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Solid lipid nanoparticles highly loaded with brazilian biodiversity amazon butters: One alternative to improve their product sensory and rheology.

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1. Introduction

Amazon forest has countless oleaginous plant species rich in fatty acids, with potential use in the food, pharmaceutical, and cosmetic industries, even though rainforest plant materials have been extensively used by indigenous groups for millennia, it was only in recent times that the Amazonian ethnobotanical culture started to be discovered and considered for the development of phytopharmaceuticals [1]. *Viola surinamensis*, known as ucuuba, is widely used by the riverside inhabitants to treat different disorders, seed oil is used topically for inflammatory skin conditions and as a preventive for microbial infections during wound healing [2]. *Astrocaryum murumuru*, commonly known as murumuru, has a long history of use by traditional Amazonian populations, the pulp of the fruit served as food, and the seeds were processed to extract butter and oil, which were used as natural moisturizers [3]. *Theobroma grandiflorum* called by Cupuassu, presents a taxonomic relationship with cocoa (*Theobroma cacao* L.) and is one the most popular native fruits cultivated in the Brazilian Amazon region, has been traditionally consumed as food, valued for its nutritional and energetic properties and recently has been explored by cosmetic industry [4].

Ucuuba fat is rich in myristic acid (77.48 %), which is rarely found in other oleaginous plants, making it a unique source of this saturated fatty acid [5]. Lauric (C12:0) and myristic (C14:0) are the main fatty acids in ucuuba raw seed butter, representing a sum of of approximately 85% of total fatty acid contente. Capric (C10:0), myristoleic (C14:1), palmitic (C16:0), oleic (C18:1) and linoleic (C18:2) acids are also present in concentrations higher than 1% of total fatty acid content [6].

Murumuru butter was analyzed by gas chromatography and revealed that the major component of *Astrocaryum murumuru* butter is contained by lauric acid (40%) and myristic acid (29.3%) [1]. It also shows high oxidative stability due to its high content of saturated fatty acids (90%) and antioxidants such as tocopherols and β-carotene. Murumuru fat contains all tocopherol isomers, with α- and β-tocopherol together accounting for about 92% of the total methyl tocols [5].

Cupuassu seed represents about 30–45% of the fruit's weight and is mainly discarded as industrial waste, the recycling of these residues may reduce the environmental impact associated to their disposal, hence adding value to the whole production chain. The seeds are highly rich in proteins, minerals, bioactive compounds, and fat, presenting a varied content of fatty acids (60%). Oleic acid is an important constituent of Cupuassu seeds and has been demonstrated to induce a faster wound closure when compared to linolenic and linoleic acids [7].

Fatty acids are essential metabolites with crucial cellular functions, including cell migration, development, differentiation, and proliferation, also influencing human cell processes [7]. Unsaturated fatty acids, such as linoleic acids, are crucial arachidonic acid precursors, an essential inflammatory mediator in wound healing, play a direct role in tissue regeneration through the formation and deposition of collagen fibers [1]. They can modulate the release of pro-inflammatory cytokines, affecting neutrophil migration, increasing the wound healing tissue mass while decreasing the thickness of the necrotic cell layer edge around the wound, and ultimately modulating the closure of skin wounds [7]. Solid lipid nanoparticles (SLNs) are a colloidal delivery system made from solid (under room temperature) lipids with particle sizes varying from 50 to 500 nm, generally comprise single lipids or blends such as fatty acids which are stabilized by a layer consisting of a single surfactant or through a mixture of surfactants which result in smaller particle size and improved storage stability [8]. Depending on the nanosystem characteristic it can promote tissue interaction and active penetration, especially for highly lipophilic compounds, which generally show a low penetration into the inner skin layers. In this way, bioavailability and, consequently, formulation effectiveness can be increased [7].

These characteristics make Ucuuba, Murumuru and Cupuassu fats valuable for their unique lipid compositions and potential applications in various industries. Studies to optimize the processing of oils and fats are needed to obtain a product of uniform quality and to add commercial value [5].

Therefore, this study aimed first to develop SLNs of vegetable butters in water to improve rheology aspects of final products, transforming what would be solid creams into liquid milky lotion and second to enhance sensory and consumer's perception of Ucuuba formulation.

2. Materials and Methods

2.1 Development Formulation

Three different SLNs were prepared using isolated Amazon butters each one: Ucuuba (INCI: Virola surinamensis seed butter), Cupuassu (INCI: Theobroma grandiflorum seed butter) and Murumuru (INCI: Astrocaryum murumuru seed butter). The butters were supplied by a local cooperative of collectors in Pará state, in Brazil, and followed the compliance with Brazilian National regulations for biodiversity protection and sanitary production. Their level of application was 15%, w/w. The emulsifier system was one specific proportional mix of steareth-2 and steareth-21, and butters were dispersed in caprylic capric triglycerides. Tocopherol acetate was added for antioxidant protection and a mix of Benzyl Alcohol and Dehydroacetic Acid were used as preservative. Purified water was used as vehicle. The SLNs were prepared using high-pressure homogenization technique using hot process. The emulsions were prepared using minimal shear by rotor-stator at 85°C for the necessary time for the mixing in a separate vessel, and right after, keeping the temperature, they were passed through the high-pressure homogenization. The pressure used was 1,200bars for first stage and 120bar for second stage, and two cycles of homogenization were made. The product was collected and kept under low naval propeller mixing until reach room temperature (25°C). The preservative was added and preparation was finished.

2.2 SLN characterization and stability

The SLN of ucuuba butter particle size was characterized in triplicate using Electrophoretic Light Scattering (ELS). The three SLNs were included in accelerated stability program following Brazilian National Sanitary Vigilance Agency (ANVISA) guidelines, exposing them to high (45°C) and cold (4°C) temperature for 3 months to verify their properties. The viscosity was checked using LVT (low viscosity) rotation viscometer method.

2.3. Clinical study

This study was designed as a single-center, single-blind, non-comparative clinical trial, aimed at verifying the dermatological safety and perceived efficacy of the investigational product, the SLN of Ucuuba. The trial was conducted in adherence to ethical guidelines, including the principles outlined in Resolution 466/2012 by ANVISA (Brazilian Health Regulatory Agency).

Panel was formed by 32 female participants aged between 21 and 65 years. Participants had intact skin in the experimental area and exhibited skin characteristics ranging from mixed to dry and diverse Fitzpatrick phototypes ranging from I to VI, thereby representing the intended user profile for this product, all kind of types, regarding population demographic and consumer profile appreciability in Brazil, occasional users of products in this category was included in inclusion criteria. Safety requirements evaluated by dermatology physicians were included and all participants signed informed consent, in compliance with Ethical Compliance and

Consent. SLN of Ucuuba was delivered to participants during the initial visit. Each participant was instructed to apply the product daily for seven days to the body and/or face.
Perception assessment was studied through participants responses collected at Day 7 with self-reported questionnaires evaluating parameters related to hydration, elasticity, tone uniformity, and reduction of roughness, on a scale of perceived improvements. These assessments allowed the collection of subjective data regarding the product's cosmetic acceptability.

Table 1. Perception assessment: Self-reported questionnaire.

PARAMETER	QUESTION	RESPONSES
Skin condition before the test	How do you feel about your skin before starting this test?	1 = Dry, 2 = Normal, 3 = Oily
Dry touch feeling	How do you evaluate the dry touch sensation on your skin?	1 = Very bad, 2 = Bad, 3 = Indifferent, 4 = Good, 5 = Very good
Absorption	How do you evaluate the product absorption on your skin?	1 = Very bad, 2 = Bad, 3 = Indifferent, 4 = Good, 5 = Very good
Soft skin	How do you evaluate the sensation of softness on your skin?	1 = Very bad, 2 = Bad, 3 = Indifferent, 4 = Good, 5 = Very good
Improved skin appearance	How do you evaluate the improvement in skin appearance?	1 = Very bad, 2 = Bad, 3 = Indifferent, 4 = Good, 5 = Very good
Hydration for body skin	How do you evaluate the hydration that the product provides to your body?	1 = Very bad, 2 = Bad, 3 = Indifferent, 4 = Good, 5 = Very good
Hydration for facial skin	How do you evaluate the hydration that the product provides to your face?	1 = Very bad, 2 = Bad, 3 = Indifferent, 4 = Good, 5 = Very good
Texture description	How would you describe the product texture in one word?	1 = Light, 2 = Fluid, 3 = Concentrated
Application areas	In which areas of your body did you use the product?	1 = Entire body, 2 = Face, 3 = Dry areas of the body
Frequency of usage	How often would you use this moisturizer in your skincare routine?	1 = Morning, 2 = Night, 3 = Throughout the day
Uniform skin tone	Did the product even out your skin tone?	Yes / No
Increased skin elasticity	Did the product increase the elasticity of your skin?	Yes / No

Reduced fine lines	Did the product reduce fine lines?	Yes / No
Reduced roughness and flaking	Did the product reduce roughness and flaking?	Yes / No
Reduced skin cracks	Did the product reduce cracks on your skin?	Yes / No
Improved skin tone and firmness	Did the product improve skin tone and firmness?	Yes / No
Reduced itching	Did the product reduce itching?	Yes / No
Induced skin oiliness	Did the moisturizer cause oiliness on your skin?	Yes / No
Other benefits	Have you noticed any other benefit? If yes, specify: _____	Open-ended
Improvement suggestions	What would you like to change in the moisturizer and packaging to make it more appealing?	Open-ended

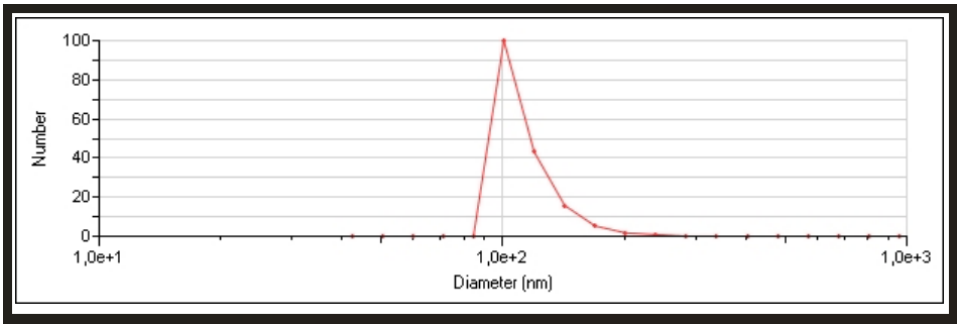
3. Results

Homogeneous and liquid formulations were obtained successfully. Results are shown in Table 2 and Figure 1.

Table 2. Particle size (nm) and polydispersion index results for SLN – Ucuuba butter. Results are in triplicate.

SAMPLE	DIAMETER (NUMBER) – NANOMETERS (nm)	POLYDISPERSION INDEX
1	201,06	0,205
2	214,82	0,409
3	209,21	0,409
AVERAGE	208.36	0,37
S.D.	6,92	0,15

Figure 1. Average particle size distribution in number of SLN made with Ucuuba butter.



Stability of three SLNs was performed, and results confirmed the stable profile of particles. Results are shown in Table 3.

Table 3: Accelerated stability results of SLNs.

		SPECIFICATION	INITIAL	UCUUBA 90 DAYS	CUPUASSU 90 DAYS	MURUMURU 90 DAYS
Aspect (23±3ºC)	5ºC	LIQUID EMUL-SION	CON-FORM	CON-FORM	CONFORM	CONFORM
	ROOM		CON-FORM	CON-FORM	CONFORM	CONFORM
	45ºC		CON-FORM	CON-FORM	CONFORM	CONFORM
Color (23±3ºC)	5ºC	WHITE TO BEIGE	CON-FORM	CON-FORM	CONFORM	CONFORM
	ROOM		CON-FORM	CON-FORM	CONFORM	CONFORM
	45ºC		CON-FORM	CON-FORM	CONFORM	CONFORM
Odor (23±3ºC)	5ºC	CHARACTERIS-TIC TO THE BUTTER	CON-FORM	CON-FORM	CONFORM	CONFORM
	ROOM		CON-FORM	CON-FORM	CONFORM	CONFORM
	45ºC		CON-FORM	CON-FORM	CONFORM	CONFORM
pH (23±3ºC)	5ºC	4,0 – 5,0	CON-FORM	CON-FORM	CONFORM	CONFORM
	ROOM		CON-FORM	CON-FORM	CONFORM	CONFORM
	45ºC		CON-FORM	CON-FORM	CONFORM	CONFORM

The primary rheological distinction between the SLN of each butter and its traditional emulsion form is the relative viscosity, as shown in Table 4.

Table 4. Viscosity comparison between SLNs and their correspondent traditional emulsion.

VISCOSITY (24h after production)	**SLN method: LVT, #61, 3 rpm, 5 min, 23°C**	**TRADITIONAL EMULSION method: LVT, #64, 1.5 rpm, 3 min, 23°C**
UCUUBA	LIQUID: 200 - 500cP	THICK CREAM: 85.000 - 120.000cP
MURUMURU	LIQUID: 200 - 500cP	THICK CREAM: 85.000 - 120.000cP
CUPUASSU	LIQUID: 200 - 500cP	THICK CREAM: 85.000 - 120.000cP

In order to verify consumer evaluation and sensory experience, clinical study was performed with SLN of Ucuuba, results of self-questionnaire are shown in Figure 2 and Figure 3.

Figure 2. Appreciability study: Hydation, Dry touch and Texture.

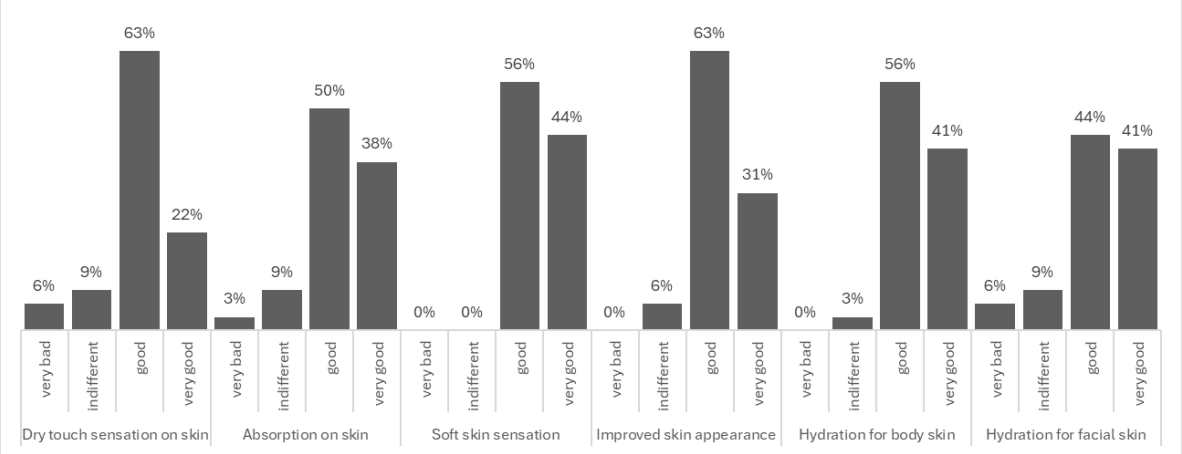
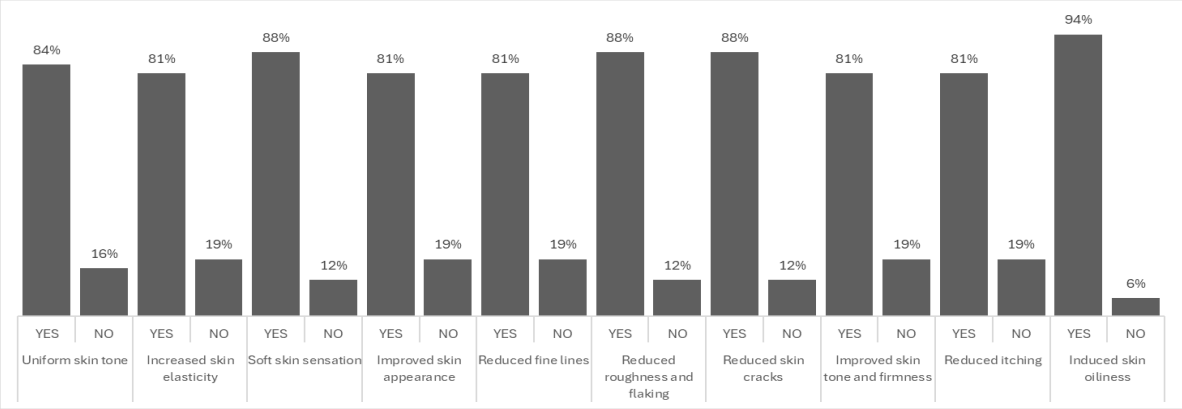


Figure 3. Appreciability study: Improvement in skin condition and Oilness.



4. Discussion

Homogeneous and liquid stable formulations were obtained successfully. Ucuuba butter SLN was chosen to perform particle size, due to the fact it has the highest melting point among the three SLNs made, thanks to its lipid composition, therefore it is expected to have the worst-case scenario for particle size, considering the fact butter composition was the only difference amongst the three SLNs. The results evidenced the nanoscale size of particles. Results are shown in Table 2, Table 3 and Figure 1.

The main rheological difference between the SLN of each butter correspondingly to it version without being transformed to SLN (traditional emulsion) is relative viscosity. The high level of butter load to these formulations (15% w/w) in traditional emulsions results in products with thick cream appearance, thanks to their composition rich in long carbon chain lipids and high melting points. This is a dilemma; these thick creams can be a consumer experience barrier once often are related to unpleasant texture experiences however high level of butters are necessary for better skin benefits. Unfortunately, due to the own limitation of the LVT technique, results nod made under the same viscosity method are not able to be fairly compared, however, they can be demonstrated for trend analyses and characterization purposes in table 4. The results and much more the aspect observation evidenced the transformation that SLN creation does to the aspect of product, from thick cream to liquid emulsions, even with exact same levels of butters in composition. The SLNs creation is a physical method able to transform the aspect of formulations without touching the levels of butters.

Consumer evaluation and sensory experience performed with SLN of Ucuuba indicated moisturizing benefits, at the same time, a soft texture, rapid absorption, velvet dry touch [6]. Findings demonstrated high aprecciability (Figure 2) related to Hydration on face (85%) and body (97%), Dry touch skin (85%) and Absorption on skin (88%), combined with Texture described by volunteers as Fluid (53%) and Light (28%), confirming Ucuuba composition and benefits decribed in Introduction and also the Hypothesis that SLNs of vegetable butters in water would improve sensory to enhance consumer’s perception of formulations.

In addition, Improvement in Skin Condition was well evaluated (Figure 3), after 7 days of usage for skin appearance, firmness, elasticity and reduction in fine lines, contributing to know data composition and the skin rennovation potential described in literature [9]. Oilness perception was evaluated (Figure 3) to identify if SLN of Ucuuba could present any restriction of use on face, and 94% reported that the product did not induce oiliness. Besides that, in the beginning of study 21% classified their skin as oily prior to using the product and post-product use, 15% of participants felt their skin was oily, indicating the product didn’t cause oilness in skin.

According to Figure 3, SLN of Ucuuba was able to reduce Itching (81%), Skin cracks (88%) and Roughness/Flaking (88%), indicating it has potential to sensitive skin.

These results underscore the product's ability to maintain or improve skin hydration and condition without inducing greasy sensations or visual oiliness.

5. Conclusion

Results showed SLNs were made successfully with particle size within what established for SLNs and stable under accelerated studies. The main goal for rheology characteristic was reached, to transform thick creams into milky-liquid format, while keeping the high levels of Amazon butters in the composition. Human clinical trials confirmed the format appreciability in both sensory and performance. Perception study with volunteers demonstrated that SLN of Ucuuba offers hydration benefits while ensuring compatibility with diverse skin types, including those prone to oiliness. In addition, there was improvement in skin condition, related to firmness, elasticity and reduction of fine lines after 7 days of usage. The technique of SLNs was able to transform the Amazon biodiversity butters into more appealing-to-use final products.

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