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Physical, physicochemical and phytochemical characterization of the latex of the Janaúba plant (Euphorbia *Umbellata*) of the varieties Synadenium granti *hook* and Synadenium umbellatur *pax*

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ABSTRACT
The use of medicine plants for the healing is used since the begginings, but the rise of the reseraches and the advance of the science, most of the these plants already have the evidenced effectiveness by scientific evidences checked. Therefore, a study about the plant Euphorbia umbellata and its varieties would have great relevance, since it is popularly very known when it comes to its physiotherapeutic action in the ancologic treatment. The species belonging to this group posses great highlight not inly in the economic acticity directly related to the human alimentation but also in the popular medicine based on the empiric knowledge. To characterize physical-chemical and phatochemical the latex of the Janauba plant (Euphorbia umbellata) of the varieties Synadenium grant Hook and Synademium umbellatur Pax. The sampling stock used in the research was collected in Belém and municipalities and Castanhal city, in Pará state, Brazil, between April and November pf 2022. It was taken to the controll and quality laboratory of Centro Universitário da Amazônia (UniEsamaz) located in Belém, PA, for the execution of the analyzes. The anatomic characterization is fairly important because it must be done before the use related to the medicine plant, in what way it can be idetified in other not to occur a wrong consume of the specie. The sample results demonstrate that the latex of Janauba is a product classified as medium acidity, the difference of PH, based on the results obtained do not demonstrate great impact. Thus, it is concluded that despite they have not detected in the current analyses and comparing to the previous results, the Janauba plant and its varieties can be considered as a strong alternative to help the cancer comba and being extremaly essential when it is used due to the presence of cumarinas which can cause hepatic problems for the use of big quantities.

Keywords: Medicinal plants, Phytotherapy, Phytochemicals, Coumarins.

1 INTRODUCTION

According to Nothias-Scaglia, as cited by Siane and Santos (2023), the origin of the plant's name occurred from the History of King Juba II of Mauritania (year 25 B.C.) who made use of a remedy that was produced from the latex of a succulent plant and gave it its healing power, he suggestively

named it Euphorbium, after his Roman physician, Euphorbius, who was equally corpulent (Euphorbio = well-nourished in ancient Greek).

As the years passed and the studies evolved, Bruyns, when developing research with the plant, discovered some species, naming it *Euphorbia umbellata (Pax) Bruyns* (current) (Siani and Santos, 2023). And among these studies, the great highlight was around the latex produced by it. This material can be found on the stem, and even on the leaves abundantly. A plant of African origin, but belonging to most of the Brazilian territory, where it is known as milkweed or janaúba, or even with a variety of other names.

However, all the studies found until the 2000s talked about the botanical origin, however, when talking about folk medicine, we hear a lot about the Plant and its actions in the treatment of different types of diseases, as cited by Ortêncio (2012) and Oliveira (2013), who state, popular use to treat allergies, gastric disorders and, especially, several types of cancer.

It is worth mentioning the importance of studies and scientific evidence about the use of this plant as an herbal medicine, so it is essential to know the chemical composition of this latex that will be ingested, in order to identify the possible harms, cytotoxicity that it can affect the body, as well as the improvement of its benefits. For this, there is the IFAV, which is the standardization of pharmaceutical inputs of plant origin, according to RDC No. 26 of May 13, 2014, which provides for the registration of herbal medicines, which establishes minimum requirements for this registration. The document emphasizes the importance of knowing the composition of the plant and the analyses, as provided for in section III – Technical Reports (RDC nº26. P. 5, 2014), where there is a series of documents necessary to prove this phytotherapeutic action, as well as several reports of physicochemical analysis, ashes, among others.

The use of medicinal plants for the purpose of obtaining a cure has been used since the beginning, but with the growth of research and the advancement of science, many of these plants already have, by scientific evidence, their proven effectiveness. Therefore, a study on the plant Euphorbia *Umbellata and its varieties would be of great relevance, since, which is popularly known for its phytotherapeutic action in cancer treatment (Alves* et al*., 2021), therefore, this work aims to physicochemically and phytochemically characterize the latex of the Janaúba plant (*Euphorbia umbellata*) of the varieties* Synadenium granti Hook and *Synadenium umbellatur* Pax.

2 MATERIAL AND METHODS

2.1 OBTAINING THE RAW MATERIAL

The sample raw material used in the research was collected in the municipalities of Belém and Castanhal, located in the State of Pará, Brazil, from April to November 2022. It was taken to the quality control laboratory of the University Center of the Amazon (UNIESAMAZ), located in Belém, PA, for

analysis.

2.2 ANATOMICAL CHARACTERIZATION OF PLANTS

The leaves of the plants were obtained at 5 cm from the apex of the plant of the species *Synadenium umbellatur*, The leaves were photomicrographed using an Olympus BX-40 light microscope equipped with a digital camera.

2.3 SAMPLE EXTRACTION

According to the information contained in the studies found, the extraction of the latex (Figure 1A) began with an incision in the stem of the plant to remove the latex (Figure 1A), depositing it directly in a glass of water for solubilization (Figure 1B). For the dilution conditions, the one described by Ortêncio (2007) was used, which considers the following concentration of use: 18 drops of latex in 1 liter of water, consumed three times a day, in the measure of a small cup of coffee. Storage should be done under refrigeration. These conditions were used in the preparation of the initial extract of the present study. In figure 1C, we have the demonstration of how, after the removal of a leaf, the plant remains, that is, there is the presence of latex throughout its structure.

Figure 1 - Collection of latex from Janaúba.

Source: Authors (2022)

The sample was collected in a glass container sanitized with sodium hypochlorite at 50 ppm for 15 minutes, and then placed in sterile 500ml amber containers. The samples were stored under refrigeration and taken to the Uniesamaz laboratory to begin the analyses.

2.4 PHYSICOCHEMICAL CHARACTERIZATION

The physicochemical composition was determined in triplicate according to methodologies described by AOAC (2019), namely: pH using a digital potentiometer of the QUIMIS(R) brand and

acidity after titration with NaOH (1mol. L-1).

The qualitative test to evaluate the presence of polysaccharides was performed by adding 5 mL of the ethanolic extract of the fruit at a concentration of 0.2mg/mL plus 3 drops of lugol reagent, the blue color indicates the presence of polysaccharide chains in the extracts.

2.5 ELABORATION OF THE DIFFERENT DILUTIONS

In order to evaluate the influence of latex dilution on its phytochemical composition, different dilutions of the extract were prepared to evaluate the influence of dilution on phytochemical parameters, as described in Table 1.

Table 1. Dilutions used in the study.

Code	Concentration
E0	100% solution containing plant latex
E80	80% of the solution containing the plant's latex
E60	60% of the solution containing the plant's latex
E40	40% of the solution containing the plant's latex
E20	20% of the solution containing the latex of the plant

Source: Authors (2022)

2.6 PHYTOCHEMICAL CHARACTERIZATION

2.6.1 Preparation of hydroalcoholic extracts

The ethanolic extracts were prepared using 10 ml of the solution diluted in 90 ml of ethyl alcohol at 70% v/v, the extracts were stored under refrigeration and kept at rest for 15 days for further analysis.

2.6.2 Alkaloids

1 mL of 92% hydroalcoholic extract at a concentration of 0.2mg/mL, 6 mL of distilled water, 1 mL of hydrochloric acid (HCl) and four drops of Bouchardat reagent (iodine and potassium iodide solution) were added to a test tube. The expected result in case of a positive reaction is the presence of amorphous or crystalline precipitates, with color differentiation ranging from white to orange-brown.

2.6.3 Steroids/triterpenes

The Liebermann-Burchard reaction (acetic anhydride – concentrated sulfuric acid) was used to identify the steroids/triterpenes. In a test tube, 1 mL of the extract at a concentration of 0.2mg/mL was placed, 6 mL of distilled water mixed with 2 mL of chloroform, then 1 mL of acetic anhydride, stirring gently, carefully adding three drops of concentrated sulfuric acid, shaking gently to check for the appearance of color. In case of a positive reaction, evanescent blue color followed by green is expected.

2.6.4 Flavonoids

For the detection of flavonoids, the Cyanidin or Shinoda (concentrated hydrochloric acid and magnesium) test was used. In a test tube, 1 mL of the extract at a concentration of 0.2 mg/mL, 6 mL of distilled water, 2 mL of hydrochloric acid, approximately 0.5 cm of magnesium were added in a 2 mL strip. In case of a positive reaction, a color ranging from brown to reddish is expected after the end of the effervescence (end of the reaction).

2.6.5 Tannins/Phenols

In a test tube, 1 mL of the extract at a concentration of 0.2mg/mL was added and 6 mL of distilled water was added. Blue precipitate indicates the presence of hydrolyzable tannins, and green the presence of condensed tannins.

2.6.6 Saponins

In 1 mL of the extract at a concentration of 0.2mg/mL, 6 mL of water, 2 mL of distilled water and three drops of hydrochloric acid were added. Then the solution was stirred permanently for 3 minutes, the presence of persistent and abundant foam (collar) indicates the existence of saponins.

2.6.7 Coumarins

Three drops of the extract were dripped onto filter paper, awaited for it to dry, and then three drops of an aqueous solution of sodium hydroxide were added to one molar. It was expected to observe the appearance of bright blue or green fluorescence under ultraviolet light (360 nm). Coumarins in alkaline solution develop a yellow color due to the disruption of the lacton ring.

2.6.8 Anthraquinones

For this determination, 0.5 mL of benzene was added to 1 mL of the extract at a concentration of 0.2 mg/mL and 6 mL of distilled water, followed by ten drops of 10% ammonium hydroxide solution. The appearance of pink, red or violet coloration in the aqueous phase will indicate the presence of anthraquinones.

2.7 STATISTICAL ANALYSIS

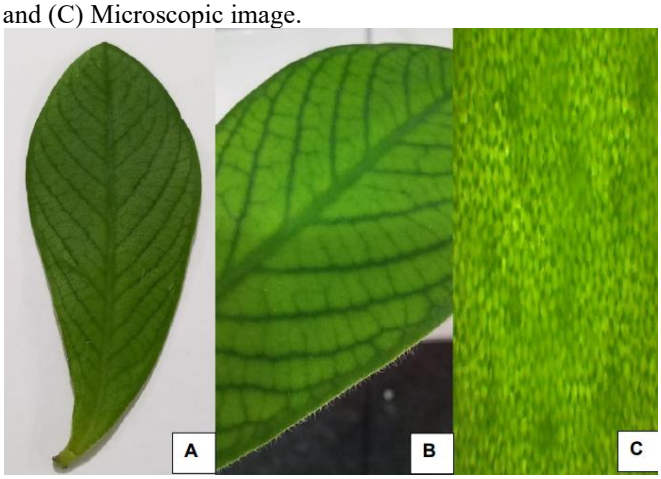
All results were expressed as arithmetic mean and standard deviation (SD). The data were submitted to analysis of variance (ANOVA), considering Tukey's test at a 5% significance level, to compare the means.

3 RESULTS AND DISCUSSION

3.1 ANATOMICAL CHARACTERIZATION OF PLANTS

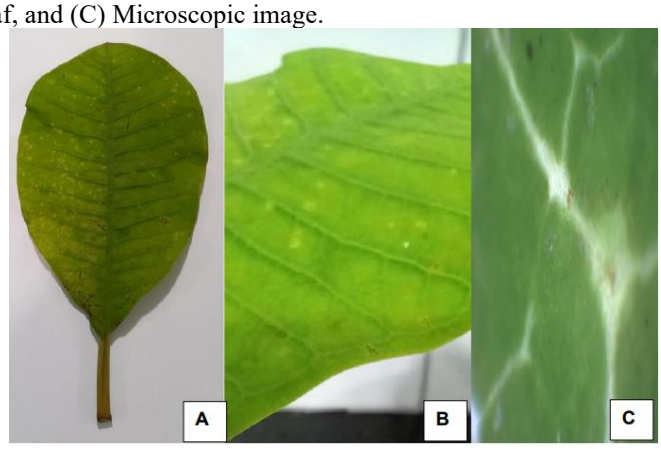
The anatomical characterization is very important, as it must be done before the use related to medicinal plants, which can be used as herbal medicine, so that it can be identified more easily so that there is no erroneous consumption of the species, because although they belong to the same family group, they are of different species and each one has its particularities. As we can see in images 2 and 3.

Figure 2. Anatomical characterization of the plant *Synadenium grantii.* (A) Macroscopic view of the entire leaf, (B) Macroscopic view of the leaf, and (C) Microscopic image.



Source: Authors (2022)

Figure 3. Anatomical characterization of the plant *Synadenium umbellatur.* (A) Macroscopic view of the entire leaf, (B) Macroscopic view of the leaf, and (C) Microscopic image.



Source: Authors (2022)

The images present in figure 3 morphologically characterize the leaves of the plant of the species Synadenium *umbellatur*, in the macroscopic view 3B we can notice the presence of a layer at the tips of the leaves that bring a velvety aspect different from that observed in figure 2B macroscopic view of the species *Synadenium grantii*. This is due to the fact that the *Synadenium umbellatur* species has epidermal cells covered by a thin and smooth cuticle.

However, although the leaves differ in shape and pigmentation (see Fig 2A and 3A), both show

epidermal cells with sinuous anticlinal walls (Fig. 2B and Fig. 3B) on both sides, while the leaves of the species Synadenium umbellatur, *however, have epidermal cells with a polygonal shape (see Figure 2C), which is not observed in the species* Synadenium grantii *(see Figure 3C).*

3.2 PHYSICOCHEMICAL CHARACTERIZATION

The results for physicochemical composition are shown in Table 2, related to pH, polysaccharides and acidity.

Table 2. Physicochemical characterization of the Janaúba plant extract of the two varieties. JB*: Synadenium umbellatur*, JC: *Synadenium grantii,* ND: not detected.

Component	JU	JG
Ph	4.71±1.015A	4.19±0.34A
Acidity	0.05±0.0A	0.05±0.0A
Polysaccharides	ND	ND

Source: Authors (2022)
Different letters between the columns represent a statistical difference of 5% significance.

The pH value is an important parameter, as it is associated with storage and conservation conditions of the product. According to Nelson and Cox (2019), pH is nothing more than the concentration of H+ present in food or in a solution, as is the case with Janaúba latex. For its determination, a pH scale ranging from zero to fourteen is used, where the higher the concentration of H+, the higher the pH value, there is neutrality that is determined by the scale in seven, a value that corresponds to the neutrality of water.

The result of the samples shows that Janauba's latex is a product classified as medium acidity, The difference in pH, based on the results obtained does not show great impact, leaving both JB (*Synadenium Umbellatur*) and JC (*Sinadenium grantii*) with similar values and classifying with the same pH according to the reference scale, such as 4.71±1.015 and 4.19±0.34 respectively. In this acidic way, that is, these values do not favor pathogenic bacterial growth, similar, since there was no statistical difference at the level of 5% significance from one variety to the other, these results are in agreement with what is cited by Brito *et al*. (2021), who state in their studies that these pH values provide balance to the product after its removal from the stem, thus delaying microbial development and multiplication.

The same result was found for the determination of acidity, where Table 2 shows that all analyses showed the same result, as shown in the example. Acidity is a parameter used to guide the quality of the sample, that is, an excellent and very important tool to determine signs of the presence of organic acids, as mentioned by Brito *et al*. (2021), which is not indicated by the results in Table 2.

As well as pH, acidity, qualitative analyses with regard to polysaccharides, i.e., starch, are also of paramount importance, however, Table 2 shows that both the varieties Syandenium Umbellatur and

Synadenium Grantii did not present positive results for polysaccharides in the dilute samples analyzed.

3.3 PHYTOCHEMICAL CHARACTERIZATION

The literature states about the presence of bioactive principles in the Janaúba plant, as cited by Ortêncio (1997), the plant has anticarcinogenic activity, his research demonstrates the presence of terpenes in the composition of the plant among other phytochemicals.

Facchini (2001) states that these secondary metabolites can be divided into three different groups, phenolics, terpenes, and alkaloids. And they need phytochemical analysis to identify each of them. According to Kanunfre et *al*. (2019), few cytotoxic studies exist on Janauba latex, this information is important to describe possible cytotoxicity mechanisms. Table 3 shows the results for the qualitative evaluation of the phytochemicals present in the latex of the Janaúba plant (Euphorbia umbellata) in its varieties (Synadenium umbellatur *Pax and* Synadenium umbellatur Hook).

Thus, in table 3, the qualitative results for the phytochemical tests performed on the hydroalcoholic extracts of the varieties of the janaúba plant (Euphorbia Umbellatur) are presented.

Table 3. Qualitative result of phytochemical analysis of the two varieties of Janaúba. + Positive \ - Negative, JB*: Synadenium umbellatur*, JC: *Synadenium grantii.*

Phytochemicals	**JC**					**JB**				
Coumarins	+	+	+	+	+	+	+	+	+	+
Alkaloids	-	-	-	-	-	-	-	-	-	-
Tannins	-	-	-	-	-	-	-	-	-	-
Steroids	-	-	-	-	-	-	-	-	-	-
Flavonoids	-	-	-	-	-	-	-	-	-	-
Saponins	-	-	-	-	-	-	-	-	-	-
Anthraquinones	-	-	-	-	-	-	-	-	-	-

Source: Authors (2022)

In the literature, we found some studies that make use of this plant species as well as its extracts that result in a high cytotoxic potential, according to Andrade *et al*. (2021) and Oliveira *et al*. (2013), affirm this cytotoxicity in relation to melanoma, both in vivo and in vitro latex. Based on the studies described by Rosa *et al*. (2022) where he tells us that extracts obtained with nonpolar solvents (hexane and chloroform) are more active, as Luz *et al*. (2015) In their studies, we noticed that latex extracts are more promising, demonstrating a potency and a greater action against types of cancer related to the cervix, and especially leukemia. Thus, phytochemical analyses are a great step to complement the studies we already have available.

Of all the phytochemicals analyzed, both JB (Janaúba de Belém) and JC (Janaúba de Castanhal) showed negative results for Alkaloids, Tannins, Steroids, Flavonoids, Saponins and Anthraquinones. Presenting a positive result for coumarins in both the JB variety and the JC variety, and in all dilutions of different concentrations, all results were favorable to detect the presence of coumarins in the dilutions from 20% to 100%, there was the presence of neon halo in all analyses.

Coumarins are directly related to liver toxicity, i.e., depending on the amount of coumarins present in the solution to be ingested, harm and liver damage may occur, as demonstrated by Ueraha *et al.* (2008) in his study on coumarin-induced hepatotoxicity. There is a great interest in the pharmaceutical industry's economic activity in using this phytochemical for drug development, which is directed to this interest due to its pharmacotherapeutic prominence (Patil; Gouramma; Jalde, 2021; Borges *et al*., 2005).

Thus, Lake (1999) reported on the absorption of coumarins, which, after oral administration, passes through the GIT (gastro-intestinal tract) where it is fully absorbed and fully metabolized in the liver, but only 2 to 6% of what was absorbed is intact to the systemic circulation.

Some studies found in the literature bring different types of analyses regarding phytochemicals, in addition to being tested in different species of the Euphorbiaceae family in relation to different models of cancer, as reported by Hsieh *et al.* (2011) and Hsieh *et al.* (2015), the methanol extract from the latex of the *plant Euphorbia antiquorum* L. expressed the ability to induce apoptosis in HeLa cells, reaching an IC50 value close to 2 µg/mL. In addition, a change in the cell cycle was observed, with an increase in the cell population in the S phase.

Knowing that this family of Euphorbiaceae has about 200 species, the literature brings us a variety of analyses and clinical trials. Ghramh, Khan and Ibrahim (2019), evaluated the hydroalcoholic extract (70%) of E. peplus, and it was observed that a concentration of 25 µg/mL caused the inhibition of almost 50% (48.55%) in the population of cells taken from the spleen of rats after 72 hours of treatment. Kwan *et al.* (2015) performed morphological analysis that revealed evidence of apoptosis, while a cell cycle analysis indicated a cell cycle arrest with increased cell population in the S phase.

A study carried out by Choene and Motadi (2016), investigated the cytotoxic potential of the stem extracts of the Euphorbia tirucalli L. plant in relation to the MCF-7, MDA-MB 231 and MRC-5 cell lines, and the results were that cell prevention ranged between 30-100 µg/mL for the MCF-7 line and between 50-100 µg/mL for the MDA-MB 231 lineage. In addition, they observed a disruption of cells in the G0/G1 phase and induction of apoptosis.

It is important to emphasize that the fact that the above study ends up inducing some cells of the cancer model tested to apoptosis, a determining factor for the continuity of research on the subject, is directly related, as mentioned by Ichim and Tait (2016) and Kim and Kim (2018), to the mechanisms of occurrence and progression of cancer, which, although not yet fully understood, But through the

most diversified studies that we have previously, the progression of the disease is also due to the ability of cancer cells to avoid apoptosis. Because it is related to cell death, so if cancer cells are being induced to this factor, it is relevant that the plant is attributed the function of contributing to the reduction of cancer.

4 CONCLUSIONS

In view of the above, the present study brings relevant data about the chemical, physicochemical and phytochemical characterization of the latex of the Janaúba plant, which despite the little study on the subject, it seeks to add to science and other studies on the subject. It is extremely important that the study be taken into consideration for future research, because it was possible to perceive that although different authors affirm the presence of phytochemicals, in the present study carried out from the dilution of latex in pure water, according to the popular orientation, described in the literature, with the aid of reagents for the analysis may have been another contribution to science. that the analyses need to be carried out in a different way, and even a strong contribution in the sense that although the studies allege the presence of different bioactive principles, even so in the dilution suggested for ingestion it is not possible to detect all the phytochemicals mentioned in the other studies, thus bringing a new look for the future, with a new set of analyses that may, in the future, serve as a basis for future research.

Thus, it can be concluded that although they have not been detected in the current analyses, but compared with past studies, the janaúba plant and its varieties can indeed be considered as a strong alternative to help in the fight against cancer, and it is extremely essential to be careful when being used due to the presence of coumarins that can cause liver problems. for use in large quantities. I suggest that new research be done, including clinical trials, and that more research be started from then on so that we can contribute to society and several families who receive a diagnosis of cancer, to achieve a cure, in addition to having nature as our main supplier of raw material for the cure of different diseases.

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