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# Development and stability evaluation of an emulsified system containing *Stryphnodendron adstringens* (Mart) *Coville* (Fabaceae) extract from the Brazilian Cerrado

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**Abstract**
Brazilian flora biodiversity is object of study and research of medicinal plants with healing and emollient therapeutic potential. On this basis, *Stryphnodendron adstringens* (Mart) *Coville* stands out and was the aim for the development and stability evaluation of an emulsified system. The formulation was prepared, bottled in plastic and glass containers and stored at room temperature, refrigerator and incubator. The accelerated stability test was carried out at $T_0$, $T_{15}$ days, $T_{30}$ days and $T_{60}$ days. And a microbiological analysis in accordance with the Brazilian Pharmacopoeia 5$^{th}$ was also performed. Results evidenced that the formulation remained stable during the evaluated period, especially at a refrigerated environment and bottled in glass container. Regarding microbiological aspects, no microorganism's growth was observed, meeting quality standards. Accordingly, results will serve as a subsidy for study continuity and definition of the formulation validity period.

**Keywords:** Emulsified system, *Stryphnodendron adstringens* (Mart) *Coville*, stability, cerrado, Brazil

## 1. Introduction
The advancement in scientific investigations regarding human skin has provided the awareness that it is more than a simple protective barrier, the skin is an organ of the integumentary system with peculiar properties and functions [1]. Relevant scientific and technological advancement brought the responsibility of developing innovative and safe products [2]. In this context, natural actives with proven effectiveness have been increasingly researched [3].

Considering the Brazilian flora biodiversity and medicinal plants popular use, there is an interest in studying pharmacological properties of various plants. So, pharmaceutical industries recognized such importance and have been developing products with medicinal plants in recent decades [4]. Ergo, based on the pharmacological characteristics of plants with healing and emollient action and therapeutic potential for skin disorders, one stands out, *Stryphnodendron adstringens* (Mart) *Coville* (*S. adstringens*) [5].

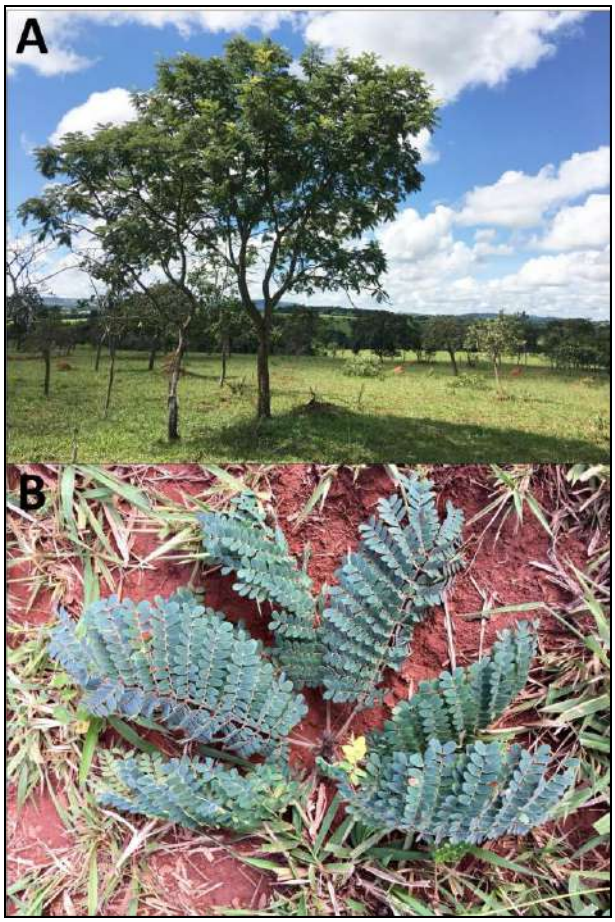
*S. adstringens*, popularly known as barbatimão, barba-de-timão, borãozinho-roxo, bark-da-virgindade, uabatimô, abaramotemo, casca-da-mocidade, faveiro and fill-cangalha, is a species belonging to the family Fabaceae and the subfamily Mimosoideae, widely distributed through the Brazilian cerrado [6]. Botanically, *S. adstringens* is considered an evergreen species with heights ranging from 2 to 8 meters [7]. Phytochemical characterizations showed that *S. adstringens* has as main secondary metabolites alkaloids, terpenes, flavonoids, steroids and specially tannins. The large amount of condensed tannins (20% to 50%) arouse the industry's interest for its pharmacological activities, such as antimicrobial [8, 9, 10], antiseptic [11], anti-inflammatory [12], antinociceptive [13], anti-ulcerative [14] and healing [15].

Due to its versatility and therapeutic potential, *S. adstringens* was included in the National List of Medicinal Plants of Interest to SUS [16] and recommended as healing herbal medicine in the Brazilian Pharmacopoeia 5$^{th}$ [17]. Based on its potential, this work aimed to develop and evaluate the stability of an emulsified system containing *S. adstringens* extract.

## 2. Material and Methods

### 2.1 Plant obtainment and extract preparation

*S. adstringens* leaves were collected in February 2021 at Latitude: 16.17469°S; Longitude: 50.30809°W (Figure 1). An exsiccate was identified by Professor Dr Edvande Xavier dos Santos Filho and deposited in the herbarium of the University Center Brasília de Goiás.




**Source:** Authors, 2021.

**Fig 1:** Botanical structures of *S. adstringens*: plant (A), leaves (B).

400 g of leaves from *S. adstringens* were taken to the Laboratory of Botany and Pharmacognosy in the University Center Brasília de Goiás, weighed and submitted to kiln-drying (Odontobras EL 1.3) at 40±0.5 °C for 5 days. Afterwards, the sample was ground in a Wiley knife micro mill (Tecnal TE-648) and 100 g of the ground powder was extracted by maceration in 500 mL of 95% methanolic solution for 7 consecutive days. The crude extract was later concentrated on a rotary evaporator (Quimis Q344M2) at 50 °C and weighed. Lastly, *S. adstringens* concentrated extract was dried in a hot-air oven (SolidSteel SSB13L) at 50±0.5 °C for 48 hours and weighed to calculate the yield (%) of the concentrated crude extract and after drying [18].

*S. adstringens* glycolic extract was prepared through static maceration of 10 g crude extract followed by percolation in 100 mL of a mixture of 70% propylene glycol (Casa dos Químicos, RS, Brazil) in water. The mixture was wetted with q.s. of the solvent for 24 hours to allow the extractor solvent to pass through the drug homogeneously [19].

### 2.2 Emulsion preparation

As described in Table 1, the hot emulsification method at 40 °C was applied [20]. By which, the components of each phase were heated separately, pouring the aqueous phase over the oily one, homogenizing them by means of vigorous agitation and, after cooling, including the complementary phase. The final preparation volume was 100 mL.

**Table 1:** The formulation composition.

| Components | Quantities |
|---|---|
| *S. adstringens* glycolic extract | 10 mL |
| Butylhydroxytoluene | 0,1 g |
| $Na_2$ EDTA | 1 g |
| Polawax® | 2 g |
| Glycerin | 10 g |
| Methylparaben | 0,6 g |
| Propylparaben | 0,6 g |
| Deionized water | q.s. 40 g |

### 2.3 Accelerated stability testing and Determination of organoleptic properties

After preparation, the formulation was subjected to physical-chemical and microbiological analyses. Samples were bottled in plastic and glass containers and stored at room temperature, in a refrigerator (5±2°C) and an incubator (37±2 °C).

The accelerated stability test was carried out in four different stages, at times $T_0$ (24 hours after production), $T_{15}$ days, $T_{30}$ days and $T_{60}$ days), as recommended by the Stability Guide for Cosmetic Products [21].

The macroscopic aspect can be classified as: paste, gel, fluid, viscous, volatile, homogeneous, heterogeneous, transparent, opaque or milky; unchanged, slightly separated, slightly precipitated, slightly cloudy, separated, precipitated or cloudy. As for color and odor, the product can be considered unaltered, slightly modified, modified or intensely modified [21]. So, the organoleptic characteristics were defined by evaluating the macroscopic appearance as viscous, homogeneous and opaque; brownish color; woody odor; tactile sensation of the emulsion in slightly unctuous and pH 4.0 - 6.0.

### 2.4 Compatibility to bottling material

#### 2.4.1 Bottling and formulation integrity

These parameters were established by observing the emulsion in the respective bottling during the study period, with the aim of recording possible deformities and/or significant changes in the formulation in relation to bottling [21].

#### 2.4.2 Content weight

The weight of the content was determined by weighing the full bottles and subtracting the values from the empty bottles. Samples analyzed were $T_0$ and $T_{60}$ days, under the three environments and the two bottling types. In addition, the maintenance or loss of water by evaporation and volatile materials was observed, as well as the declared weight on the label [21].

#### 2.4.3 Seal

The sealing of the bottles used was manually checked, observing how easy it was to open and close them and the possibility of leaks [21].

#### 2.4.4 pH determination

The emulsion Potential Hydrogen (pH) was determined in all samples by Merck® pH-indicator strips.

### 2.4.5 Microbiological analysis

In accordance with the specifications indicated in the Brazilian Pharmacopoeia 5th [17], specific culture media were used for the growth of the following microorganisms: Total aerobic mesophilic bacteria, *Escherichia coli*, *Pseudomonas aeruginosa*, *Salmonella* spp., *Staphylococcus aureus* and *Candida albicans*.

Emulsion samples at times $T_0$ and $T_{60}$ days, stored in plastic and glass containers, were distributed on each media following the technique of sowing by exhaustion in striations. And, for the Plate Count Agar (PCA) culture media, the sweeping seeding technique was applied. Forthwith, test and control dishes were incubated at 37 ºC and analyzed after 24 and 48 hours.

It is noteworthy that analyzes were performed in triplicate and, as recommended, 10% of the media produced were used for sterility testing [17, 21]. Herewith, it was guaranteed that the methodology used in the media preparation was adequate, avoiding a false-positive result from microorganisms arising from the culture medium itself.

## 3. Results and Discussion

### 3.1 *S. adstringens* crude extract obtainment

The crude methanolic extract from *S. adstringens* leaves produced a yield (w/w) of 20.14%, with an extractives content determination of 11.88%.

### 3.2 Accelerated stability testing, aspect and organoleptic properties

Results obtained in the stability test, aspect, organoleptic properties and pH are presented in Table 2.

**Table 2:** Physicochemical analysis of the emulsified systems containing *S. adstringens*.

| Environment / Parameters | | Formulation bottled in plastic container | | | | Formulation bottled in glass container | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | $T_0$ | $T_{15}$ | $T_{30}$ | $T_{60}$ | $T_0$ | $T_{15}$ | $T_{30}$ | $T_{60}$ |
| RT | Aspect | NC | NC | NC | SP | NC | NC | NC | NC |
| | Color | NC | NC | NC | NC | NC | NC | NC | NC |
| | Odor | NC | NC | NC | NC | NC | NC | NC | NC |
| | Tactile sensation | NC | NC | NC | NC | NC | NC | NC | NC |
| | pH | 4.0-5.0 | 4.0-5.0 | 4.0-5.0 | 4.0-5.0 | 4.0-5.0 | 4.0-5.0 | 4.0-5.0 | 4.0-5.0 |
| R | Aspect | NC | NC | NC | NC | NC | NC | NC | NC |
| | Color | NC | NC | NC | NC | NC | NC | NC | NC |
| | Odor | NC | NC | NC | NC | NC | NC | NC | NC |
| | Tactile sensation | NC | NC | NC | NC | NC | NC | NC | NC |
| | pH | 4.0-5.0 | 4.0-5.0 | 4.0-5.0 | 4.0-5.0 | 4.0-5.0 | 4.0-5.0 | 4.0-5.0 | 4.0-5.0 |
| I | Aspect | NC | SP | SP | P | NC | SP | SP | P |
| | Color | NC | SM | SM | M | NC | NC | SM | M |
| | Odor | NC | NC | SM | SM | NC | NC | SM | SM |
| | Tactile sensation | NC | M | M | M | NC | M | M | M |
| | pH | 4.0-5.0 | 4.0-5.0 | 4.0-5.0 | 4.0-5.0 | 4.0-5.0 | 4.0-5.0 | 4.0-5.0 | 4.0-5.0 |

Description: Environment (RT: room temperature, R: refrigerator, I: incubator); Aspect (NC: no change; SP: slightly precipitated, P: precipitated); Color, odor and tactile sensation (NC: no change; SM: slightly modified, M: modified).

The emulsified system containing *S. adstringens* freshly prepared ($T_0$) presented a viscous macroscopic appearance, homogeneous and opaque, slightly brownish, with a woody Odor, slightly unctuous to the touch and pH 4.0-5.0.

It is described that Polawax®, a non-ionic emulsifier, manifests a rheological behavior characterized as a time-dependent non-Newtonian fluid, which classifies it as thixotropic. This property establishes that the formed emulsion expresses a high viscosity when at rest and increasing fluidity when subjected to shear stress over time [22].

Samples conditioned at room temperature did not undergo considerable changes. Only slight surface hardening and a slightly precipitated at $T_{60}$ were observed on the formulation bottled in a plastic container. Souza & Ferreira (2010) [23] when evaluating the stability of emulsions, also observed a slight modification manifested by the surface hardening from 15th day on. The authors mentioned this occurred due to the loss of hydrophilic components by evaporation during heating, which occurred more intensely on the surface, thus increasing the concentration of less volatile components, which are generally more consistent.

Samples stored in the refrigerator did not change independent of the container they were stored, which demonstrates the emulsified system behaved stably at low temperatures. The most visible aspect in the samples was the maintenance of viscosity and the emulsion lightness to touch. According to Aulton (2005) [24], a product storage at low temperatures (above the freezing point) can increase its viscosity on a continuous phase. However, in the present work, this was not observed. The author mentions the maintenance of viscosity and kinetic energy, that is, the aspect of constancy and the absence of cremation must also be considered.

Related to samples stored at the incubator under a controlled temperature of 37 ºC, cremation (cream formation on the surface) was observed from $T_{15}$ onwards. This process occurs when dispersed droplets, under the influence of gravity, tend to float due to the difference in densities of the dispersed and dispersing phases. This occurrence is common in oil-in-water (O/W) or water-in-oil (W/O) emulsions, when the internal phase has a lower density than the external one. Even though it is reversible, and can be restored by mechanical agitation, an emulsified system under the creaming process can change the uniformity of the active concentration and even become aesthetically unacceptable [25, 26]. Furthermore, in the two conditioned containers, the emulsion color was modified on the surface due to cremation; the odor was changed and, especially, the tactile sensation was altered by the more apparent oily perception.

It is known that the pH of a pharmaceutical form has therapeutic importance for topical treatment [27]. Related to pharmacotechnical specification, emulsions must present the

pH according to the purposes for which they were formulated, keeping the value between 4.0 and 7.0, since the skin pH has values between 4.5 to 5.5 [28]. Therefore, it was noted that in all analyzes of the emulsified system containing *S. adstringens*, the pH did not change, always remaining between 4.0 and 5.0.

### 3.3 Compatibility with bottling material

By reason of direct contact with the formulation, containers are decisive in the product stability since they must not interact with each other, physically or chemically. If that occurs, there may be a compromise in the product quality, as well as in the concentration or purity of the bottled formulation [26]. Glass has qualities for bottling products, as it is a rigid, resilient material that does not deteriorate over time and is considered chemically inert. Plastic, on the other hand, can show permeability to atmospheric oxygen and humidity, leaching (ingredients transfer from the container to the stored product), active sorption to the plastic packaging, in addition to being more susceptible to external interference [27]. On that account, the alterations that occurred in this study are justified, such as loss of water by evaporation and the droplets found in some samples conditioned in the incubator, more accentuated on those conditioned for a longer time ($T_{60}$ days).

### 3.4 Bottling and formulation integrity

Bottling must provide adequate stability for carrying out studies and, thereby, provide information about the physical and chemical characteristics of the container, lids and other packaging components for the proposed product [25]. Accordingly, the integrity of the bottle was reflected in the stability of the formulations here, since they did not exhibit apparent changes such as deformation, softening or other factors that could affect their integrity.

### 3.5 Content weight

Emulsions bottled in plastic, aluminum or glass containers when well-sealed – prevent the product's water evaporation. Therefore, sealing becomes one of the interfering factors in reducing the weight of an emulsified system over time. However, when subjected to elevated temperature environments, they tend to accelerate the physicochemical reactions, altering emulsion stability [20]. The results obtained in this study reveal that, when comparing the average weight $T_0$ and $T_{60}$ days, the greatest loss occurred in the samples conditioned in the incubator, with values of 11.84% for the formulation bottled in a plastic container and 9.26% for the formulation bottled in glass container. In view of this, it is considered that the slight modification (surface hardening) was a result of components hydrophilic loss by evaporation during storage. Corroborating these facts, in the emulsions stored in the refrigerator, the smallest water loss due to evaporation was observed, with values of 3.88% for the formulation bottled in plastic container and 1.73% for the formulation bottled in glass container. And, at room temperature, the variation in weight loss was 6.14% for the formulation bottled in plastic container and 2.29% for the formulation bottled in glass container.

### 3.6 Seal

Conforming to Loyd (2013) [25], containers are classified according to their ability to protect the contents from external conditions. The alterations verified in the emulsified systems bottled in plastic containers suggest that the sealing in these packages may have been a limiting factor in this research. Plastic bottling protected the formulation from foreign solid particles, but did not prevent oxygen permeation and, therefore, loss of water by evaporation. The emulsified system containing *S. adstringens* bottled in glass container demonstrated greater stability.

### 3.7 Microbiological analysis

Table 3 determinates microbiological analysis results with the readings performed after 24 and 48 hours of incubation, at both established times ($T_0$ and $T_{60}$ days). It is observed that there was no growth of any of the microorganisms surveyed, demonstrating that time and humidity were not factors capable of influencing bacterial and fungal proliferation.

**Table 3:** Microbiological growth of the emulsified systems containing *S. adstringens*.

| Microorganism | Culture media | Formulation bottled in plastic container | Formulation bottled in glass container |
|---|---|---|---|
| Total aerobic mesophilic bacteria | Plate Count Agar | negative | negative |
| *Escherichia coli* | Eosin Methylene Blue Agar | negative | negative |
| *Pseudomonas aeruginosa* | Salmonella-Shigella Agar | negative | negative |
| *Salmonella* spp. | MacConkey Agar | negative | negative |
| *Staphylococcus aureus* | Manitol Agar | negative | negative |
| *Candida albicans* | Sabouraud Agar | negative | negative |

An ideal system should contain preservatives that are effective and stable in different pH ranges, compatible with other components and quick in inactivating microorganisms, consequently preventing deterioration caused by microorganisms from altering physical and chemical characteristics of the product [29, 30]. In the present study, it was observed that the selected preservatives were efficient and ensured the formulation to maintain adequate conservation.

At the end, it is noteworthy that, due to the antiseptic and antimicrobial properties attributed to *S. adstringens*, there is the possibility that it inhibited the growth of microorganisms during the analysis [5, 18]. Several studies have investigated and demonstrated the potential antimicrobial and antiseptic activity of *S. adstringens* [8, 9, 10, 11, 31], and the main compounds produced by its secondary metabolism and identified as responsible for its biological activities are alkaloids, terpenes, flavonoids, steroids and tannins, the latter being its predominant constituent [32; 33].

## 4. Conclusion

The emulsified system containing *Stryphnodendron adstringens* (Mart) *Coville* (Fabaceae) extract from the Brazilian cerrado were well developed and remained stable

during the evaluated period, especially in a refrigerated environment and bottled in glass container. Regarding microbiological aspects, no microorganism's growth was observed, meeting quality standards. Accordingly, results will serve as a subsidy for study continuity and definition of the formulation validity period.

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**6. Declaration of interest statement**
The authors report no declarations of interest. The authors alone are responsible for the content and writing of the paper.

**7. References**
1. Byrd AL, Belkaid Y, Segre JA. The human skin microbiome. Nature Reviews Microbiology. 2018 Mar;16(3):143-55.
2. Lim KM. Skin Epidermis and Barrier Function. International Journal of Molecular Sciences. 2021;22(6):3035.
3. Binic I, Lazarevic V, Ljubenovic M, Mojsa J, Sokolovic D. Skin ageing: natural weapons and strategies. Evidence-based Complementary and Alternative Medicine. 2013, 827248.
4. Ferreira PMP, Arcanjo DDR, Peron AP. Drug development, Brazilian biodiversity and political choices: Where are we heading? Journal of Toxicology and Environmental Health - Part B: Critical Reviews. 2023;26(5):257-274.
5. Souza-Moreira TM, Queiroz-Fernandes GM, Pietro RCLR. *Stryphnodendron* Species Known as "Barbatimão": A Comprehensive Report. Molecules. 2018;23(4):910.
6. Occhioni EML. Considerações taxonômicas no gênero *Stryphnodendron* Mart. (leguminosa e mimosoideae) e distribuição geográfica das espécies. Botanica Brasilica. 1990;4:153-158.
7. Felfili JM, Silva Júnior MC, Dias BJ. Rezende AV. Estudo fenológico de *Stryphnodendron adstringens* (Mart.) *Coville* no cerrado sensu stricto da fazenda água limpa no Distrito Federal, Brasil. Revista Brasileira Botânica. 1999;22:83-90.
8. Ishida K, Mello JC, Cortez DA, Filho BP, Ueda-Nakamura T, Nakamura CV. Influence of tannins from *Stryphnodendron adstringens* on growth and virulence factors of *Candida albicans*. Journal of Antimicrobial Chemotherapy. 2006;58(5):942-949.
9. Soares SP, Vinholis AHC, Casemiro LA, Silva MLA, Cunha WR, Martins CHG. Atividade antibacteriana do extrato hidroalcoólico bruto de *Stryphnodendron adstringens* sobre microorganismos da cárie dental. Revista Odonto Ciência. 2008;23(2):141-144.
10. Luiz RLF, Vila TVM, Mello JCP, Nakamura CV, Rozental S, Ishida K. Proanthocyanidins polymeric tannin from *Stryphnodendron adstringens* are active against *Candida albicans* biofilms. BMC Complementary and Alternative Medicine. 2015;15:68.
11. Souza TM, Moreira RRD, Pietro RCLR, Isaac VLB. Avaliação da atividade antisséptica de extrato seco de *Stryphnodendron adstringens* (Mart.) *Coville* e de preparação cosmética contendo este extrato. Brazilian Journal of Pharmacognosy. 2007;17:71-75.
12. Lima JC, Martins DT, de Souza Jr PT. Experimental evaluation of stem bark of Stryphnodendron adstringens (Mart.) Coville for anti-inflammatory activity. Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives. 1998 May;12(3):218-20.
13. Melo JO, Endo TH, Amado LEB, Svidzinski AE, Baroni S, Mello JCP, *et al*. Effect of *Stryphnodendron adstringens* (barbatimão) bark on animal models of nociception. Revista Brasileira de Ciências Farmacêuticas. 2007;43(3):465-469.
14. Audi EA, Toledo DP, Peres PG, Kimura E, Pereira WK, Mello JC, *et al*. Gastric antiulcerogenic effects of *Stryphnodendron adstringens* in rats. Phytotherapy research. 1999 May;13(3):264-6.
15. Eurides D, Mazzanti A, Belleti ME, Silva LAF, Fioravante MCS, Troncoso Neto NS, *et al*. Morfologia e morfometria da reparação tecidual de feridas cutâneas de camundongos tratadas com solução aquosa de barbatimão (*Stryphnodendron barbatiman* Martius). Revista da Fzva. 1996;3(1):30-40.
16. National List of Medicinal Plants of Interest to SUS - RENISUS. 1 ed, Ministério da Saúde, Brasília, 2009, p. 1 and 2.
17. Brazilian Pharmacopoeia. 5 ed, ANVISA, Brasília, 2010, vol. 1 & 2.
18. Carvalho GG, Peres GC, Mendonça RMC, dos Santos Filho, EX. Phytochemical prospection and antibacterial activity of native plants from the cerrado of Goiás, Brazil. Journal of Pharmacognosy and Phytochemistry. 2020;9(4):29-37.
19. Ardisson L, Godoy JS, Ferreira LAM, Stehmann JR, Brandão MGL. Preparação e caracterização de extratos glicólicos enriquecidos em taninos a partir das cascas de *Stryphnodendron adstringens* (Mart.) *Coville* (Barbatimão). Revista Brasileira de Farmacognosia. 2002;12(1):27-34.
20. Ferreira AO, Brandão MAF, Polonini HC. Guia Prático da Farmácia Magistral. 5 ed, São Paulo, Editar, 2018, 4-20.
21. Agência Nacional de Vigilância Sanitária - ANVISA. Guia de Estabilidade de Produtos Cosméticos. 1 ed (updated). ANVISA, Brasília, 2020, 5-52.
22. Valverde TM, Soares BNGS, Nascimento AMD, Andrade ÂL, Sousa LRD, Vieira PMA, *et al*. Anti-Inflammatory, Antimicrobial, Antioxidant and Photoprotective Investigation of Red Propolis Extract as Sunscreen Formulation in Polawax Cream. International Journal of Molecular Sciences. 2023;24(6):5112.
23. Souza VB, Ferreira JRN. Desenvolvimento e estudos de estabilidade de cremes e géis contendo sementes e extratos do bagaço da uva Isabel (*Vitis labrusca* L.). Revista de Ciências Farmacêuticas Básica e Aplicada. 2010;31(3):17-22.
24. Aulton ME. Delineamento de Formas Farmacêuticas. 2 ed, Porto Alegre, Artmed, 2005, 97-276.
25. Loyd VAJ. Formas farmacêuticas e sistemas de liberação de fármacos. 9 ed, Porto Alegre, Artmed, 2013, 155-310.
26. Xavier-Junior FH, Vauthier C, Morais AR, Alencar EN,

Egito ES. Microemulsion systems containing bioactive natural oils: an overview on the state of the art. Drug Development and Industrial Pharmacy. 2017;43(5):700-714.
27. Derwin R, Patton D, Avsar P, Strapp H, Moore Z. The impact of topical agents and dressing on pH and temperature on wound healing: A systematic, narrative review. International Wound Journal. 2022;19(6):1397-1408.
28. Lukić M, Pantelić I, Savić SD. Towards Optimal pH of the Skin and Topical Formulations: From the Current State of the Art to Tailored Products. Cosmetics. 2021;8(3):69.
29. Halla N, Fernandes IP, Heleno SA, Costa P, Boucherit-Otmani Z, Boucherit K, Rodrigues AE, Ferreira ICFR, Barreiro MF. Cosmetics Preservation: A Review on Present Strategies. Molecules. 2018;23(7):1571.
30. Herman A. Antimicrobial Ingredients as Preservative Booster and Components of Self-Preserving Cosmetic Products. Current Microbiology. 2019;76(6):744-754.
31. Ishida K, Rozental S, de Mello JC, Nakamura CV. Activity of tannins from Stryphnodendron adstringens on Cryptococcus neoformans: effects on growth, capsule size and pigmentation. Annals of Clinical Microbiology and Antimicrobials. 2009 Dec;8(1):1-0.
32. Panizza S, Rocha AB, Gecchi R, Souza e Silva RAP. *Stryphnodendron barbadetiman* (Vell.) *Martius*: teor de taninos na casca e sua propriedade cicatrizante. Revista Brasileira de Ciências Farmacêuticas. 1988;10:101-106.
33. Lima TCD, Cardoso MV, Modesto T, Oliveira ALB, Silva MN, Monteiro MC. Brief review ethnobotany, phytochemistry and pharmacology of *Stryphnodendron adstringens* used in the Amazon. Revista Fitos. 2016;10(3):220-372.