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Pharmacognostic evaluation of *Libidibia ferrea* extracts and analysis of semi-solid dosage forms

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Abstract

A medicinal plant known as Jucá (*Libidibia ferrea*) is a Brazilian tree that possesses several therapeutic uses, including wound healing actions, due to the presence of polyphenols. Fruits from *Libidibia ferrea* var. *leiostachya* (Benth.) L.P. and *Libidibia ferrea* (Mart. ex Tul.) L.P. Queiroz var. *ferrea*, were collected in Teresina (PI) and Jardinópolis (SP), respectively, and were used to prepare hydroethanolic and hydroglycolic extracts, produced in a 1:10 ratio. The extracts from the fruits from *L. ferrea* var. *ferrea* were used for the preparation of creams and ointments, containing 10 % (w/w) of these extracts. The extracts prepared with the fruits from *L. ferrea* var. *ferrea* (PI) are twice as concentrated in gallic acid content and in the percentage of dry residue, in comparison with those obtained from the fruits *L. ferrea* var. *leiostachya*. Among the formulations prepared, creams and ointments showed, statistically, the same concentration of total phenols, regardless of the type of extract used. The spreadability evaluation, which refers to the distribution of the pharmaceutical form by application area, showed that creams and ointments had very similar behaviors, except for the ointment produced with hydroglycolic extract, which was very fluid, making its therapeutic use unfeasible.

Keywords: *Libidibia ferrea*. Brazilian Ironwood. Production of *Herbal Medicines.* Quality control.

Introduction

The Brazilian tree known as "*Jucá*", is a tree up to 10 meters in height. The traditional name comes from an indigenous Tupi word (*yucá*), whose translation means "to kill". This meaning is due to the fact that the indigenous people use solid wood of this plant species to manufacture instruments (tacapes) used in wars[1]. Currently the name *Jucá* is used to officially designate this medicinal plant in the Brazilian Pharmacopoeia (6th Ed)[2]. Another traditional name is "Pau-ferro" (*Iron Wood*), and the botanical name is *Libidibia ferrea* (Mart. Ex Tul.) L.P. Queiroz also has a synonym *Caesalpinia ferrea* Mart. ex Tul.[3].

In Brazil there are only two species of *Libidibia*: *L. paraguariensis* (D. Parodi) G.P. Lewis, occurring in the State of Mato Grosso do Sul, and *L. ferrea* (Mart. Ex Tul.) LP Queiroz, which occurs naturally in all states in the northeast region, and in the states of Minas Gerais, Espírito Santo, and Rio de Janeiro[4].

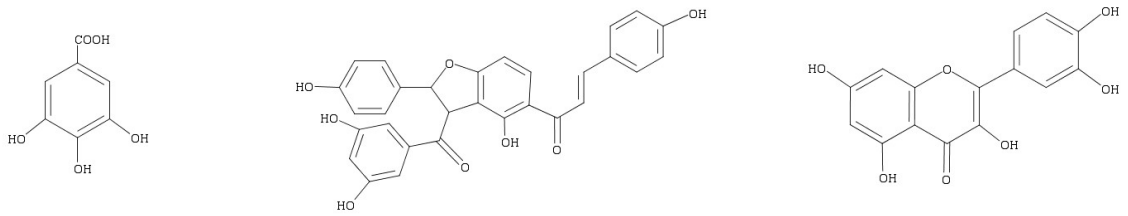
The taxonomic concept of *L. ferrea* is complex and remains practically the same since the work carried out by Bentham in 1870[5], in which the species circumscription included only the specimens from eastern Brazil, proposing the existence of four varieties that are not easy to distinguish. One of them, *L. ferrea* var. *leiostachya* (Benth.) L.P. Queiroz occurs in the Atlantic Forest of Bahia and the southeast, while the other three varieties *L. ferrea* (Mart. ex Tul.) L.P. Queiroz var. *ferrea*, *L. ferrea* var. *glabrescens* (Benth.) L.P. Queiroz, and *L. ferrea* var. *parvifolia* (Benth.) L.P.Queiroz] occur mainly in the northeast[6] **(FIGURE 1)**.

FIGURE 1: Morphological differences between *Libidibia ferrea* fruits: (A) *Libidibia ferrea* var. *leiostachya* (Benth.) L.P.; (B) *Libidibia ferrea* (Mart. ex Tul.) L.P.Queiroz var. *ferrea*.

The ethnopharmacological use of the species *Libidibia ferrea* is distributed in popular medicine, with several pharmacological claims for preparations using its fruits[7,8]. The use of fruits as topical wound healer is one of the most frequent indications. An ideal wound healer agent generally has several different pharmacological properties such as the anti-inflammatory, antimicrobial, antioxidant, epithelial, and analgesic effect. Some of these actions have already been evidenced for the fruits of *Jucá*[9-11], which is why several topical dosage forms were developed from extracts of this botanical drug[12-14].

In phytochemical studies carried with botanical extracts from this species, several classes of secondary metabolites were detected **(FIGURE 2)**, including polyphenols such as hydrolyzable tannins - derivatives of gallic [I] and ellagic acids; flavonoids - chalcones (pauferrol B) [II], catechin and quercetin [III], in addition to terpenes, steroids, and polysaccharides. It is emphasized that the phenolic compounds present are suggested to be the main responsible for the healing effects of the extracts[8,15], and for this reason they are used as chemical markers of quality of pharmaceutical herbal ingredients derived from *L. ferrea*[2].

FIGURE 2: Chemical constituents isolated from *L. ferrea.*



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Thus, it is essential that the active phytopharmaceutical ingredients (botanical drugs and plant extracts) used in the preparation of herbal medicines are rigorously carried out, so the requirements of efficacy and safety are preserved[16]. In this respect, many process factors have influence on the quality of raw materials, such as origin of the drug or the extraction method used[17].

A phytomedicinal preparation using *Libidibia ferrea* requires prior botanical identification, since the species have different varieties that may present chemical variability both quantitatively and qualitatively in relation to the production of secondary metabolites.

Another important aspect regarding the development of herbal formulations is the evaluation of pharmacotechnical parameters on dosage form, considering the requirement to provide patients with a stable preparation, regarding acceptable levels of active principles[18].

Considering semi-solid dosage forms for topical use, the main options are cream and ointment. The former is based on an emulsive system stabilized by surfactants, making administration possible in a single mixture of hydro and fat-soluble actives, while the latter is usually used when intense penetration of the actives into the deeper layers of the skin is required, as it is composed of a lipophilic vehicle, with less polar characteristics[19].

The objective of present paper was to analyze the quality of drugs and extracts from the fruits of two varieties of *Jucá* - *Libidibia ferrea* var. *leiostachya* (Benth.) L.P. and *Libidibia ferrea* (Mart. ex Tul.) L.P. Queiroz var. *ferrea*, from two Brazilian locations, extracted with different solvents. In addition, we conducted preliminarily evaluation of two types of topical dosage forms using *L. ferrea*. In this regard, it is expected that the knowledge related to these themes will be expanded as well as the greater variety of stable and efficient formulations for production of herbal medicines.

Material and Methods

Herbal material

Vegetable-type fruits (pods) were collected from different geographical coordinates. One of the samples was collected from Teresina, in the state of Piaui (latitude 05°22'28 ”S; longitude 95°00'35” W), in November 2018, and the other was obtained from Jardinópolis, in the state of São Paulo, in August 2018 (latitude 24°04'11”S; longitude 47°44'07”W). The examples of these materials were identified by Dr. José Elvino do Nascimento Júnior from the Federal University of São João del Rei, Department of Natural Sciences, and exsiccatae were deposited in the Herbarium of Medicinal Plants of the Biotechnology Department at the University of Ribeirão Preto (UNAERP), receiving the voucher HPMU-3228 for material from Teresina, and HPMU-3229 for material collected in Jardinópolis.

The parts of the seedless mature pericarp were dried in a circulating air oven (45°C for 72 h). After this process the material was ground in a knife mill and sieved in a 0.25 mm granulometer.

Obtention of botanical extracts

Two herbal drugs were subjected to two extraction processes: the first, by maceration with hydroethanolic solvent (7: 3, ethanol: water, v/v), for 7 days, using a ratio of 1 part of the drug to 10 parts of extractor liquid; and the second, by maceration with hydroglycolic solvent (7: 3, propylene glycol: water, v/v), for 7 days, using a ratio of 1 part drug to 10 parts extractor liquid. After extraction, the extracts were filtered using filter paper and stored in amber flasks.

Botanical extracts analysis

Organoleptic characteristics (sensory evaluation)

The organoleptic characteristics were performed following the method of the Brazilian Pharmacopoeia 6th edition[20,2]. The extracts were evaluated in their general aspect in relation to their color and odor.

Relative density, pH, dry residue and chromatographic profile

All physical-chemical analyzes with the extracts were performed according to descriptions in the Brazilian Pharmacopoeia 6th edition[20,2]. The relative density was obtained by the pycnometer method. The pH survey was carried out after checking with a pH meter and using results that did not vary by more than 0.05 units.

The dry residue was calculated from the drying of the extract, associating the use of a hot water bath with subsequent heating in the oven for complete evaporation of the solvent (100 °C for 1 h).

The chromatographic profile was performed using thin layer chromatography (TLC), using silica as a stationary phase (Alugram, Macherey Nagel, Silica Gel 60, UV 254 nm). The mobile phase used was ethyl acetate: formic acid: water (90: 5: 5, v/v/v); as an analytical reference, standard gallic acid (Sigma-Aldrich, CAS nº 149-91-7) was used. The derivatization method used was carried out with ferric chloride 1 % (m/v) nebulization.

All analyzes were performed in triplicate. Those that produced numerical results were expressed as the arithmetic mean and standard deviation. The coefficient of variation was also calculated.

Gallic acid concentration

The analytical technique used to quantify the chemical marker was high performance liquid chromatography (HPLC), using a Shimadzu chromatograph (SCL-10A VP), with diode array detector (SPDM-10A VP). The analysis developed for the measurement of the marker (gallic acid) is essentially determined in the Pharmacopeial Monograph of *Jucá*[2]. The analyses were carried out using an octadecylsilane stationary phase column (C18, Fenomenex Luna, 250 x 4.6 mm, particle 5 µm) and detection of the chemical marker at a wavelength of 270 nm. The official method was adapted, changing the mobile phase and the elution gradient **(TABLE 1)** because the chromatographic analysis using the original method was not satisfactory.

TABLE 1: Comparison between mobile phases and elution gradients for HPLC analysis techniques for extracts from *Jucá,* following the Brazilian Pharmacopoeia (6th ed.) method, and that performed in this work.

Pharmacopial Method		**Developed Method**	
Solvent A: H_2O + TFA 0.05% Solvent B: Methanol + TFA 0.05%		**Solvent A: H_2O + TFA 0.1% Solvent B: Acetonitrile + TFA 0.1%**	
Time (min.)	**% Solvent B**	**Time (min.)**	**% Solvent B**
0 – 10	15 – 25%	0 – 25	10 – 25%
10 – 12,5	25 – 40%	25 – 27	25 – 34%
12.5 – 15	40 – 75%	27 – 30	34 – 42%
15 – 17.5	75 – 15%	30 – 33	42 – 65%
17.5 – 18	85%	33 – 35	65 – 10%

* TFA: Trifluoracetic acid

For the determination of the chemical marker content, the calibration curves were produced using commercial analytical standard of gallic acid (Sigma Aldrich, CAS # 149-91-7). The analytical validation of the method was performed by linear regression of the chromatographic peak areas, using solutions of the standard in the concentrations of 3.12, 6.25, 12.50, 25.00, 50.00, and 100.00 µg/mL. The data were analyzed using the Excel program, determining the linear equation, linearity (R^2), correlation (R), quantification limit, and detection limit **(TABLE 2)**, as recommended by current legislation[21].

TABLE 2: Analytical validation method.

Validation Parameters	
Equation	**y = 42882x + 45960**
R^2	0.9991
R	0.9995
Limit of Quantification (LOQ)	2.75 µg/mL
Limit of Detection (LOD)	0.90 µg/mL

Development of topical dosage forms

Creams and ointments were produced similar to the official formulations for these dosage forms in the Brazilian National Formulary[22], containing 10 % (w/w) of *Jucá* extracts. This concentration is usually used for similar formulations present in the National Herbal Medicines Formulary of Brazilian Pharmacopoeia [23].

Creams (oil / water emulsion)

As listed in **TABLE 3**, the cream formulations were prepared using the usual emulsion development technique. The constituents were divided according to hydro or liposolubility. The constituents were fused by heat at 70ºC, independently. After the melting of the oily components, the hydrophilic components were dissolved, slowly adding the aqueous phase to the oily phase, with mechanical agitation, for 30 min. After cooling (below 40°C), the *Jucá* extract was incorporated.

Ointment (lanolin and vaseline based)

The ointments were prepared to incorporate the extracts into the previously melted excipient (prepared by solution). The constituents were fused by heat at 70 ºC, together with the antioxidant adjuvant, butylated hydroxytoluene (BHT). After obtaining adjuvant solubilization in the medium where the excipients were melted, a mixture of lanolin and vaseline was cooled to below 50°C. At this moment, 10 % of *Jucá* extract (w/w) was incorporated, as shown in **TABLE 3**.

TABLE 3: Formulations of creams and ointments with *Jucá* extracts of the *ferrea* and *leiostachya* varieties (% w/w).

Cream	Control	Hydroethanolic extract	Hydro-glycolic extract
Nonionic self-emulsifying wax	15	15	15
Propylene glycol	5	5	5
Methylparaben	0.15	0.15	0.15
Propylparaben	0.05	0.05	0.05
Jucá extract	0	10	10
Purified water	100	100	100
Ointment			
Solid Vaseline	60	60	60
Lanolin anhydrous	30	30	30
BHT	0.02	0.02	0.02
Jucá extract	0	10	10

Three samples were prepared for each of the dosage forms (n = 3). They were packed in polyethylene bottles and stored at room temperature, for later analysis.

Analysis of dosage forms

Organoleptic analysis

For organoleptic analyzes of the dosage forms, the general aspect was observed in relation to color and odor of the preparations.

Chemical marker (total phenolics)

The methodologies created by De Paula[24] and Brasileiro[25] were adapted for the extraction of samples (total phenolics) from pharmaceutical forms. Prior to the analysis of the cream, 1 g of the product was weighed in a falcon tube (15 mL) and 10 mL of water were subsequently added. The sample was homogenized and submitted to a heating bath at 85ºC for 30 min. After cooling, 2 mL were pipetted into an Eppendorf tube, and centrifugation occurred at 12,000 rpm for 10 min. An aliquot of 1 mL the aqueous phase was removed and filtered through a 45 µm pore nylon syringe filter.

For the extraction of the ointment samples, 1 g of the product was weighed in a falcon tube (15 mL) and made up to 10 mL with water. The sample was homogenized and submitted to a heating bath at 85ºC for 30 min. After cooling the sample, a 1 mL aliquot of the aqueous phase was removed, filtered through a nylon syringe filter, with a 45 µm pore.

The quantification of assets was carried out with these previously processed samples, using spectrophotometry as an analytical technique, following the methodology of analysis of total phenols, carried by Ferreira *et al*.[26]. Quantification was performed using a UV-VIS spectrophotometer (Model S-2150, brand Unico®). The samples were analyzed after a Follin-Ciocalteu reaction at 760 nm. Gallic acid solution was used as a reference standard.

This analysis was performed in three samples, for each product (n = 3). All were conducted in triplicate. For presentation of the results obtained, the arithmetic mean and standard deviation were used. The coefficient of variation was also calculated.

Spreadability

The determination of the maximum spreadability and the limit effort for the pharmaceutical forms was carried out according to the method developed by Milan *et al*.[27], in which are used increasing weights (50 g and 100 g) that are placed over a plate of glass (20 cm x 20 cm) that covers the sample of the pharmaceutical form, in certain time intervals, with constant evaluation of the occupied area. The maximum spreadability was considered to be the point at which the addition of mass over the sample did not cause significant changes in the calculated area values. The limit effort corresponds to the mass compensated at the maximum spreading value. The relationship between the area of maximum spreadability and the mass corresponding to the limit effort was obtained to obtain numerical values ($mm^2.g^{-1}$) that represent the spreadability of the pharmaceutical form. Three repetitions were performed for each sample and the results obtained as arithmetic mean and standard deviation, together with the coefficient of variation were also calculated.

Statistical analysis

The results of the determinations were corrected by analysis of variance (ANOVA), followed by the Tukey multiple comparison test ($p < 0.05$). This statistical analysis was performed using GraphPad Prism 5 software.

Results and Discussion

Analysis of *Jucá* extracts

In the organoleptic evaluation, the hydroglycolic extracts extracted from herbal drugs of *L. ferrea* var. *ferrea* and *L. ferrea* var. *leiostachya* presented an intense reddish-brown color, as well as the hydroethanolic extract calculated from the material of the *L. ferrea* var. *ferrea*. The hydroethanolic extract of the *leiostachya* variety showed brown color. All of the extracts presented sweet fragrance, characteristic of the herbal drug.

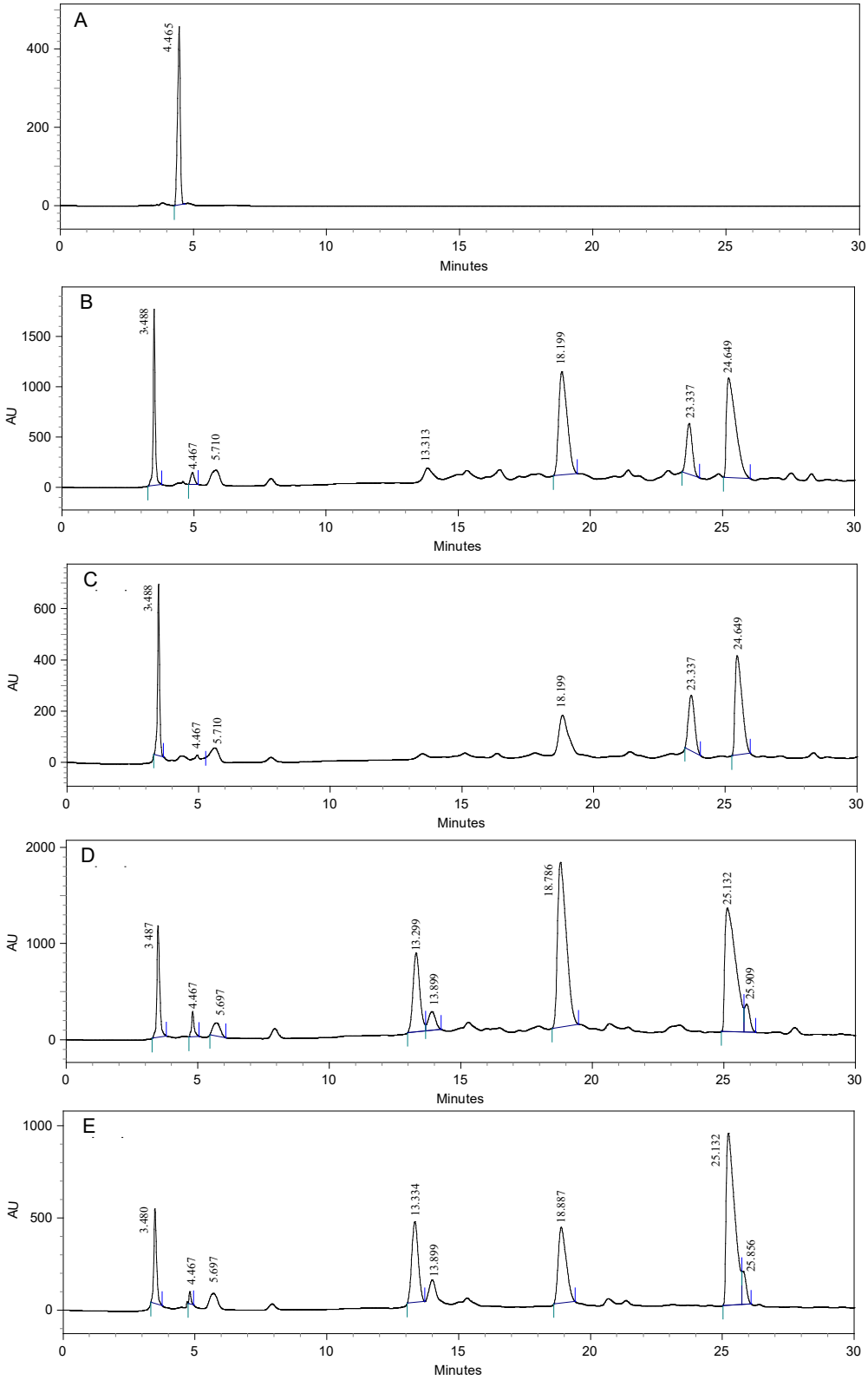
Regarding the chromatographic profiles obtained by TLC, in both hydroglycolic and hydroethanolic extracts gray spots were detected with Rf = 0.2, 0.4, 0.6, and 1.0, for all extracts analyzed. These spots were denser in the extracts found with the fruits coming from the *ferrea* variety. The gray spot of Rf = 1.0 corresponds to the marker used (gallic acid). The upper spots present in the TLC analysis of the extracts are also one of the parameters assigned for the analysis of the herbal drug of *Jucá* present in the Brazilian Pharmacopeia [2].

The pH of the different samples varied within an acid range (4.36 - 4.61), mainly due to the presence of dissolved polyphenols in these different extracts, which are acidic compounds. The relative density presented by the extracts is related to the type of solvent that was used in the extractive process, with results below 1 g/mL for those that contained ethanol: water mixture, and above 1 g/mL for those containing propylene glycol: water.

Regarding the dry residue, both the hydroalcoholic and hydroglycolic extract of both varieties used showed a significant difference between them, and the highest values were obtained with extracts of the *ferrea* variety, showing that the herbal drug from this variety presents greater wealth of chemical components. This information is important for the production of herbal medicines, since the extracts with a greater mass possibility have a higher content of active compounds.

This was confirmed by the results presented in the quantification of gallic acid, obtained by HPLC. The hydroethanolic and hydroglycolic extracts obtained with the herbal drug from *L. ferrea* var. *ferrea* had twice the content when compared to *L. ferrea* var. *leiostachya*, however the chemical profile was very similar **(FIGURE 3)**.

FIGURE 3: Standard chromatogram in HPLC (A) gallic acid standard, (B) Hydroethanolic extract of *L. ferrea* var. *ferrea*, (C) Hydroethanolic extract of *L. ferrea* var. *leiostachya*, (D) Hydroglycolic of *L. ferrea* var. *ferrea*, and (E) Hydroglycolic extract of *L. ferrea* var. *leiostachya.*



Previously, analysis conducted by Ferreira *et al*.[26] and Santos[28] concluded that for *L. ferrea*, there are several factors that can influence the content of polyphenols in the different parts of the plant.

Ferreira *et al*.[26] investigated the variation in the concentration of gallic acid in 14 fruits from *Jucá*, from locations in the northeast and north of Brazil, in addition to Brasília and Mato Grosso do Sul (with higher latitudes). The results, obtained by the analysis of aqueous extracts, demonstrated that the highest and the lowest contents came from samples collected in northeast Brazil, while those from the north region, Brasília and Mato Grosso do Sul (both center west region) resulted in intermediate levels.

Santos[28], when analyzing methanolic extracts from the leaves and stem barks of a single sample from Recife (PE), for 12 months, concluded that the total phenol levels increased during the months of drought and decreased in the months of high rainfall.

This information indicates how important it is to standardize extracts of *Libidibia ferrea*, considering that several factors interfere in the concentration of this chemical marker. Thus, the present work elucidates that characterizing the species variety is also an important factor, since the content of the active substances, especially the gallic acid concentration, as well as the percentage of dry residue of extracts vary significantly from one variety to another **(TABELA 4)**.

TABLE 4: Results of physicochemical-specific analyzes related to the concentration of the marker in relation to the researched extracts.

Extract (Variety)	pH	Relative Density (g/mL)	Dry residue (% m/m)	Gallic acid content (µg/mL)
Hydroethanolic (*ferrea*)	4,37a (0.005; 0.13)	0.91a (0.0005; 0.06)	5,09a (0.288; 5.66)	215,35a (0.215; 0.10)
Hydroethanolic (*leiostachya*)	4.59b (0.010; 0.21)	0.89b (0.001; 0.13)	2.15b (0.128; 5.95)	95.65b (0.366; 0.38)
Hydroglycolic (*ferrea*)	4.36a (0.015; 0.34)	1.06c (0.0006; 0.05)	4.43c (0.025; 0.57)	208.66c (0.846; 0.41)
Hydroglycolic (*leiostachya*)	4.61b (0.005; 0.12)	1.05d (0.004; 0.04)	2.14b (0.026; 1.19)	102.01d (0.404; 0.40)

n = 3; p <0.05 - ANOVA followed by Tukey's multiple comparison test. Averages followed by the same lower case letters in the column do not differ statistically. Numbers in parentheses below the averages, refer respectively to the standard deviation and coefficient of variation (%).

Analysis of dosage forms

The conclusion that extracts obtained from fruits of *L. ferrea* var. *ferrea* have the highest percentage of dry residue and are the most concentrated, in relation to the chemical marker, led these to be chosen for the evaluation of pharmaceutical forms.

The examination of the visual aspect of the formulations reveal that the creams had an intense orange-brown color and the ointments had a dark brown color. The preparations did not present a characteristic aroma of *Jucá* extracts. The ointments containing hydroglycolic extracts exhibit fluid consistency, almost liquid.

Considering the results presented in **TABLE 5**, the contents of total phenols in the samples of the pharmaceutical forms, statistical difference was not detected when comparing creams and ointments

containing hydroethanolic or hydroglycolic extracts. Both extracts, produced in a 1:10 ratio, could be used in the formulations, as they demonstrate to contain similar content of the evaluated marker.

The total phenolics content and area/limit effort ratio for creams and ointments are shown as an area ratio and limit effort, in **TABLE 5**.

TABLE 5: Average values obtained for total phenolics and the relationship between areas and the limit effort (spreadability) in semi-solid pharmaceutical forms containing extracts of *Jucá* (*L. ferrea* var. *ferrea*).

Dosage Form Extract	Total Phenolics (% m/m)	Area /Limit Effort Ratio (mm^2/g)
Cream – Hydroethanolic extract	0.32a (0.027; 8.35)	8.79a (1.510; 17.18)
Cream – Hydroglycolic extract	0.26a (0.036; 13.83)	8.26a (3.178; 38.46)
Control – Cream	-	12.17a (1.519; 12.49)
Ointment– Hydroethanolic extract	0.27a (0.018; 6.87)	8.04a (0.769; 9.57)
Ointment – Hydroglycolic extract	0.35a (0.158; 44.97)	22.29b (1.625; 7.29)
Control – Ointment	-	12.95a (1.317; 10.17)

n = 3; p <0.05 - ANOVA followed by Tukey's multiple comparison test. Averages followed by the same lower case letters in the column do not differ statistically. Numbers in parentheses below the averages, refer respectively to the standard deviation and coefficient of variation (%).

No statistical difference between the formulations tested was observed, including a comparison to the controls. The exception of the ointment prepared with hydroglycolic extract, which showed an excessively high value, evidenced the great fluidity of this preparation, also noted in the visual evaluation.

A very fluid ointment is uncomfortable for the patient and irregular distribution may occur due to the great fluidity, spreading it to areas where the application is not necessary. Products that occupy a restricted region of the skin are more adequate.

A possible explanation for the high fluidity of the ointment prepared with hydroglycolic extract is an interaction between the solvent (hydroglycolic), the active ingredients present in the extract, and the components of the excipient of the ointment. This may be plausible, as the same aspect did not occur in the ointment located with the hydroethanolic extract.

For this reason, the use of *Jucá* hydroethanolic extract (1:10) is only recommended for formulations of lanolin and vaseline ointments, at a concentration of 10 % (w/w), not the hydroglycolic extract.

Previously, a preparation of oral paste ointment was performed by Matos[12], the excipient of which is essentially lipophilic, containing dry extract from the *Jucá* barks. In this work, instability of the preparations was observed, with phase division after centrifugation, when stored for several periods in different storage environments, revealing that it is even possible that there is incompatibility between the substances present in the extract and the excipients of the ointment. In contrast, the Federal University of Pernambuco[14] has

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patented another ointment with antimicrobial action, containing fluid extract (1: 1) from *Jucá* seeds. The excipients used were very similar to those in the present work but there were no reports of incompatibilities.

In relation to creams, these formulations have good spreading, with results close to the control, both with the use of hydroethanolic and hydroglycolic extracts.

Magalhães *et al.*[13] developed cosmetic preparation (liquid soap), using surfactants and fluid extract (1: 1) from *Jucá* leaves, using hydroglycolic solvent, in concentrations of 3 %, 5 % and 10 % (m / m) and did not report incompatibilities, and antimicrobial activity was evidenced in these products.

The 1st edition of the National Herbal Medicines Formulary of Brazilian Pharmacopoeia [29] presents a gel formulation (at 5 % w/w) produced with glycolic extract of *Jucá* fruits, with healing and antiseptic properties, but without mentioning the proportion between herbal drug and solvent used for the preparation of the glycolic extract for this formulation, and also without observations regarding the possible incompatibilities. The 2nd edition, published in 2021, excluded the formulation using gel and included the cream, using 10 % v/w of hydroglycolic extract.

Conclusion

Botanical varieties of *Libidibia ferrea* showed diversity in the abundance of secondary metabolites. The *L. ferrea* var. *ferrea* demonstrated to be more chemically productive, with a higher percentage of dry extract and higher content of gallic acid than the leiostachya variety.

Creams and ointments can be formulated using extracts produced with the herbal drug from the ferrea variety, as they resulted in preparations with the same concentrations of active and have good spreadability, except for ointments containing hydroglycolic extract, which were excessively fluid, making it difficult to be used by patients.

Based on this presentation, the importance of an accurate process of quality control and production of formulations from extracts of *Libidibia ferrea* is emphasized, in order to assure the efficacy and safety of herbal medicines obtained.

Financing source

None.

Conflict of interests

There is no conflict of interests.

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Contribution

Study design: LJFM; AMSP; JCB

Data curation: LJFM; AMSP; IMCD

Data collection: LJFM; IMCD; JENJ

Data analysis: LJFM; JENJ

Writing of the original manuscript: LJFM

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