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Analysis of hydrophilicity degree in chitosan membranes produced from the incorporation of extract from the stalk of Anacardium microcarpum Ducke

Análise do grau de hidrofilicidade em membranas de quitosana produzidas a partir da incorporação de extrato da casca do caule do Anacardium microcarpum Ducke

Análisis del nivel de hidrofilicidad en las membranas de quitosano producidas a partir de la incorporación de extracto del tallo de Anacardium microcarpum Ducke

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Abstract
The skin is the organ that protects the internal organism against pathogenic agents from the external environment. Therefore, rapid wound healing becomes an important target against exposure of the organism to pathogens. Thus, the use of biopolymers as dressings has been gaining prominence, among them, chitosan. Chitosan is a biomaterial that has high biological compatibility, biodegradability, low toxicity and healing effect. The objective of this research was to produce a chitosan-based biomaterial, incorporated with a hydroalcoholic extract from the bark of Anacardium microcarpum Ducke. The membranes were characterized in terms of color, homogeneity, flexibility, thickness, wettability and degree of swelling. The membranes were transparent, homogeneous and flexible with an average thickness of 5 micrometers. In swelling, there was absorption of 50%, mass loss below 6% and durability greater than 21 days. As for wettability, the membranes were moderately hydrophilic. The membranes showed promising chemical and physical characteristics to be a curative biomaterial.
Keywords: Dressing; *Anacardium microcarpum* Ducke; Chitosan; Hydrophilicity.

Resumo
A pele é o órgão que protege o organismo interno contra agentes patogênicos do meio externo. Portanto, a rápida cicatrização de lesões se torna um alvo importante contra a exposição do organismo aos patógenos. Assim, a utilização de biopolímeros como curativos vem ganhando destaque, dentre eles, a quitosana. A quitosana é um biomaterial que possui alta compatibilidade biológica, biodegradabilidade, baixa toxicidade e efeito cicatrizante. O objetivo deste trabalho foi produzir um biomaterial à base de quitosana, incorporado com extrato hidroalcóolico da casca do *Anacardium microcarpum Ducke*. As membranas foram caracterizadas quanto à coloração, homogeneidade,

flexibilidade, espessura, molhabilidade e grau de intumescimento. As membranas mostraram-se transparentes, homogêneas e flexíveis com espessura média de 5 micrômetros. No intumescimento, houve absorção de 50%, perda de massa abaixo de 6% e durabilidade superior a 21 dias. Quanto a molhabilidade, as membranas apresentaram-se moderadamente hidrofílicas. As membranas apresentaram características químicas e físicas promissoras para ser um biomaterial curativo.
Palavras-chave: Curativo; *Anacardium microcarpum* Ducke; Quitosana; Hidrofilicidade.

Resumen
La piel es el órgano que protege al organismo interno contra los agentes patógenos del medio externo. Por lo tanto, la cicatrización rápida de heridas se convierte en un objetivo importante contra la exposición del organismo a patógenos. Así, ha ido cobrando protagonismo el uso de biopolímeros como apósitos, entre ellos, el quitosano. El quitosano es un biomaterial que tiene alta compatibilidad biológica, biodegradabilidad, baja toxicidad y efecto curativo. El objetivo de este trabajo fue producir un biomaterial a base de quitosano, incorporado con un extracto hidroalcohólico de la corteza de Anacardium microcarpum Ducke. Las membranas se caracterizaron en términos de color, homogeneidad, flexibilidad, espesor, humectabilidad y grado de hinchamiento. Las membranas fueron transparentes, homogéneas y flexibles con un espesor promedio de 5 micrómetros. En el hinchamiento hubo absorción del 50%, pérdida de masa inferior al 6% y durabilidad superior a 21 días. En cuanto a la humectabilidad, las membranas eran moderadamente hidrófilas. Las membranas mostraron características químicas y físicas prometedoras para ser un biomaterial curativo.
Palabras clave: Adhesivo; *Anacardium microcarpum* Ducke; Quitosano; Hidrofilia.

1. Introduction

Chitosan is a linear polysaccharide consisting of β-(1-4)-D-glucosamine and N-acetyl-D-glucosamine units. It is considered a polymer of natural origin derived from the chitin deacetylation process, it has a differentiated functionality due to the presence of amino groups responsible for the polymer properties (Anjos, 2017; Machado, 2021). This biomaterial has several applications in the health area and one of these applicability is in wound dressings. After cellulose, chitosan is one of the most important compounds in nature, whose properties have been explored in industrial applications (Azevedo, et al., 2007).

Due to its properties that contribute to tissue regeneration, this biomaterial can be used as wound dressings in various forms, such as hydrogels, nanoparticles and membranes (Peng et al., 2022). In the study developed by Queiroz and Tomaz (2020), when inducing wounds on the skin of animals, diabetic wounds and wounds with infection, they identified that chitosan-based dressings reduce healing time and increase the quality of scar tissue, contributing to knowledge regarding its use on wounds. In addition, it can undergo physical-chemical improvements, generating more biocompatible, bioactive, non-toxic derivatives and even with antibacterial properties, anticancer and antiviral pharmacological effects, among others (Zhao et al., 2020).

Several types of additives are mixed with chitosan in order to produce more efficient dressings, such as: Jacques grape berry extract (Almeida, 2017), banana peel powder (Kamel, et al., 2014), nanoparticles (Silva et al, 2018), hydroalcoholic extract of Stryphnodendron adstringens (Barral, 2014), foliar extracts of Combretum duarteanum Cambess (Sousa, 2017), cashew bark extract Anacardium occidentale (Lacerda, et al., 2020), extract from Aloe Vera (Sousa, et al., 2019).

The cashew fruit (Anacardium microcarpum Ducke) is a wild plant found in the cerrado and highlands in the coastal regions of Brazil in the states of Ceará, Maranhão, Pará, Piauí and Rio Grande do Norte (Vieira, et al., 2014). The bark of this species is commonly used in traditional Brazilian medicine to treat various diseases, including inflammation, infectious diseases, rheumatism and even tumors. These beneficial actions are due to the presence of phenolic compounds, such as phenolic acids: gallic acid, caffeic acid, chlorogenic acid and ellagic acid; and the flavonoids: quercetin, quercetin, catechin, epicatechin, isoquercitrin, rutin, kaempferol and kaempferol glycoside, identified from extracts of the stem bark of Anacardium microcarpum Ducke (Posser et al, 2014; Posser et al, 2017).

In other parts of the cashew tree, such as in the leaves, flowers and chestnut bark, flavonoids have already been identified, such as apigenin, myricetin, agatisflavone, robustaflavone, amentoflavone and ethyl gallate. In addition to these compounds, other flavonoids were also found, such as aurones and flavones, and compounds from other classes, such as tannins,

xanthones, chalcones, phenolic lipids, alkaloids, steroids such as campestrol, etigmasterol and sitosterol, triterpenoids, saponins, among others. This rich chemical composition has anti-inflammatory, antibacterial, antifungal, antitumor and neuroprotective potential, which may justify the use of this species in folk medicine (Andrade et al, 2021; Baptista, 2018; Coutinho et al, 2017; Filho, 2015; Müller, 2014).

Although cashew (Anacardium occidentale L.) has a richness in phenolic compounds similar to cashew and, consequently, similar bioactivity (Baptista, et al., 2021), the hydroethanolic extract of the cashew fruit has a superior microbial proliferation inhibitory effect than the hydroethanolic extract of the cashew cashew, according to the work by Andrade et al. (2021).

Lima, et al., (2018) prepared chitosan membranes with cashew tree bark tea that showed a slight decrease in polarity, an increase in the dispersive component and less swelling compared to the chitosan membrane. Despite this, the membranes with tea had an increase in polarity and swelling proportionally to the amount of tea incorporated into the membrane. The membranes produced by Silva, et al., (2018) were made with aqueous extract of the cashew tree bark (Anacaradium occidentale) and resulted in an increase in hydrophilicity by adding the extract compared to those without extract, observed by the decreasing contact angle, increasing surface energy and increasing swelling values.

In Pereira, et al., (2021) work, chitosan membranes with incorporated hydroalcoholic cashew fruit extract had increased hydrophilicity according to wettability and surface energy in relation to those without extract, important characteristics that are related to adhesion and cellular proliferation, already in the swelling the result showed a smaller absorption of water in relation to the ones without extract. As for the macroscopic characteristics, the membranes produced were 11 μm thick, homogeneous and transparent, the membranes with the extracts showed shades of red tending towards brown, with an intensification of the shade as the amount of extract increased.

In this work, chitosan membranes were prepared without and with incorporation of hydroethanolic extract from the stem bark of Anacardium microcarpum Ducke at different concentrations. Then they were subjected to characterizations regarding their thickness, macroscopic aspects, degree of swelling, degradation, wettability by contact angle and surface energy, physical and chemical characteristics that must be analyzed, as they are important for a dressing that aims to be applied to epithelial lesions. Therefore, the objective of this research was to produce a low-cost biomaterial based on chitosan and hydroethanolic extract of the bark of Anacardium microcarpum Ducke that presents suitable characteristics for its application as a dressing.

2. Methodology

2.1 Preparation

2.1.1 Plant Material

The stem bark of Anacardium microcarpum Ducke was collected from trees belonging to the municipality of Ipiranga do Piauí, state of Piauí, Brazil (00° 00'00" S and 00°00'oo"W, altitude 000m) ((-6,806, -41,861) and (-6,795, -41871)) as of 2/24/2019. The research was registered on the SisGen platform (National System for the Management of Genetic Heritage and Associated Traditional Knowledge) as genetic heritage with registration number ACE183B.

2.1.2 Hydroethanolic Extract Preparation

The plant material (Anacardium microcarpum Ducke) was washed and dried in an oven at 40°C for 5 days, then ground in a manual mill to obtain powdered material.

To produce the hydroethanolic extract, 25g of powder were extracted with 250 mL of EtOH/H2O 7:3 (v/v), in an ultrasound bath, three times for 20 minutes. Subsequently, the resulting material was subjected to vacuum filtration, finally

obtaining the liquid extract, which was dried, leaving approximately 7g of crude extract at the end of the process (Zanatta, et al., 2021).

2.1.3 Chitosan Membranes Preparation

For the preparation of the membranes, chitosan from the company Exodus Scientific Chemical Fine Industry and Trade, Sumare - SP, Brazil, was used, with a degree of deacetylation of 92.6%. Initially, powdered chitosan was mixed at a concentration of 2% (w/v) in a 2% (v/v) lactic acid solution, then stirring for 24 hours to effectively dissolve the chitosan. Then, the solution was subjected to two filtrations to remove impurities, the first through a nylon screen filter and the second through a Mille Millipore® filter (45μm).

From the filtered chitosan solution, two types of membranes were produced: chitosan membranes without extract (P) and membranes incorporated with the hydroethanolic extract of the bark of Anacardium microcarpum Ducke in three different concentrations of mass of extract per membrane (Ci 1 containing 1 .25 mg of extract, Ci 2, containing 2.5 mg of extract, and Ci 3, 3.75 mg per membrane). The extract membranes were made by dissolving the respective amounts of solid extract in a 30/70 hydroethanolic solution (water/ethanol; v/v).

The chitosan solutions, without and with extract, were poured into Petri dishes in a volume of 25 mL per dish, and placed to dry in an oven for 24 h, at a temperature of 50 °C. After drying, they were left to neutralize with a 5% (w/v) sodium hydroxide (NaOH) solution for a period of 4 h. After being neutralized, they were washed with distilled water, to remove residues of the neutralization, and placed to dry in the open air for 24 h at room temperature. After 24 h, the membranes were harvested and stored for characterization (Lacerda et al., 2020).

2.2 Characterizations

2.2.1 Thickness

Thickness was measured using a Starret® micrometer. Measurements were taken at 5 points, crossing the membrane. The values presented are an average for the measurement of 7 membranes of each condition (Q, Ci 1, Ci 2, Ci 3) (Santos, 2018).

2.2.2 Qualitative Analysis

The qualitative analysis was made from observations, with the naked eye and tactile, of macroscopic characteristics, such as: color, transparency, homogeneity and flexibility. The information obtained was organized in a table.

2.2.3 Swelling

This technique aims to measure the amount of water absorbed by the membranes in a given time. First, the dry membranes were weighed and then immersed in 400 mL of distilled water at 37 °C. Every hour the membranes were weighed until completing 8 h. After 8 h, the membranes were weighed at intervals of 24 h, up to 144 h (Sousa, 2017). This test was done in triplicate. The calculation of the absorbed mass was done using Equation (1):

$$S\ (\%) = \frac{m_w - m_d}{m_d} \times 100\ \% \qquad \text{Equation (1)}$$

S (%) = degree of swelling in percentage;

m_w = wet mass;

m_d = dry mass.

2.2.4 Degradation

After 144 hours of the swelling test, the membranes were dried in an oven at 50 °C for 24 h. Then, the final mass was weighed and the percentage of loss was calculated using Equation (2):

$$D\ (\%) = \frac{m_d - m_f}{m_d} \times 100\ \% \quad \text{Equation (2)}$$

D (%) = percentage degradation;

m_d = dry mass;

m_f = final mass.

2.2.5 Wettability by Contact Angle

The technique used was the sessile drop using a goniometer from the Laboratory of Research in Biomaterials of the IFPI - Campus Picos, where a drop of 20 μL of 3 different liquids (water, formamide and glycerol) was deposited in pieces of membranes of approximately 2. 0 cm x 2.0 cm. This characterization was performed in triplicate.

The behavior of the gout was monitored and recorded on video. The videos were made from images of 10 s in 10 s, until the stabilization of the drop in 60 s. The measurement of the contact angle was performed using the Surftens software, DEMO version. 7 measurements were performed on each image, the highest and lowest values obtained were eliminated, and the averages and standard deviations for each image were calculated from the remaining 5 values (Sousa et al, 2019).

2.2.6 Surface Energy

The surface energy consists of the sum of the intermolecular forces that exist between the liquid and the surface of the membrane. This characterization was carried out using Fowkes' method, Equation (3), which consists of a sum of the polar and non-polar components present in the interaction, factors related to surface cohesion or dispersion (Sousa, et al., 2019).

$$\left(\frac{1+\cos\theta}{2}\right) \times \left(\frac{y_l}{\sqrt{y_l^d}}\right) = \sqrt{y_s^p} \times \sqrt{\frac{y_l^p}{y_l^d} + \sqrt{y_s^d}} \quad \text{Equation (3)}$$

y_l = total liquid-air surface tension;

y_l^d = dispersive coordinate of the surface tension of the liquid;

y_s^p = polar coordinate of the surface tension of the solid under study;

y_l^p = polar coordinate of the surface tension of the liquid;

y_s^d = dispersive coordinate of the surface tension of the analyzed solid;

θ = liquid contact angle.

3. Results and Discussion

3.1 Thickness

Membrane thicknesses, both without and with extracts, showed values close to 5 μm, as shown in Table 1. The values shown are an average of 35 measurements on 7 different membranes. The high values of the standard deviation are due to the method used in the manufacture of the membranes, which was solvent evaporation, already pointed out in the literature as the cause of this great dispersion (Sobral, 2000; Assis & Silva, 2003; Santos, 2018).

Table 1 - Mean thickness of each type of membrane.

	P	Ci 1	Ci 2	Ci 3
Average thickness (µm)	5,40	5,14	5,09	4,86
Standard deviation	0,93	0,81	0,95	0,77

Source: Authors.

The thickness obtained was satisfactory, since the dressings must have a thickness compatible with that of the skin, generally being smaller than the dermis (Gonzaga, 2018). The epidermis has a thickness that varies from 0.07 mm to 1.4 mm and the dermis, which varies from 1 to approximately 3 mm, depending on the part of the body (Dallan, 2005), and the membranes produced have thicknesses lower than the respective values, even lower than the thickness of the wound dressing marketed with collagen and alginate FIBRACOL*PLUS by Systagenix Wound Management Limited, which is 1 mm thick (Santos, 2018).

3.2 Qualitative Analysis

A qualitative analysis was made regarding the visual and tactile aspects of the membranes. The chitosan membranes showed a cream yellow color, while the extract membranes showed a darker cream yellow color, as the concentration of the extract in the membrane increased, as shown in Figure 1 a). All membranes were similar in terms of transparency, homogeneity and flexibility, which corroborates the results by Pereira et al. (2021). In Figure 1 b) the transparency of the membranes is shown.

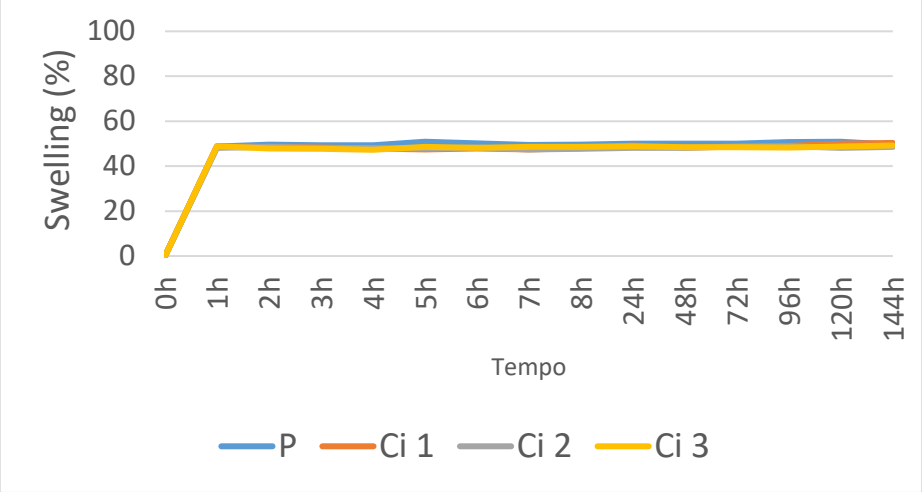
Figure 1 - a) Membranes without and with extracts of different concentrations. b) Transparency of the produced membranes.

Source: Authors.

3.3 Swelling

The swelling test was carried out by immersing the membranes in water, at a temperature of 37°C, for a period of 144 hours, where a mass gain of approximately 50% was observed in the first hour, which remained relatively constant until the end time of the study. Similar behavior in all conditions studied, as shown in Figure 2.

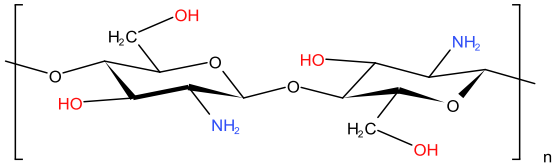
Figure 2 - Dynamics of membrane swelling without and with extracts.



Source: Authors.

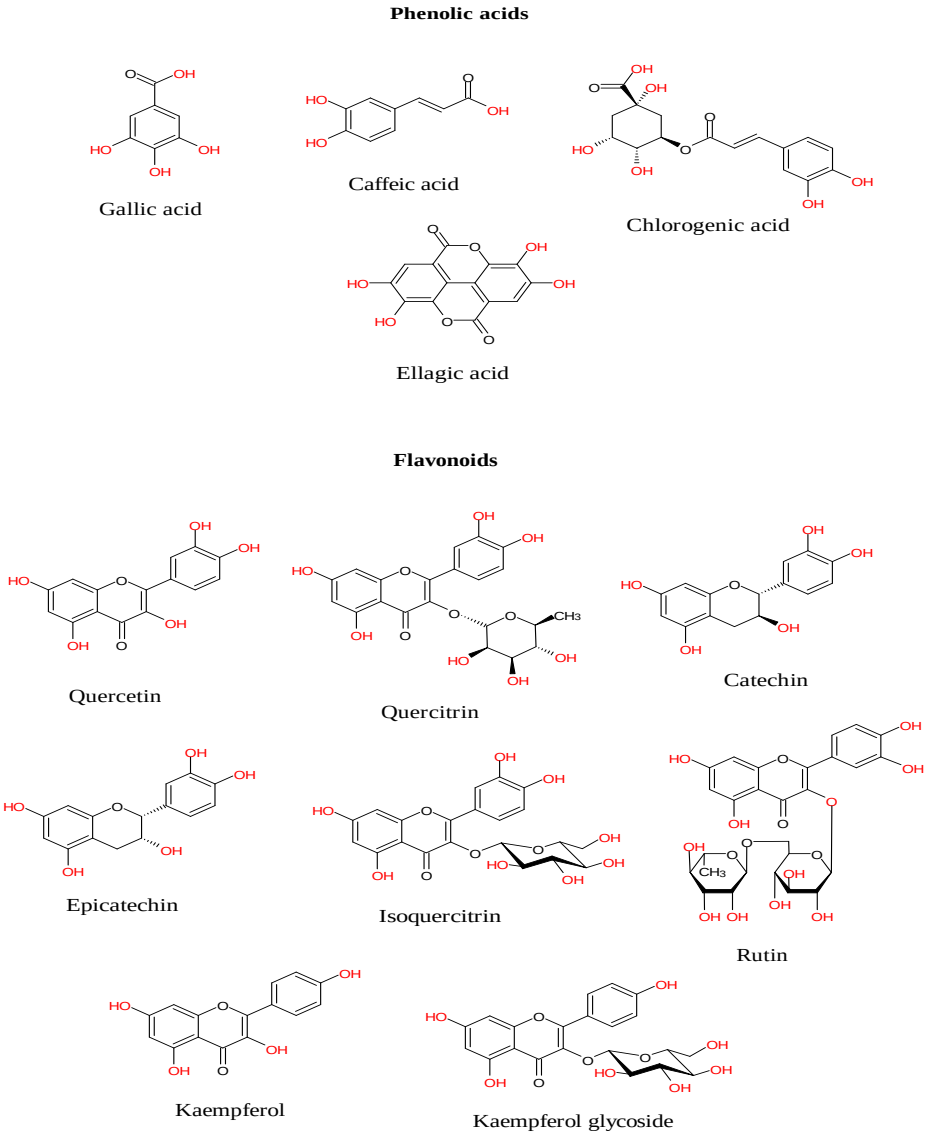
Both the structure of chitosan and the compounds present in the extracts have polar groups. Chitosan has amine (NH2) and hydroxyl (OH) groups (Macêdo, 2009) as illustrated in Figure 3, and in the extracts of Anacardium microcarpum Ducke, there is a large amount of phenolic compounds, which have hydroxyl groups (OH), of which among them are the phenolic acids: gallic acid, caffeic acid, chlorogenic acid and ellagic acid; and the flavonoids: quercetin, quercetin, catechin, epicatechin, isoquercitrin, rutin, kaempferol and kaempferol glycoside, whose chemical structures are shown in Figure 4 (Posser et al., 2014).

Figure 3 - Chemical structure of chitosan (hydroxyl groups highlighted in red and amine groups in blue).



Source: Authors.

Figure 4 - Chemical structures of the phenolic compounds present in the extract (hydroxyl groups in red).



Source: Authors.

These polar groups present in the structure shown perform hydrogen bonding, which is a strong interaction that occurs when a hydrogen, bonded either to fluorine, or to oxygen or nitrogen, is attracted to these same atoms (Atkins, et al., 2017), which makes them interact strongly with water. However, despite the presence of polar groups, both in chitosan and in extracts from Ci 1, Ci 2 and Ci 3 membranes, these presented a water absorption similar to that of chitosan membranes.

A factor that may have contributed to this happening is the fact that a lower concentration of polymeric material was used in the composition of the Ci 1, Ci 2 and Ci 3 membranes, due to the volume occupied by the extract, which, according to Assis et al. Silva (2003), may have caused less roughness and, consequently, a decrease in the available area to carry out interactions with water. In addition, during the process, membranes with extracts suffered greater degradation compared to chitosan membranes, which may also have contributed to a lower absorption of membranes with extract (Pereira et al., 2021).

3.4 Degradation

When analyzing the degradation, it was noticed that mass loss was less than 6% in all cases, showing that there was a low degradability, as shown in Table 2.

Table 2 - Weight Loss of membrane mass after swelling.

	P	Ci 1	Ci 2	Ci 3
Weight Loss (%)	0,4	3,4	5,4	3,0

Source: Authors.

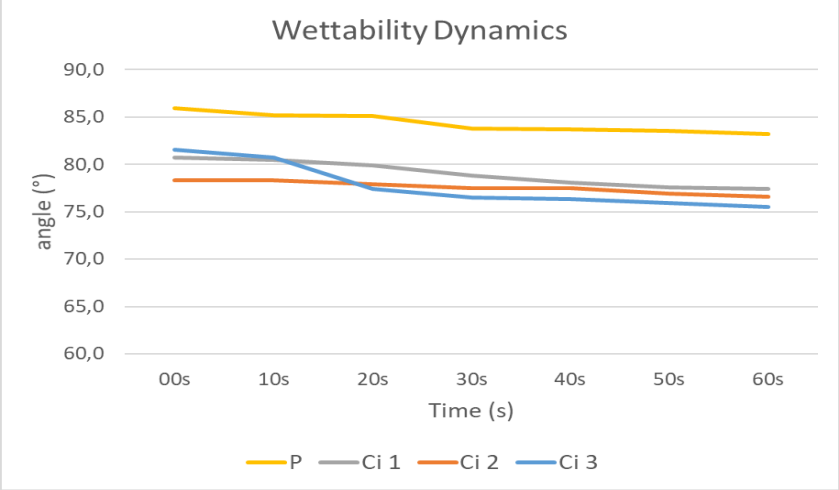
The membranes remained intact in an aqueous environment during the 21 days of the test. This period was chosen because it is sufficient (on average) for the wound healing process to reach its final stage of tissue regeneration, which is maturation, or remodeling, in which there is an attempt to normalize the tissue structure and the coating. of the injury by a new epithelium, a stage that begins around 12 days after the injury (Campos, et al., 2007), (Medonça & Coutinho-Netto, 2009).

The greater loss of mass in the Ci 1, Ci 2 and Ci 3 membranes may have been caused by the release of part of the extracts into the aqueous medium, in which it was immersed, a possibility also suggested by Pereira et al. 2021, since the phenolic compounds present in them have a hydrophilic character and may have solubilized in water due to the large number of hydroxyls in their carbon chain (Martins, et al., 2013).

3.5 Wettability by Contact Angle

The membranes produced, both with and without extracts, had contact angles below 90°, characterizing them as being partially hydrophilic (Tomaz, 2017). Figure 5 shows the behavior of the contact angle over time until stabilization in 60 seconds. It is observed that in the initial 30 seconds there are the highest values of contact angle and that it tends to decrease from then on, stabilizing at approximately 76° in the membranes with extract, while in the chitosan membrane the value of the angle contact point was approximately 83°.

Figure 5 - Wettability dynamics by contact angle of membranes using water.



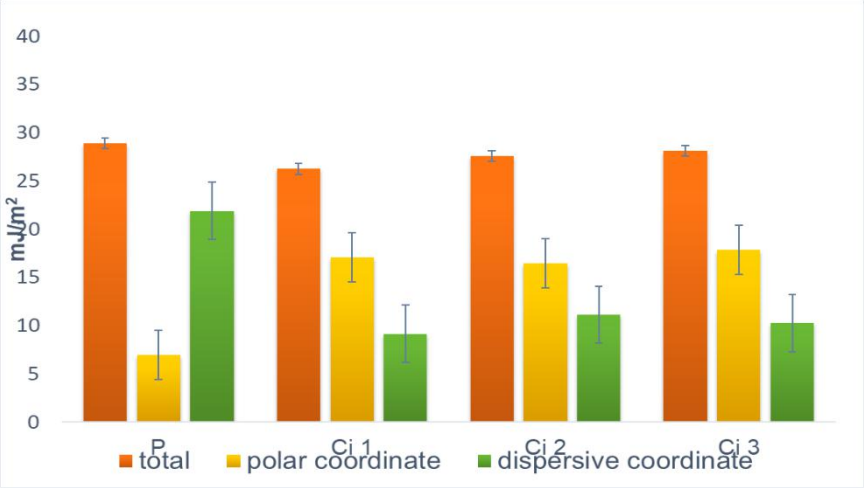
Source: Authors.

The membranes showed approximately equal hydrophilicity. However, the membranes with extracts had slightly lower contact angles in relation to the chitosan membranes, this because of the greater number of hydroxide groups, of the phenolic compounds present in the extracts incorporated into the Ci 1, Ci 2 and Ci 3 membranes. a decrease in the contact angle of the Ci 1 to Ci 3 membrane, this was due to the increase in the concentration of the extract used in the respective membranes.

3.6 Surface Energy

The surface energy is a property that is related to the adhesion/binding of the surface of the material, caused by the interaction between the free atoms of the polymer and another substance, so that the greater the surface energy, the greater the adhesion (Macêdo, 2012). This characteristic is important, as it is related to favoring cell adhesion to the surface of the material (Coutinho & Elias, 2009). Figure 6 shows the measured values for the surface energy of the produced membranes.

Figure 6 - Surface energy of chitosan and extract membranes.



Source: Authors.

A change from the dispersive character to the polar character was observed when extract was added to the membrane composition. The increase in the polar component, in relation to the one without extract, emphasizes the result obtained by wettability, in which membranes with extracts proved to be slightly more hydrophilic. The surface tension was slightly higher in the chitosan membrane, but in the Ci 1, Ci 2, Ci 3 conditions membranes, there was an increasing trend, due to the increase in the extract concentration. Assis and Silva, (2003) explain that the concentration of extract can interfere with the roughness of the membranes and consequently decrease the interaction of the membrane with water, a phenomenon also observed in the swelling test.

4. Final Considerations

The influence of the addition of the extract on the physicochemical properties of the membranes was observed. An increase in hydrophilicity in membranes with extracts was noticeable as the extract concentrated. This increase in hydrophilicity is a positive point for the absorption of liquids and the accommodation of cells in the membranes. All membranes remained intact and flexible during all manipulations during the study period.

The results obtained showed that the membranes produced, without and with the extract of Anacardium microcarpum Ducke, have promising properties compatible with the possibility of exercising the function of dressing. However, for there to be a definitive proof of the true potential of application of these membranes as dressings future research in biological field is necessary to analyze the cellular behavior on its surface

Acknowledgments

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