Analysis of studies of applications therapeutic of *Carapa guianensis* Aublet (MELIACEAE)

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Abstract

This work has the theme "Analysis of studies on the therapeutic applications of Carapa guianensis Aublet (MELIACEAE)", a plant popularly known as andiroba. This species is used in ethnomedicine, but it is not written in the Brazilian Pharmacopoeia which makes it difficult to use in prescriptions, so can andiroba be trained by health professionals? With this questioning, this work aims to compile articles and literature of this kind, where I point out studies on its medicinal use, I conceptualize its pharmacological action in order to verify that Andiroba can be prescribed by duly qualified professionals, done through bibliographic review. Studies show that andiroba oil is capable of reducing the intensity of the inflammatory response in wounds; about oral use still does not have enough studies, so the best way for andiroba oil to be prescribed is in topical form because it has more toxicity studies for this type of application.

Keywords: Medicinal plants . Ethnobotany . Phytotherapy . Guyanensis carapa

1 Introduction

Andiroba is a neotropical tree that occurs in southern Central America, Colombia, Venezuela, Suriname, French Guiana, Brazil, Peru, Paraguay and the Caribbean islands. In Brazil, it is found up to 350 meters above sea level, in terra firme forests, temporarily flooded forests, along rivers and streams and close to

mangroves throughout the Amazon basin. Belonging to the same family as mahogany and cedar, the Andiroba tree, because its wood is resistant to insect attack, is much sought after by sawmills (FERRAZ et al., 2003).

Its seeds are floating and can be dispersed sas in the stream of the courses d ' water. However, in terra firme forest, most fruits and seeds are found under the parent tree. An adult tree can reach up to 30 meters in height and produce up to 120 kilos of seeds (corresponding to an average of 50 kilos/tree). At the time of dispersion, the seeds are heavily consumed by rodents, armadillos, deer, wild pigs, etc . (FERRAZ et al., 2003) .

It was found that the seeds have 43% fat and to have a liter of oil by hand, 12 kilos of in natura seeds are needed , with the mechanical press 4 kilos of dry seed are used and when chemical solvents are applied, it is used up 3 pounds. As for the yield of Carapa guianensis oil , per tree, extracted by hand, it can reach 3 liters and up to 30 liters per industrial extraction (MORAIS, 2012) .

Due to its rapid development in the field and the high value of its wood, Andiroba is indicated for joint plantations and agroforestry systems. Monoculture plantations suffer from attack of the terminal shoot by Hypsipyla grandella , which is the biggest pest for the Meliáceas family in the Amazon region and which inhibits its growth. This ends up compromising the use of trees for wood, when Andiroba survives the attack, which is not as intense as in Mahogany, the fruit productivity remains the same (SOUZA et al., 2006) .

Herbal medicine has gained an important place in the treatment of various pathologies, however there are scientific literatures that do not provide results regarding the use of these products, causing the prescribing health professional to end up not choosing the use of this therapy, making it impossible for the patient to be involved in the process of cure. The Carapa guianensis popularly known as Andiroba, despite being very traditionally used by the population and present studies ethnomedicinal and pharmacological activities already

published proven and is not present in any Brazilian Pharmacopoeia.

And ntender as Andiroba can help in the healing process is important for patient care and safety professional at the time of prescription. The objective of this research was to create a compilation of studies demonstrating that C. guianensis Aublet has enough studied therapeutic properties so that it can be prescribed by able professionals and was divided into three specific objectives:

a) Point out studies that inform about Carapa guianensis and its medicinal use,

b) Conceptualize the chemical properties responsible for the pharmacological action of the medicinal species and

c) Verify that Andiroba can be prescribed by duly qualified professionals .

2 Methodology

It is an studo review of the literature caracterizada as descriptive (Torrelio et al., 2009). The revision will include documents between the years 2003 to 2021. The databases used were PubMed , SciELO , CAPES periodicals, dissertations, LILACS , websites Missouri Botanical Garden and Flora in Brazil plus d and personal books. The descriptors used were the following: Medicinal plants, Ethnobotany and Phytotherapy. The languages of the analyzed works were Portuguese and English . 100 articles were analyzed, however, only 38 met the criteria, the PICOT method was also used in this research, the PICOT method (P problem ; I Intervention: Represents the intervention of interest, which can be therapeutic, prognostic, administrative or related to economic issues ; C Control or comparison : Defined as a standard intervention, the most used intervention or no intervention; O (Outcome “ outcomes ”) or expected results and time T) (SANTOS et al., 2017) .

3 *Carapa guianensis* Aublet

The geographic distribution of andiroba extends over the North (Acre, Amazon, Amapá, Pará) and

Northeast (Maranhão) regions, as shown in Figure 1. Its traditional medicinal use includes anthelmintic action, use in skin diseases, febrifuge, insect bite, insect repellent, ulcer, because it is rich in tannin. And the use of seed oil on a daily basis goes to the manufacture of soap and lighting (FLORES , 2020).

Figure 1: Map of Brazil showing the locations where the species is located.

Source: Flores (2020) – adapted.

3.1 Botanical Aspects

According to Carvalho et al. (2019) andiroba is a large tree belonging to the Meliaceae family and has a large production of seeds per year. Regarding its biochemistry, it has osteotranortriterpenes , the so-called Limonoids and their C30 precursors, and the protolimonoids . Figures 2 and 3 represent the leaf excicata and the fruit of the species respectively.

Figure 2: Photo of the excicata specimen of the *Carapa guianensis* leaf

Source: Ferreira; Nelson (1980).

Figure 3: Fruit of the species *Carapa guianensis* Aubl.

Source: Stevens (2015)

In the studies carried out by Milhomem et al. (2016) describe that andiroba oil is extracted from the seeds of the andirobeira tree, and is represented by the species Carapa guianensis of the Meliaceae family found in the Amazon. This oil has various uses in folk medicine, among which are cited healing, anti-inflammatory, insect repellent, antimalarial, and antiparasitic and has been widely used in the cosmetic industry.

According to Gueye et al. (2009, p.12) “native plants are important

sources of income in rural communities, and play an important social and cultural role".

In agreement Alexandre et al. (2017, p.15) emphasizes that "all parts of the plant have been used for herbal purposes". Therefore, andiroba oil is composed of fatty acids and another part of non-saponifiable components, rich in limonoid compounds, their presence of origin in bitterness, therefore, they can be obtained through fractionation by chromatography (NONATO et al., 2018).

The book "Contemporary Phytotherapy: Tradition and Science in Clinical Practice" exposed from the perspective of Saad et al. (2016 , p.99) lists several plant species with medicinal properties. The culmination of the studies is the inclusion of Brazilian plants that, despite being little studied, are highlighted in popular medicine, among them Andiroba (*Carapa guianensis* , Meliaceae) (figure 4).

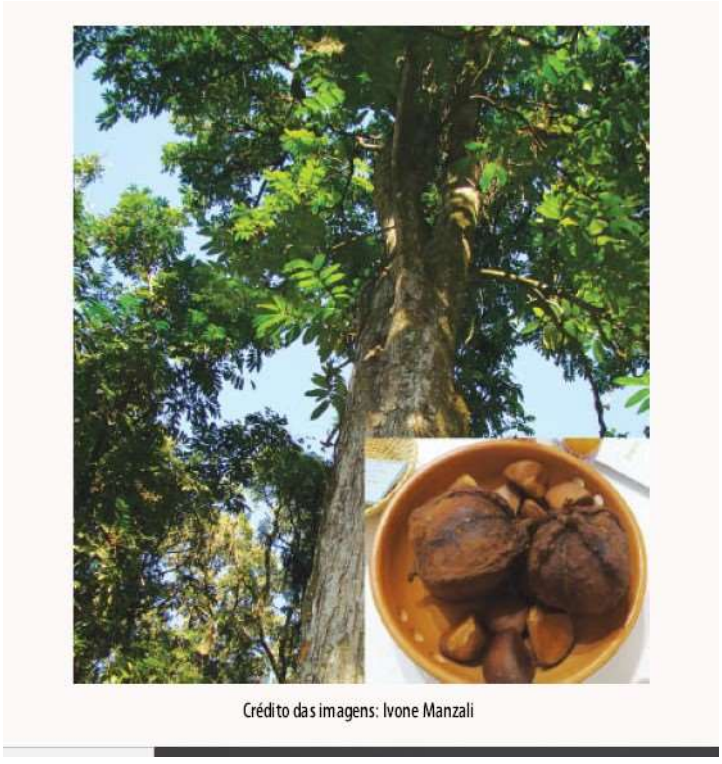

Figure 4: Andiroba tree and fruit.

Source: Ivone Manzali in book Contemporary Phytotherapy (adapted) (SAAD et al., 2016).

Studies show that the high growth rate of andiroba wood and its ability to adjust leaf characteristics in response to changing ambient light make andiroba wood a good choice in reforestation programs where rapidly developing species are warned to rush forest recovery and succession processes of deforested lands. In addition, such species can also effectively contribute to the effect of carbon dioxide deposition in the atmosphere (CAMARGO ; MARENCO, 2012).

It is noteworthy that the other use of andiroba (*Carapa guianensis* Aubl .) is its residues through the optimization of the alkaline pre-treatment to obtain fermentable sugars. Residual husks of andiroba seeds were analyzed and submitted to alkaline application, a pre-treatment that aimed to maximize the recovery of fermented sugar. The authors findaram the production of fermentable sugars from the seed husk andiroba is optimized for pre alkali-treatment with the reaction time, concentration of NaOH , and temperature effects exerted on the linear response variable, saccharification (%) , higher sugar concentration was obtained in 100 min reaction time, 4% (m/v) NaOH concentration and 120 °C temperature. These implications allowed this biomass to be considered as a suitable material for the production of fermentable sugars (SOUZA et al., 2020).

Although it has broad traditional use, it was not included in the Brazilian Pharmacopoeia Herbal Medicines Form or in any of the five editions of the Brazilian Pharmacopoeia (SAAD et al., 2016) .

3.2 Chemical components

They are found in the chemical composition of andiroba seed oil , concentrations of fatty acids, myristic , palmitic, linoneic , stearic and arachidic , limonoids and others. And it has medicinal properties with healing potential and stands out among traditional oils in the North of the country (ALEXANDRE et al., 2017).

Accordingly, in one study, conducted with five new limonoid type fragmalin, carapanolidos M and Q (1 and 5), together with two type limonoid mexicanolida , carapanolidos R and S (6 and 7) were isolated from oil

seeds from *Carapa guianensis* AUBLET (Meliaceae), a traditional product in Brazil and Latin American countries. Their structures were explained on the basis of spectroscopic analysis using 1D and 2D NMR techniques and a single crystal X-ray diffraction analysis. Compounds 1 and 7, along with 12 known limonoids , 8 and 19, isolated from the flower and seed oil of C. guianensis were tested to determine their speed in promoting triglyceride metabolism in the human hepatocellular carcinoma cell line pre-treated with high glucose content, HepG2. Gedunin -type limonoid : 14 (% control at 10 mM : 35.4 to 3.9), 13 (55.0 to 3.6 to 10 mM) and 18 (75.4 to 4.2 to 10 mM) significantly reduced levels of TG in hepatocytes (INOUE et al., 2012) .

In another study, twigs of *C. guianensis* from Yunnan province, China were collected in December 2001. The air-dried twig was extracted and isolated in powder (13.5 kg) with 3X EtOH under reflux, and the solvent was evaporated in vacuo. The residue was partitioned into H 2 O and extracted with CHCl 3 , EtOAc and n- BuOH three times, respectively. Compound 1 was obtained as a white powder, which showed molecular formula of C 35 H 56 N 2 O 4 . Nine compounds were separated from the EtOH extraction of Carapa guianensis branch , spectroscopic methods were performed and their structures were elucidated as carbon amine 1,3-di-benzene-2-octadecyl acid-glyceride, hexacosanoic acid-2,3-dihydroxyglyceride acid, ursolic , narina- Genina , scopoletin , 3,4-dihidroximetilbenzoato, 2,6-dihidroximetilbenzoato, tetratria - acetic contanóico acid and triacontanóico (HUS lQ-Hua et al., 2004).

3.3 Ethnomedical use

Used externally for its anti-inflammatory properties against rheumatic pains and muscle as well as in insect repellency, oil seed is one of the medicinal products sold over the Amazon forest for this purpose (Amaral et a l ., 2005). Mixed with honey, andiroba oil is a very popular anti-inflammatory for fighting throat infections and flu processes in general.

The oil obtained when cold shows a light yellow color, without precipitates and a characteristic aroma. Due to the growth of the market, fraud is very frequent. Soybean oil, patauá oil (*Oenocarpus bataua* - palm tree from the Amazon), animal fats, among others, is added to the oil of C. guianensis . The producers claim that the " test " to assess the quality of the oil is to spread a small portion on the skin. The " true " tends " dry " while the " doctored " continues " smearing " the skin (Homma et al., 2014).

It is also described as a substitute for quinine in combating swamp fevers. In Amazonas, the use of oil did not differ from reports in other locations. The indigenous people of French Guiana used andiroba oil mixed with annatto as a repellent for mosquitoes and bugs (*Tunga penetrans*). The oil of *C. guianensis* has been used in folk medicine in inflammatory cases, which has been proven in preclinical trials. However, the lack of a detailed evaluation profile regarding the anti-inflammatory action mechanism suggests its application only in topical formulations. Use topically in rheumatic pain, acute inflammation or in cases of topical bacterial infections. For this, it is recommended the use of topical formulations from 2 to 5% of concentration, with applications three times a day (PESCE, 1941 apud MENDONÇA et. al., 2007).

In the Amazon, in some regions, it is widely used in the treatment of uterine cancer (oil applied directly to the vaginal canal), diabetes (cortex decoction) and bark extract as a digestive stimulant. The dosage of fresh oil is that it must be applied directly to the affected region, pure or associated, in rubs and compresses. The authors did not find references regarding precautions, contraindications and extracts available in the Brazilian market (SAAD et al., 2016).

3.4 Toxicity

The oral administration of C. guianensis seed oil did not show any toxic effect in pregnant rats nor did it induce fetotoxicity , as it did not modify the biochemical and hematological parameters (COSTA et al., 2007). However, it caused an increase in serum alanine aminotransferase , in the relative

mass of the liver and testis of rats and in the number of sperm in the epididymis tail, which indicates a possible toxic effect that needs further research (SILVA, 2006).

For Brito et al. (2013, p. 478) in their "study the effects of andiroba oil on the liver function of rats submitted to injury induced by ischemia and normothermic liver reperfusion were evaluated . The pre-treatment of animals with the oil was not enough to change the deterioration of liver function".

Some studies have shown that andiroba oil does not trigger or increase morbidity and mortality when applied in the abdominal cavity of rats within a period of up to seven days, being used orally, regarding the acute and subacute toxicity of andiroba oil (BRITO et al., 2013).

In comparison in the studies by Costa-Silva et al. (2008) were found in Wistar rats increased serum ALT levels and absolute and relative increase in liver weight of treated animals, which may indicate the possibility of liver toxicity.

4 Pharmacological activities and use in clinical practice

It is pointed out that the oil of C. guianensis due to its traditional use has aroused interest since the Brazilian colonization due to its importance in everyday life in popular therapy (SAAD et. al., 2016).

Several studies have shown that the oil extracted from the plant has anti-inflammatory, analgesic and anti-allergic activities (PENIDO et al., 2006).

It is well known that the seeds' potential lies in their oil, which is extracted by hand, Brito et al. (2013, p. 478) highlights that "the oil has been widely used by extractivists, Indians and riverside dwellers in the Amazon also in cases of animal bites, which is administered orally or topically, also used by the pharmaceutical industry in the formulation of cosmetics".

It is mainly indicated for prophylaxis against insect bites, rheumatic pain, wounds and skin lesions. Due to the presence of active ingredients as cardiotonic glycosides, triterpernoides, tannins and carbohydrates, it confirms the importance of andiroba as a source of subst â pharmacologically active

TRENDS. The antifungal activity is probably associated with the presence of limonoid- like substances, which has already been proven for other species of the Meliaceae family (SAAD et al., 2016).

4.1 Superficial skin lesions

According to Saad et al., (2016) the andiroba can be used in some situations without more serious accidents, such as scratching type, cuts, small superficial edema and bruising. Stagnation: Hematoma, pain, trauma, edema and breakage in the skin.

4.2 Andiroba for wounds in diabetics

A survey carried out by Souza et al. (2017) at the Federal University of Pará, which evaluated wound healing in Alloxan- induced diabetic rats using the topical form of andiroba oil, where they presented significant results in wound healing of final wounds in rats with induced diabetes between treatments when compared to the control group.

Analyzing the article according to the PICOT method, it was noticed that the main issue of the research was the search for alternatives to improve the healing of diabetic foot ulcers, in addition to being effective and with the convenience of a lower cost similar to the treatment pattern. Carapa guianensis oil has already been described with this great potential.

The researchers used six rats disseminated in three subgroups (collagenase , andiroba and control), made at 7, 14 and 21 days. In group collagenase was used the ointment collagenase (0,6U / g) was applied every day once a day. In group andiroba were applied oil andiroba every day, once a day in a volume of 0.3 ml to euthanasia and control group was treated only with distilled water once a day, every day, with a volume of 0, 3ml, Figure 5 shows the evolution of the wound in the groups.

Figure 5: Andiroba oil is able to reduce the intensity of the inflammatory response compared to the Collagenase Group .

Source: SOUZA et. al., 2017 (adapted).

Andiroba oil showed positive results compared to the control group, reaching a lower mean wound area (Table 1). In macroscopy, the degree of almost total contraction of the wound incision was observed on day 21 and the presence of re- incision was also observed .

Table 1. Mean ± SD of wound area within days according to groups.

	Mean of wound area (mm^2)			p-value
	Control	Collagenase	Andiroba	
7^{th} Day	0.49 ± 0.01	0.47 ± 0.01[a]	0.40 ± 0.01[a,b]	0.006
14^{th} Day	0.33 ± 0.02	0.27 ± 0.01[a]	0.30 ± 0.02[a,b]	0.005
21^{st} day	0.13 ± 0.01	0.0 ± 0.0[a]	0.0 ± 0.0[a]	0.003

[a]: p<0.01 versus Control group. ANOVA (Tukey) test; [b]: p<0.01 versus Collagenase group. ANOVA (Tukey) test

Table 1: Mean + - SD wound area in days according to the groups.

Source: SOUZA et al., 2017 (adapted).

The experimental model showed greater effectiveness of the topical application of andiroba oil in tissues of epithelialization formation , angiogenesis and collagen deposition in the skin lesion compared to the control group, leading the researchers to the conclusion that andiroba oil is capable of reduce the intensity of the

inflammatory response compared to the collagenase group , proving by macroscopic results as seen in figure 5 that there was a greater wound retraction in animals treated with andiroba oil and there was no confirmation of impaired incisional wound healing.

4.3 System musculo skeletal

According to Saad et al. (2016) musculoskeletal pain encompasses a large number of pathologies with different physiologies and anatomical origins. Phytotherapy offers a therapeutic resource to reduce pain, inflammatory processes and aid in immune-mediated diseases.

It is noteworthy that among the pathologies manageable by herbal medicine, we have muscle contractures, contusions, tendonitis, degenerative joint diseases (osteoarthrosis), metabolic diseases such as gout and immunologically mediated diseases such as rheumatoid arthritis. Many of the pathologies are chronic in nature, leading to a prolonged period of treatment (SAAD et al., 2016).

It is important to highlight the importance of etiological diagnosis, as well as stressing that the combination of herbal medicines with synthetic drugs often leads to a decrease in the use of the latter, with a consequent reduction in side effects, therefore , andiroba also has action in the treatment of musculoskeletal disorders (SAAD et al . , 2016).

4.4 Antiplasmodic activity of andiroba

The results of studies carried out by MIRANDA JUNIOR et al. (2012) mention support for the usual use of andiroba oil (*Carapa guianensis* Aubl, Meliaceae) and its fraction rich in limonoids as an antiplasmodic , which additionally proved not to be toxic in bioassays performed in mices.

In contrast, Barros et al. (2012) mentions in their studies that, in order to evaluate the in vitro efficacy of andiroba oil, due to the occurrence of parasitic dermatitis in domestic cats, making it possible to obtain alternative products to combat it, in the case of andiroba oil , they presented efficacy at the concentrations tested.

4.5 Oral anti-mucositis action

Another study observed a statistically significant reduction in the degree of Oral Mucositis (OM) in children on the fourth, fifth and sixth days and in pain scores on the second, third and fourth days in the andiroba group after the onset of OM, compared to the laser group . The use of andiroba oil effectively reduced the severity of OM and relieved pain, which resulted in a decrease in the severity of signs and symptoms in patients in the andiroba group , compared to the laser group (SOARES et al., 2021).

Given the above, Fernandes et al. (2014, p. 11) states in their studies that " the oil of andiroba extracted from the seeds is used to treat edema, rheumatic, anti-inflammatory, antiallergic, aid in healing and serves as raw material for cosmetics industries " .

4.6 Intracellular glucose suppression

A limonoid of andiroba - 7-Deacetoxi-7-Oxogedunin (CG-1) andiroba (Carapa guianensis , Meliaceae) eliminated the accumulation of intracellular lipid in the initial stage of adipocyte via suppression mediated glucose production by the IRS-1 / Akt raising and lowering of GLUT4 expression through the repression of glucose uptake mediated by insulin receptor substrate-1 (IRS-1) and Akt (IRS-1 / Akt) in adipocytes (MATSUMOTO et al., 2019).

4.7 Action against liver and kidney injuries

The andiroba reduced various aspects of the severity of injuries caused by DOX, decreasing haematotoxicity and severity of histological changes in the liver and kidneys and reducing the frequency of cell death by apoptosis. The study sheds new light on the therapeutic benefits of andiroba and suggests new ways to investigate how the quantity and quality of lipid compounds affect exposed organisms (MELO et al., 2021).

4.8 Antileishmanic Activity

Oliveira et al . (2018) studied a chemist of C. guianensis , seed oil and its limonoid- rich fractions , to identify its secondary metabolites, mainly limonoids, and to investigate its anti - Leishmania potential .

The evaluation of the mass spectra contracted from the oil allowed the identification of fractions rich in

limonoids derived from C. guianensis seed oil . Fractions rich in limonoids showed leishmanicidal activity against L. amazonensis promastigotes and amastigotes . The anti - Leishmania activity was attributed to the limonoids 11-hydroxygedunin and 6,11 - diacetoxedunin , identified in the active limonoid- rich fractions of C. guianensis seed oil .

4.9 Action larvicide and repellent

The FFA2-SF emulsions derived from AO2, which mostly contained unsaturated fatty acids, showed the best results against Ae larvae . aegypti after a period of 48 h (LC 50 = 16.79 mg.mL -1), causing changes in the vector. It is estimable that the matrix biopolymer of fibroin silk increases the biodistribution and bioavailability of the active in aqueous media. The first work of this type that showed larvicide activity of the free fatty acid of C. guianensis associated with silk fibroin against Aedes aegypti (SARQUIS et al., 2020).

In a study by Miot et al. (2016) was fe ito a comparison between home repellents made with carnation, picaridin , andiroba and soybean oil against Aedes bites aegypti , where four subjects with health put his forearms on a pre - cleaned plastic nursery with 20 Aedes aegypti healthy females. Their forearms remained in the container for 5min, and if there were no bites, the volunteers waited for 25min outside the mosquito aviary until the next entry. Fifty assessments were carried out using different combinations of products and volunteers. The results were not relevant in relation to chemical repellents which led the researchers to advise not using homemade repellents, since they have less effective than those already on the market, which can lead to risky behaviors by falsely guarantee

4.10 Trypanocidal Action

The pharmaceutical forms mentioned in the studies by Baldissera et al. (2013) indicate that the use of systems such as liposomes, nanoparticles and nanoemulsions , for an action trypanocidal through activity nanoemaulsão can bring other

benefits, but still has a long way ahead and depends on advances in knowledge about the composition of phytochemical and bio -logical activity of medicinal plant extracts, as well as on the physicochemical characterization of nanostructured delivery systems containing these complex matrices .

5 Final Considerations

After reading previous research, it was found that the best way for andiroba oil to be prescribed is in the topical form, as there are more toxicity studies for this form of application. The use of C. guianensis Aublet oil as a repellent is not recommended , as researchers have felt that it is dangerous to advise repellents with lesser effectiveness. The study that induced diabetes in rats and created wounds showed that andiroba oil is able to reduce the intensity of the inflammatory response compared to the Collagenase group.

As for the prescription in the form of oral use, more ingrained studies are still needed so that health professionals who are able to prescribe it can have more security when treating their patients with andiroba oil.

Thus, it is evident that the plant has studied factors phytochemicals effective es for therapeutic treatment. The extract of the C. guianensis plant used in oil acts as an anti-inflammatory and is well known by the Amazon population, who use the empirical knowledge demonstrated in this study.

In the literature study it is clear that the use of herbal medicines in order to check the action in the healing of tissues has been frequent, especially in experimental research, this way is of utmost importance to prescribe medicinal plants and fitoterápic the s , professional pass on all the necessary guidelines according to the legislation , aiming at the prevention of the pathology and the well-being based on the needs of each patient.

From this premise, it is possible to prescription Andiroba p or duly qualified professionals , so you can articulate their efficiency in the pharmaceutical industry or

cosmetics ecêutica allowing approval of benefits.

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