life of food products. Furthermore, the low cytotoxicity of *Nopalea cochenillifera* Salm-Dyck mucilage in cell culture models reinforces its potential as a safe and versatile biomaterial. Nonetheless, further structural elucidation using advanced analytical techniques such as NMR spectroscopy, glycosyl composition analysis, or complementary methods is

recommended to fully define its molecular architecture and assess potential extraction-induced modifications.

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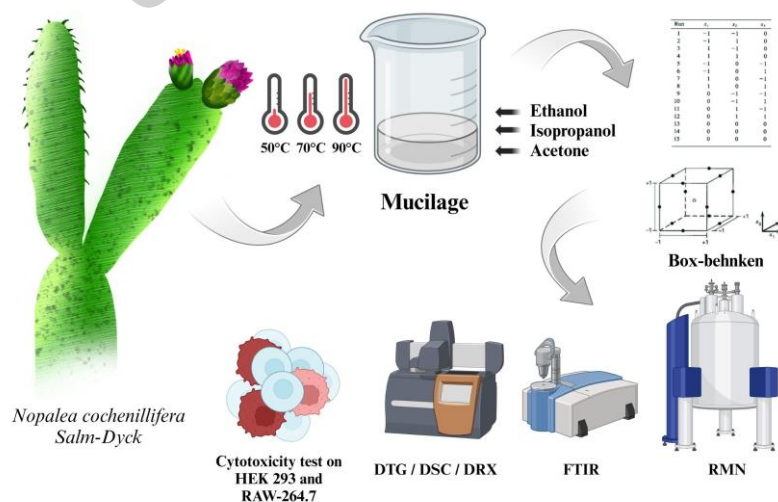
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GRAPHICAL ABSTRACT



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☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Disciplinas Obrigatórias

Ano/Per	Componente Curricular		CH	CR	Turma	Nota	Situação
2021.2	1608127	TÉCNICAS AVANÇADAS DE RMN	45	3	01	8.5	APROVADO
2021.2	SPRNA0107	FARMACOQUÍMICA II	45	3	01	7.5	APROVADO
2022.2	SPRNA0104	SEMINÁRIOS INTEGRADOS I	30	2	01	9.8	APROVADO

Disciplinas Optativas

Ano/Per	Componente Curricular		CH	CR	Turma	Nota	Situação
2021.2	1608039	MÉTODOS FÍSICOS EM FITOQUÍMICA II	45	3	01	8.5	APROVADO
2022.1	1302087	METODOLOGIA CIENTÍFICA E DA PESQUISA	30	2	01	10.0	APROVADO
2022.1	1608143	MÉTODOS FÍSICOS EM FITOQUÍMICA I	45	3	01	9.2	APROVADO
2022.1	1608146	TÓPICOS ESPECIAIS EM PRODUTOS NATURAIS E BIOSINTÉTICOS I	30	2	01	10.0	APROVADO
2022.2	1608141	BIOSSÍNTESE DE PRODUTOS NATURAIS	30	2	01	9.5	APROVADO
2022.2	1608142	ESTEREOQUÍMICA DE FÁRMACOS	15	1	01	10.0	APROVADO
2022.2	1608146	TÓPICOS ESPECIAIS EM PRODUTOS NATURAIS E BIOSINTÉTICOS I	30	2	01	9.6	APROVADO
2022.2	1608151	RELAÇÃO ESTRUTURA QUÍMICA-ATIVIDADE BIOLÓGICA	45	3	01	9.0	APROVADO
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2023.1	1608120	FARMACOQUÍMICA I	30	2	01	8.0	APROVADO
2023.1	1608122	PROCESSOS DE EXTRAÇÃO, ISOLAMENTO E PURIFICAÇÃO DE PRODUTOS NATURAIS	30	2	01	9.5	APROVADO
2023.1	1608123	TECNOLOGIA E CONTROLE DE MEDICAMENTOS FITOTERÁPICOS	30	2	01	8.5	APROVADO
2023.1	SPRNA0101	FARMACOLOGIA E TOXICOLOGIA PRÉ-CLÍNICA	30	2	01	--	TRANCADO
2023.2	1608148	TÓPICOS ESPECIAIS EM PRODUTOS NATURAIS E BIOSINTÉTICOS III	30	2	01	9.8	APROVADO

Disciplinas Extra Curriculares

Ano/Per	Componente Curricular		CH	CR	Turma	Nota	Situação
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Informações Adicionais de Disciplinas

Disciplina	Ano	Periodo	Turma	Subtítulo
1608146	2022	1	01	Gênese de Fármacos
1608146	2022	2	01	Nanotecnologia aplicada aos produtos naturais e biossintéticos
1608148	2023	2	01	Inovação Tecnológica no Desenvolvimento de Medicamentos Fitoterápicos

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2025/1	MATRICULADO			

Exames de Qualificação				
Descrição		Ano/Per	Data de Conclusão	Resultado
EXAME DE QUALIFICAÇÃO		2023.1	29/08/2023	APROVADO

Exames de Proficiência				
Idioma		Ano/Per	Data do Exame	Situação
14DCV1000	EXAME DE PROFICIÊNCIA EM INGLÊS	2022.1	19/09/2019	APROVEITADO
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Universidade Federal da Paraíba	Universidade Federal da Paraíba	Invoice date	20-AUG-2025
Centro de Ciencias da Saude	Centro de Ciencias da Saude	Due date	19-SEP-2025
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Line	Product reference	Item	Qty	Net unit price	Net amount	Tax	Total amount
1	EPR-114MCF	Carbohydrate Polymer Technologies and Applications Article Publishing Charge Article: Optimized Extraction, Characterization, and Cytotoxicity Assessment of Biodegradable Nopalea cochenillifera Salm-Dyck Mucilage Author: Prof Francisco Humberto Xavier-Júnior PII: S2666893925003214 Tax @ 0.00%	1	2,600.00	2,600.00	0.00	2,600.00
Total					2,600.00	0.00	2,600.00
Total due					USD		2,600.00

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Humberto Xavier-Júnior <fhxj@academico.ufpb.br>

**IMPORTANT PLEASE TAKE ACTION, Production has begun on your article
[CARPTA_100980] in Carbohydrate Polymer Technologies and Applications**

Humberto Xavier-Júnior <fhxj@academico.ufpb.br>
Para: s.singh.7@elsevier.com

15 de agosto de 2025 às 21:00

Dear ,

I hope this message finds you well.

I am writing to kindly request a discount on the article processing charges (APC) for our recent manuscript
CARPTA_100980.

As a researcher from Paraíba Federal University (UFPB/Brazil), I am currently facing financial constraints that make it difficult to cover the publication fees. Despite this, I am committed to making our research accessible through your esteemed journal, which we believe is the most suitable platform for reaching our target audience.

I would be grateful if you could consider offering a partial discount on the APC.

Thank you for considering my request. I look forward to your kind response.

Best Wishes

Prof. Dr. Francisco Humberto Xavier Júnior

Universidade Federal da Paraíba

Departamento de Ciências Farmacêuticas/ Laboratório de Biotecnologia Farmacêutica (BioTecFarm)
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Humberto Xavier-Júnior <fhxj@academico.ufpb.br>

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Dear Dr. Xavier-Junior,

Article ref. No – CARPTA 100980

Article title - Optimized Extraction, Characterization, and Cytotoxicity Assessment of Biodegradable Nopalea cochenillifera Salm-Dyck Mucilage.

Thank you for contacting us regarding your Article Publishing Charges.

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Thank you for contacting us, and should you require any additional assistance, please do not hesitate to contact us.

Kind regards,
Lakshmie C

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Nº do Protocolo: NÃO PROTOCOLADO

João Pessoa-PB, 21 de Agosto de 2025

Trata-se de solicitação de pagamento referente à taxa de publicação de artigo científico, conforme os termos estabelecidos na Chamada Interna PROPESQ nº 03/2025 - Pró-Publicação.

Após análise da documentação apresentada, verificou-se que o artigo objeto da solicitação já se encontra disponível em versão *preprint*, com DOI, desde o dia 16/08/2025. Constatou-se, ainda, que o nome do proponente consta na invoice apresentada, a qual deveria mencionar apenas o nome da universidade.

Diante disso, e considerando a necessidade de comprovação de que o artigo ainda não foi publicado em sua versão final, solicitamos:

1. Apresentação de declaração oficial emitida pela revista, atestando expressamente que o artigo encontra-se apenas em versão *preprint* e ainda não foi publicado em sua forma final;
2. Substituição da invoice apresentada por uma nova versão que contenha exclusivamente o nome da universidade, sem a menção ao nome do proponente.

Após o cumprimento das solicitações acima, o processo será encaminhado para análise do Pró-Reitor de Pesquisa, para posterior deliberação quanto ao pagamento da taxa.

Atenciosamente,

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Line	Product reference	Item	Qty	Net unit price	Net amount	Tax	Total amount
1	EPR-114MCF	Carbohydrate Polymer Technologies and Applications Article Publishing Charge Article: Optimized Extraction, Characterization, and Cytotoxicity Assessment of Biodegradable Nopalea cochenillifera Salm-Dyck Mucilage Author: Prof Francisco Humberto Xavier-Junior PII: S2666893925003214 Tax @ 0.00%	1	2,600.00	2,600.00	0.00	2,600.00
Total					2,600.00	0.00	2,600.00
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Humberto Xavier-Júnior <fhxj@academico.ufpb.br>

Re: Problems to [250822-001436]

Open Access Support <oasupport@elsevier.com>
Responder a: Open Access Support <oasupport@elsevier.com>
Para: fhxj@academico.ufpb.br

21 de agosto de 2025 às 13:46

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Dear Xavier-Junior,

Article ref: CARPTA_100980

Title: Optimized Extraction, Characterization, and Cytotoxicity Assessment of Biodegradable Nopalea cochenillifera Salm-Dyck Mucilage

I hope this message finds you well.

I'm writing to provide clarification regarding the status of your article currently listed as a Journal Pre-proof. Please find below the official explanation:

Journal pre-proofs are Articles in Press that have been peer reviewed and accepted for publication by the Editorial Board. These versions have undergone enhancements after acceptance, such as the addition of a cover page, metadata, and formatting for readability, but they are not yet the definitive versions of record.

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Once the final article is assigned to a volume and issue, the Article in Press version will be removed, and the final version will appear in the associated published volume/issue. The original online publication date will be retained.

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Kind regards,

Elvin Cantor

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Nº do Protocolo: NÃO PROTOCOLADO

João Pessoa-PB, 21 de Agosto de 2025

Prezados,

Agradeço pela análise realizada e pelas orientações referentes ao processo nº 23074.083540/2025-16, vinculado à Chamada Interna PROPESQ nº 03/2025 - Pró-Publicação.

Adicionei ao processo a invoice contendo exclusivamente o nome da Universidade Federal da Paraíba, conforme solicitado.

Também adicionei o email enviado pela editora explicando o que é o status do artigo de preprint, em que destaca que o trabalho não está publicado em sua versão final, ele apenas foi aceito. Segue o destaque traduzido enviado pela revista:

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Optimized Extraction, Characterization, and Cytotoxicity Assessment of Biodegradable Nopalea cochenillifera Salm-Dyck Mucilage

Paulo Sérgio da Silva Pereira , Ana Maria Campelo de Araújo ,
Ludmila Emilly da Silva Gomes , Álisson Emannuel Franco Alves ,
Anny Letícia Marinho Ramos Cardoso , Ana Flávia Chaves Uchoa ,
Graziela Maria de Araujo Pereira , Allessya Lara Dantas Formiga ,
Karla Samara Rocha Soares , José Maria Barbosa-Filho ,
Marcelo Sobral da Silva , Francisco Humberto Xavier-Júnior



PII: S2666-8939(25)00321-4
DOI: <https://doi.org/10.1016/j.carpta.2025.100980>
Reference: CARPTA 100980

To appear in: *Carbohydrate Polymer Technologies and Applications*

Received date: 12 June 2025
Revised date: 14 August 2025
Accepted date: 15 August 2025

Please cite this article as: Paulo Sérgio da Silva Pereira , Ana Maria Campelo de Araújo , Ludmila Emilly da Silva Gomes , Álisson Emannuel Franco Alves , Anny Letícia Marinho Ramos Cardoso , Ana Flávia Chaves Uchoa , Graziela Maria de Araujo Pereira , Allessya Lara Dantas Formiga , Karla Samara Rocha Soares , José Maria Barbosa-Filho , Marcelo Sobral da Silva , Francisco Humberto Xavier-Júnior , Optimized Extraction, Characterization, and Cytotoxicity Assessment of Biodegradable Nopalea cochenillifera Salm-Dyck Mucilage, *Carbohydrate Polymer Technologies and Applications* (2025), doi: <https://doi.org/10.1016/j.carpta.2025.100980>

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João Pessoa-PB, 22 de Agosto de 2025

À Assessoria de Comércio Exterior/PRA

De acordo com análise de documentos que consta na lista de verificação, solicito conversão da moeda e autorizo o pagamento da Invoice em anexo com recursos da ND 2025ND000939, conforme Chamada interna PROPESQ/UFPB - Pró-Publicação nº 03/2025.

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MINISTÉRIO DA EDUCAÇÃO
UNIVERSIDADE FEDERAL DA PARAÍBA

DESPACHO Nº 151/2025 - PRA-ACE (11.01.08.02.05)

Nº do Protocolo: NÃO PROTOCOLADO

João Pessoa-PB, 22 de Agosto de 2025

À

PROPESQ - COORDENAÇÃO GERAL DE PESQUISA

Prezados,

Devolvemos o presente processo, para que seja incluída a assinatura do Pró-Reitor de Pesquisa no documento de autorização. Após atendido, solicita-se encaminhar à esta unidade para dar continuidade ao atendimento do pleito. Atenciosamente,

(Assinado digitalmente em 22/08/2025 15:16)

GILMARA DE LIMA NOBREGA

DIRETOR(A)

Matrícula: 2035601

Processo Associado: 23074.083540/2025-16

Para verificar a autenticidade deste documento entre em <https://sipac.ufpb.br/documentos/> informando seu número:

151, ano: **2025**, documento (espécie): **DESPACHO**, data de emissão: **22/08/2025** e o código de verificação:
e464ebca95

MINISTÉRIO DA EDUCAÇÃO
UNIVERSIDADE FEDERAL DA PARAÍBA

DESPACHO Nº 132/2025 - PROPESQ - CGPQ (11.00.79.01)

Nº do Protocolo: NÃO PROTOCOLADO

João Pessoa-PB, 25 de Agosto de 2025

À Assessoria de Comércio Exterior/PRA

De acordo com análise de documentos que consta na lista de verificação, solicito conversão da moeda e autorizo o pagamento da Invoice em anexo com recursos da ND 2025ND000939, conforme Chamada interna PROPESQ/UFPB - Pró-Publicação nº 03/2025.

Solicitamos que a Pró-Reitoria de Administração analise os documentos de regularidade fiscal da empresa.

Constam ainda no processo e-mail enviado pela revista explicado que o artigo não está publicado na sua versão final (doc.11).

Critério de elegibilidade	Sim	Não	
01. O proponente é servidor efetivo da UFPB, credenciado como docente permanente de PPG da UFPB (verificar na página do PPG e Portal da Transparência).	x		
02. O proponente não possui pendências em programas de apoio desta Pró-Reitoria	x		
03. O artigo possui coautoria de um discente de Programa de Pós-Graduação desta instituição ou de um discente da graduação vinculado ao PIBIC (aluna doutorado)	x		
04. Periódico classificado com Percentil 75 (89%)	x		
05. O artigo possui na folha de rosto a identificação "Universidade Federal da Paraíba" ou "Federal University of Paraíba", sem nenhuma abreviação	x		
06. O artigo não está publicado	x		
Check list de documentação obrigatória			
Documento	Sim	Não	NA
01. Formulário de solicitação assinado pelo coordenador do PPG e pelo proponente	Doc.1		
02. Comprovante da revista informando a aprovação do manuscrito para publicação	Doc.2		
03. Galley-Proof (ou equivalente) do artigo a ser publicado	Doc.3		

04. Comprovante de vínculo do discente	Doc.4		
05. Invoice, exclusivamente em dólar ou euro , em nome da Universidade Federal da Paraíba, informando os dados bancários, valor da despesa externa e NIF	Doc.5		
06. Declaração de regularidade fiscal da empresa no seu país de origem	Doc.6		
07. Comprovante de percentil 75	Doc.7		
08. E-mail ou outro documento que comprove a solicitação de desconto no valor da taxa de publicação junto à revista	Doc.8		
09. Comprovante de que os proprietários da empresa residem nos EUA , em caso de empresa LLC			x

(Assinado digitalmente em 25/08/2025 08:45)
 JOSE ROBERTO SOARES DO NASCIMENTO
 PRO-REITOR(A)
 Matrícula: 337210

Processo Associado: 23074.083540/2025-16

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MINISTÉRIO DA EDUCAÇÃO
UNIVERSIDADE FEDERAL DA PARAÍBA

SOLICITAÇÃO Nº 28/2025 - PRA-ACE (11.01.08.02.05)

Nº do Protocolo: NÃO PROTOCOLADO

João Pessoa-PB, 25 de Agosto de 2025

À Pró-Reitoria de Administração

Prezado Pró-Reitor,

O presente processo trata do Edital Pró-Publicação Chamada Interna nº 03/2025 - PROPESQ, conforme doc. (ordem 16) em anexo. Solicitamos autorização para emissão de empenho estimativo em favor do fornecedor estrangeiro **Elsevier B.V.** referente à publicação do artigo "**Optimized Extraction, Characterization, and Cytotoxicity Assessment of Biodegradable Nopalea cochenillifera Salm-Dyck Mucilage**, do Prof **FRANCISCO HUMBERTO XAVIER JÚNIOR**, Siape 1859738.

I n v o i c e :						O A D 0 0 0 0 6 2 5 1 7 9	
Valor	em	moeda	estrangeira:	USD	2,600.00		
Valor	convertido	em	Real:	R\$	15.000,00	(10 %	variação cambial)
Nota de Dotação: 2025ND000939							

Atenciosamente,

(Assinado digitalmente em 25/08/2025 10:22)

GILMARA DE LIMA NOBREGA

DIRETOR(A)

Matrícula: 2035601

Processo Associado: 23074.083540/2025-16

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28, ano: **2025**, documento (espécie): **SOLICITAÇÃO**, data de emissão: **25/08/2025** e o código de verificação:

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MINISTÉRIO DA EDUCAÇÃO
UNIVERSIDADE FEDERAL DA PARAÍBA

AUTORIZAÇÃO Nº 4157/2025 - PRA (11.00.47)

Nº do Protocolo: NÃO PROTOCOLADO

João Pessoa-PB, 25 de Agosto de 2025

À ASSECAD,

Considerando a necessidade e solicitação da Unidade demandante, na condição de Ordenador(a) de Despesas, no exercício da função delegada pelo ordenador originário, nos termos do art. 80, do Decreto-Lei nº 200/67 e Portaria nº 155, de 19 de novembro de 2024 do Gabinete da Reitoria, encaminho para análise quanto à instrução processual. Se adequada, autorizo empenhamento/dedução do empenho.

Atenciosamente,

(Assinado digitalmente em 25/08/2025 12:28)
GEORGE RODRIGO BELTRAO DA CRUZ
PRO-REITOR(A)
Matrícula: 3301269

Processo Associado: 23074.083540/2025-16

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MINISTÉRIO DA EDUCAÇÃO
UNIVERSIDADE FEDERAL DA PARAÍBA

AUTORIZAÇÃO Nº 4251/2025 - PRA (11.00.47)

Nº do Protocolo: NÃO PROTOCOLADO

João Pessoa-PB, 26 de Agosto de 2025

À ACE,

Considerando a necessidade e solicitação da Unidade demandante, na condição de Ordenador(a) de Despesas, no exercício da função delegada pelo ordenador originário, nos termos do art. 80, do Decreto-Lei nº 200/67 e Portaria nº 155, de 19 de novembro de 2024 do Gabinete da Reitoria, encaminhando para análise quanto à instrução processual. Se adequada, autorizo empenhamento/dedução do empenho.

Atenciosamente,

(Assinado digitalmente em 26/08/2025 10:54)
GEORGE RODRIGO BELTRAO DA CRUZ
PRO-REITOR(A)
Matrícula: 3301269

Processo Associado: 23074.083540/2025-16

Para verificar a autenticidade deste documento entre em <https://sipac.ufpb.br/documentos/> informando seu número: **4251**, ano: **2025**, documento (espécie): **AUTORIZAÇÃO**, data de emissão: **26/08/2025** e o código de verificação: **dc53b43de5**