RESEARCH ARTICLE

Antioxidant, Photoprotective and Thermoresponsive Nanoemulgel based on Pluronic® F127 and *Hymenaea courbaril* Extract

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Abstract

Introduction: The objective of the present work was to prepare a thermoresponsive nanoemulgel based on a natural extract extracted from the stem of *Hymenaea courbaril* for photoprotective cosmetic application. Topical photoprotection is restricted due to the short half-life of synthetic active ingredients on the skin, which requires frequent reapplications and presents potential risks of side effects.

Methods: The *H. courbaril* extract was initially obtained and characterized for the total phenolic and flavonoid content. A nanoemulsion based on the extract was prepared, identified and incorporated into a Pluronic® F127 gel to obtain the nanoemulgel. The antioxidant and photoprotective activities of the nanoemulgel and the extract were determined. The tube inversion method identified the sol-gel transition temperature of the nanoemulgel. The extract obtained showed a high value of total phenolics and flavonoids. The nanoemulsion containing the encapsulated extract presented zeta potential, diameter and polydispersity index values compatible with colloidal stability.

Results: The nanoemulgel showed antioxidant and photoprotective activity with an SPF of 2.3 ± 0.1 and thermoresponsive characteristics with a sol-gel transition temperature of 23 to 24°C, showing promise as a new cosmetic photoprotector that can contain lower concentrations of substances synthetic due to the SPF complementation attributed to the *H. courbaril* stem extract.

Keywords: *Hymenaea courbaril*, Antioxidant, Photoprotector; Nanoemulgel, Pluronic® F127.

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Introduction

Topical photoprotection is a first-line prevention strategy for skin cancer, including melanoma and non-melanoma skin cancer. However, topical photoprotection may have limitations due to its especially short half-life on the skin, which requires frequent reapplications and poses potential risks of side effects.[1] Additionally, a clinical study demonstrated that people who used sunscreen formulations containing the active synthetic photoprotectors oxybenzone, cinnamates, PABA derivatives (p-aminobenzoic acid) and azo-naphthol showed allergic skin reactions.[2] Furthermore, there are reports in the literature of studies on the photoprotective activity of natural extracts with the prospect of reducing the amount of synthetic chemical sunscreens in photoprotective formulations.[3,4]

A promising issue is the search by substances of plant origin with photoprotective activity to be incorporated in sunscreen formulations. The concept of green cosmetics has excellent public acceptance, and there is a growing tendency to incorporate plant compounds with pharmacological properties in sunscreen formulations.[5]

Studies show that the hydrophilic extract of the leaves of *Polypodium leucotomos*, the extract of the stem bark of *Spondias purpurea*, the extract of the leaves of *Marcetia macrophylla* exhibit photoprotective activity associated with the presence of flavonoids and phenolic compounds.[3,6,7]

Hymenaea courbaril, popularly known as Jatobá, belongs to the Fabaceae family, subfamily Caesalpinioideae, is well distributed throughout Brazil, occurring in almost all regions. Costa *et al*. (2021) reported that Jatobá stem sap extract has the potential to induce the healing of skin wounds due to its antioxidant activity associated with the presence of phenolic and flavonoid compounds such as catechins, proanthocyanidins, quercetin and taxifolin.[4,6,8]

Given what was exposed by Costa *et al.* (2020) and in line with what has been reported by other authors regarding extracts from plant species containing flavonoids and phenolic compounds, the hypothesis can be suggested that the extract from the stem of *H. courbaril* may have antioxidant and photoprotective activity, which may be experimentally proven.[3,6,7] Matos *et al* (2024), also demonstrated that the *H.*

courbaril extract has pharmacological potential and for use in the food industry.[9]

At the same time, other studies demonstrate that antioxidant actives from plant extracts are unstable when exposed to sunlight due to photodegradation.[10] A viable strategy to improve the stability of photosensitive actives is encapsulation in nanocarriers such as nanoemulsions. The simultaneous encapsulation of sunscreens, antioxidants and actives in nanoemulsions can also generate an efficient, stable and longer-acting photoprotective cosmetic formulation.[11] Martin *et al* (2023), reported a topical formulation containing a natural compound (rutin), in association with solid lipid microparticles from the UVA filter, with the aim of evaluating whether the photoprotection of the sunscreen was impaired by the microencapsulation process caused by UVA radiation. The topical formulation showed that the microencapsulation process promoted photoprotection, showing that the microencapsulation process is promising for use in sunscreens.[11]

An already known nanostructured strategy for encapsulating drugs is nanoemulsions, which are oil-in-water or water-in-oil dispersions with droplets in the range of 20 to 500 nm, formed by a dispersed phase in a continuous phase, stabilized with the use of surfactants.[10] Nanoemulsion drug delivery systems are a shows potential tool for delivering and improving the bioavailability of hydrophobic drugs.[12]

A versatile surfactant in the preparation of nanoemulsions that has thermoresponsive characteristics is Pluronic® F127. Pluronic® F-127 is a triblock copolymer containing in its structure a central block with 69 units of poly(propylene oxide) and two blocks at the ends containing 99 units of poly(ethylene oxide). It forms a thermoreversible aqueous gel and has been used in routes of oral and topical, intranasal, vaginal and rectal, ocular and parenteral drug administration.[13,14] Aqueous solutions of Pluronic® F127 of 20 to 30% (w/w) are liquid at refrigerated temperatures (4–5°C) and as a gel at room temperature, which can prolong the pharmacological action at body temperature.[15]

Linseed oil (*Linum usitatissimum*) was used as the oil phase in the present work, a source of essential fatty acids *α*-linolenic acid (50–60%), due to its antioxidant properties and carriers of drugs in emulsions.[13,16,17]

Nanoemulgels are suitable for drug delivery as they comprise a nanoscale emulsion and a gel base, combined in a single formulation. The nanoemulgel's nanoemulsion protects the drug, preventing enzymatic degradation and certain reactions such as hydrolysis. The gel base attributes thermodynamic stability to the nanoemulsion by increasing the viscosity of the aqueous phase, stabilizing the emulsion.[18]

In the literature, reports of oil-in-water nanoemulsions based on ethanolic extract of plant species such as *Centella asiatica*, propolis and *Catharathus roseus* were prepared and showed stability.[19-21] Nanoemulgel based on ethanolic extract of *Garcinia mangostana* in coconut oil was prepared for topical use with antioxidant properties.[22]

In view of the above, the hypothesis is that phenolic compounds from *H. courbaril* may have photoprotective and antioxidant activity and can be carried in nanoemulgel for topical use.

In the present study, the extract of the stem bark of *H. courbaril* was obtained and incorporated into nanoemulgels through encapsulation in nanoemulsion based on linseed oil. The antioxidant and photoprotective properties of the extract and the nanoemulgel containing the extract were evaluated. The results obtained in this research may contribute to the development of photoprotective and antioxidant formulations based on natural substances as a future alternative for replacing or reducing the amount of synthetic photoprotective substances in sunscreen formulations.

Materials and Methods

Linseed oil (*L. usitatissimum*) purchased from Campestre (Sao Paulo, Brazil) previously characterized in a previous study, containing 49% α-linolenic acid. Pluronic® F127 (molecular mass 12,600 Daltons, 98%), Quercetin (pharmaceutical grade, 99%), DPPH (1,1-diphenyl-2-picrylhydrazyl), Folin-Ciocalteu Reagent and Gallic Acid (98%) purchased from Sigma-Aldrich (St. Louis, USA). Aluminum chloride hexahydrate PA and Ethyl acetate PA purchased from Dinâmica (São Paulo, Brazil). MilliQ ultrapure water.

Plant specie

Samples of stem bark of *H. courbaril* were acquired in September 2022 from commerce in the municipality of Maracanaú (Ceará, Brazil) and the use of this specie was registered in the *Sistema Nacional de Gestão do Patrimônio Genético e Conhecimento Tradicional Associado* (SisGen) by the number A4E7973. The stem bark samples were dried and ground at 20°C for seven days.

Stem bark extract

The extract was obtained by macerating the dry material (each batch with 5 g of stem bark and 300 mL of ethyl acetate under constant agitation for 48 hours). The crude extract was concentrated in a rotary evaporator at 45°C, filtered on 0.28 µm, and freeze-dried. The obtained dry extract was characterized according to the content of total phenolics and total flavonoids.

Total Phenolics

The total phenolic value was determined by the Folin-Ciocalteu method.[23] An aliquot (0.025 mL) of the hydroethanolic extract solution (1-mg mL^{-1}) was diluted to 0.5 mL and mixed with 0.5 mL of Folin-Ciocalteu reagent, 1.0 mL of 20% m/v of sodium carbonate (Na_2CO_3) and 1.0 mL of distilled water. The mixture was vortexed and allowed to stand for 30 minutes at room temperature and out of the reach of light. Absorbance was then measured at 700 nm using the spectrophotometer (Genesys 10S, Thermo Scientific, USA). Gallic acid (10–1000 µg mL^{-1}) was used in the construction of the standard curve. Values (in triplicate) were expressed in milligrams of gallic acid equivalents (mg EAG) per gram of extract.

Total Flavonoids

The total content of flavonoids was determined according to the aluminum chloride colorimetric method.[3] Aliquots of *H. courbaril* extract solution (0.5 mL) were mixed with 1.5 mL of 95% ethanol, 0.1 mL of 10% w/v aluminum chloride hexahydrate ($AlCl_3$. $6H_2O$), 0.1 mL of 1 mol L^{-1} sodium acetate (CH_3COONa) and 2.8 mL of deionized water. After 40 min at room temperature, the absorbance of the mixture was measured at 415 nm using ultrapure water as a blank in a spectrophotometer (Genesys 10S, Thermo Scientific, USA). Quercetin solutions (1–500 µg mL^{-1}) were used in constructing the standard curve. Data (in triplicate) were expressed in milligram quercetin equivalents (EQ)/g extract.

Nanoemulgel preparation

Approximately 65 mg of dry extract of *H. courbaril* was weighed, according to the maximum solubility achieved in the oil, added to 2.50 g of *L. usitatissimum* seed oil, and heated to 40°C under stirring for 1-hour. Then, 10.6 g of an aqueous solution of Pluronic® F127 at 30% m/m at 3 to 5°C and 0.335 g of extract were added, vortexed for 10 seconds and subjected to sonication in a Branson Sonifier 450 ultrasonicator for 1-minute in amplitude 70%, 5 seconds on and off under ice bath. A nanoemulgel composed of 2.5 g of *L. usitatissimum* seed oil was prepared to compare the antioxidant activity. Then, 10.6 g of an aqueous solution of Pluronic® F127 at 30% m/m was added at 3 to 5°C, stirred on a vortex for 10 seconds and subjected to sonication in a Branson Sonifier 450 ultrasonicator for 1-minute at 70% amplitude 5 seconds on and off under an ice bath and only after the nanomulgel was formed was 0.400 g of extract added.

Particle size, zeta potential and polydispersion index

Nanodroplet size, estimated by mean hydrodynamic diameter, polydispersion index (PdI) and zeta potential (ζ), were determined by dynamic light scattering (DLS) and doppler microelectrophoresis using a NanoZS® (Malvern Instruments, Worcestershire, UK). Measurements were taken at a 90° angle after dispersing 50 µL of nanoemulsions in 5.0 mL of Milli-Q water. All measurements were performed in triplicate at 25°C with comparable conductivity to determine the zeta potential.[13]

Tube inversion test

Sol-gel phase transition behavior of the nanoemulgel was determined using the tube inversion method. A volume of 1.5 mL of solution was placed in a glass tube with an internal diameter of 17 mm. The sample was subjected to a temperature increase in the range of 10 to 37°C, at a rate of 1°C/observation, and the lowest critical gelling temperature (transition from sol to gel) was determined. Each step consisted of a 1°C temperature increase, followed by isothermal maintenance for 5 minutes and tube inversion, which allowed a visual inspection of the phase transition occurrence. Sol and gel were identified as liquid sol with flow and gel as solid without flow in the 30 s inspection.[24]

Antioxidant activity

The antioxidant activity of the extract and the nanoemulgel was investigated by the radical DPPH$^{\cdot}$ method in triplicate.[3] Two curves were prepared for the extract and for the nanoemulgel. 2.5 mL of each concentration was mixed with 1.0 mL of a 0.3 mmol L^{-1} of ethanolic DPPH solution at room temperature in the dark for 30 min. Absorbance was measured at 518 nm in a UV-vis spectrophotometer (Genesys 10S, Thermo Scientific, USA). Ethanol was used as a blank solution. The assessment of antioxidant activity was expressed as the mean maximum inhibitory concentration (IC_{50}). Quercetin was used as a standard. The DPPH$^{\cdot}$ radical scavenging capacity of the sample was calculated according to Equation 01:

$$\text{Scavening capacity } (\%) = \frac{Ac-As}{Ac} x100 \qquad \text{(Equation 01)}$$

Where, Ac is the absorbance of the control and As is the absorbance of the sample with DPPH solution. The inhibitory concentration (IC50) was calculated using a linear equation.

In-vitro photoprotective activity

In-vitro, UVB photoprotection was evaluated using the spectrophotometric method described by Sayre *et al.* (1979) of the dry extract and the nanoemulgel.[25] The SPF determination is the correlation between the erythemogenic effect (EE) and the radiation intensity in each wavelength (I) (Table 1).

Initially, 1.0 g of the sample was weighed, transferred to a 100 mL volumetric flask, diluted to volume with ethanol, followed by ultrasound for 5 minutes, filtered through cotton, discarding the first 10 mL. A 5.0 mL aliquot was transferred to a 50 mL volumetric flask and diluted to volume with ethanol. Then, a 5.0 mL aliquot was transferred to a 25 mL volumetric flask and the volume was completed with ethanol. Subsequently, a spectrophotometric scan was performed at wavelengths between 290 to 320 nm, with 5 nm intervals, and readings were performed using a quartz cell (1-cm), and ethanol used as a blank. The calculation of the sun protection factor (SPF) was obtained according to Equation 02:

$$SPF = 10 \text{ x } \sum_{290}^{320} EE\ (\lambda) \text{x I x Abs} \qquad \text{(Equation 02)}$$

EE is the erythermogenic effect, I is the radiation intensity, and Abs is the absorbance read at the specific wavelength.

Preliminary Stability Study

The nanoemulgel containing the encapsulated extract, the nanoemulgel containing the non-encapsulated extract and

Table 1: Normalized product EE x I

Wavelength (λ)	*EE x I*
290	0.0150
295	0.0817
300	0.2874
305	0.3278
310	0.1864
315	0.0839
320	0.0180

EE: erythermogenic effect; I: radiation intensity.

the extract were packaged in transparent glass tubes and stored at a controlled temperature and protected from light in room temperature, 25 ± 2°C; and in an oven at 37 ± 2°C, for a period of 15 days, for preliminary stability assessment.[26]

The nanoemulgels were analyzed regarding the sun protection factor. The analyses were carried out in the 1st and 15th days after preparation.

Statistical analysis

The results were statistically analyzed using a student's t-test. Values with $p<0.05$ were considered statistically significant.

Results And Discussion

The yield obtained was 3.34% ± 0.56 of dry extract of *Hymenea courbaril* in relation to the plant material used (stem bark). The total phenolics value of the *H. courbaril* stem bark extract expressed as gallic acid equivalent was 419.4 mg ± 2.2 EAG/g of extract. The gallic acid calibration curve equation is y = 0.0129x + 0.0049 and R2 = 0.9984. Santos *et al.* (2022) found a value of 516.89 ± 2.63 EAG mg/g extract, greater than that found in this study.[27]

The total flavonoid content of the dry extract of the stem bark of *H. courbaril* expressed as quercetin was 4.4 mg ± 0.1 EQ/g of extract, higher than the value found by Santos *et al.* (2022) of 3.9 mg ± 0.1 EQ/g of *H. courbaril* stem extract.[25] The calibration curve equation was y = 0.009 x +0.0065 and $R^2 = 0.9903$.

In the characterization of the nanoemulsion, an average particle size of 186.3 nm ± 10.4 was obtained, a zeta potential of -24.5 mV ± 2.5 and a polydispersion index of 0.11 ± 0.03. The graph of intensity versus diameter showed only one peak (monomodal) as shown in Figure 1.

These values are characteristic of stable nanoemulsions. The zeta potential value of the formulation was negative and favorable to colloidal stability. Zeta potential values greater than +25 mV or less than -25 mV indicate electrostatic stability, favoring repulsion between nanoparticles. The negative surface charge is due to the fatty acids in the oil phase. It is worth mentioning that the presence of Pluronic® F127 in the composition of nanoemulsions promotes steric hindrance due to its high molar mass of 12,500 Daltons.[13] The graph of the zeta potential obtained by Doppler microelectrophoresis is shown in Figure 2, presenting itself as monomodal.

The polydispersity index (PdI) value was also considered favorable to colloidal stability, with monodisperse distribution, with PdI < 0.2. The value (PdI) represents the size distribution and from this index some colloidal instability can be predicted, in which particles with larger sizes encompass smaller particles until coalescence (phase separation), a phenomenon called Ostwald ripening.[28]

In the tube inversion test to determine the sol-gel transition temperature, the results were observed according to Table 2.

Gioffredi *et al.* (2016) observed that solutions of Pluronic® F127 in water between 25 and 30% w/v have a sol-gel transition temperature between 18 and 25°C.[24] The prepared nanoemulgel containing 23.12% Pluronic® F127 in water and oil showed a transition temperature between 23 to 24°C. The value obtained shows that at body temperature the nanoemulgel is in the form of a gel, that is, in environmental conditions below 24°C it is in a liquid form, but when applied to the skin it is in the form of a non-dripping gel over the surface.

Antioxidant activity (IC_{50}) by the DPPH method of 140.42 ± 1.03 µg of extract/mL for the dry extract of stem bark, of 969.14 ± 0.83 µg of nanoemulgel/mL for the nanoemulgel

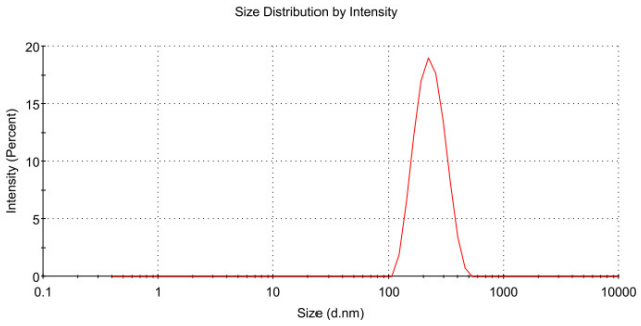

Figure 1: Particle size distribution as a function of intensity

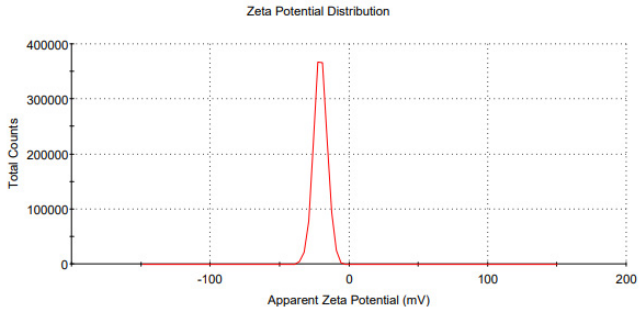

Figure 2: Distribution of the zeta potential of the nanoemulsion

Table 2: Tube inversion test results

Temperature (°C)	*Colloidal state*	*Temperature (°C)*	*Colloidal state*
10	Sol	25	Gel
11	Sol	26	Gel
12	Sol	27	Gel
13	Sol	28	Gel
14	Sol	29	Gel
15	Sol	30	Gel
16	Sol	31	Gel
17	Sol	32	Gel
18	Sol	33	Gel
19	Sol	34	Gel
20	Sol	35	Gel
21	Sol	36	Gel
22	Sol	37	Gel
23	Sol	-	-
24	Gel	-	-

containing the extract of the encapsulated stem bark and 48.05 ± 0.83 µg/mL for quercetin, the results are visually compared in Figure 3.

Veggi *et al.* (2014) found a value of 200 µg/mL and Santos *et al.* (2022), obtained an IC_{50} value of 33.97 µg/mL for the *H. courbaril* stem extract and 18.22 µg/mL for total flavonoids expressed as quercetin equivalents.[27,29] The nanoemulgel without the extract showed an antioxidant activity (IC_{50}) of 12 mg (12,000 µg) of nanoemulgel/mL ± 2 mg, that is, the antioxidant activity of the nanoemulgel is due to the *H.* extract. The mechanism by which plant extracts trigger the antioxidant activity is mainly attributed to the presence of phenolic compounds such as flavonoids, tannins and phenolic acids justified by aromatic hydroxyl groups, which eliminate free radicals through oxidation-reduction reactions.[29]

The spectrophotometric method for determining SPF is reproducible when compared to the in-vivo method recommended by the FDA.[30] According to Ručová *et al* (2023), there are two main types of in-vitro methods for measuring SPF. One involves measuring the absorption or transmission of UV radiation through sunscreen films. The other involves determining the absorption characteristics of sunscreens using spectrophotometric analysis of dilute solutions.[31] In this work the method used was through the absorption of diluted solutions in the UV region of the spectrum.

According to RDC 30/2012 ANVISA (National Health Surveillance Agency) the minimum SPF value for a cosmetic sunscreen is 6.[32] The sun protection factor value obtained for the dry extract was 9.8 and for the nanoemulgel based on the encapsulated extract was 2.3 ± 0.1 and the nanoemulgel containing the non-encapsulated extract had a lower SPF ($p < 0.05$) with a value of 1.6 ± 0.2 suggesting that the non-encapsulated extract lost in part of its photoprotective properties, the results are visually compared in Figure 4.

The nanoemulgel without extract was also prepared as a negative control and presented SPF 0.1, concluding that the nanoemulgel containing *H. courbaril* extract can be used to complement the SPF of photoprotective cosmetic products, thus reducing the amount of synthetic chemical filters in the formulation.

These findings are due to natural compounds of plant origin, which have photoprotective effects and antioxidant action. Many phenolic compounds can accumulate and reduce the penetration of UV radiation.[33] According to Veggi *et al*. (2014) the UV radiation absorption property of the Jatobá extract is due to the poly catechins.[29]

In the results of the preliminary stability tests regarding the capacity of the formulations to maintain the SPF, it was observed that at room temperature, both the extract and the nanoemulgel containing the non-encapsulated extract suffered a reduction in SPF ($p < 0.05$), while the nanoemulsion containing the encapsulated extract did not change ($p > 0.05$) as shown in Table 3.

In the test at 37ºC, the nanoemulgel and the extract showed a greater reduction in SPF compared to the temperature of 25ºC. However, the formulation containing the encapsulated extract did not show a reduction in SPF based on the statistical analysis of the data ($p > 0.05$).

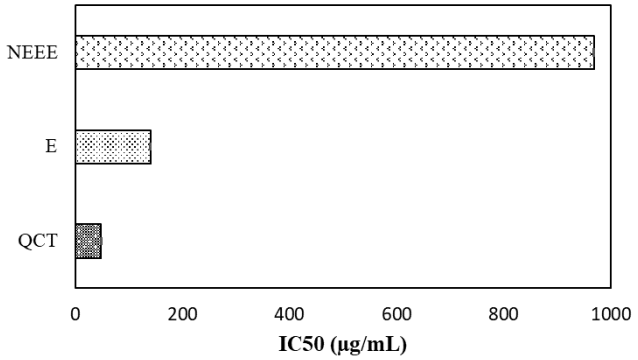

Figure 3: Results of antioxidant activity by the DPPH method. E: extract; NEEE: nanoemulsion based encapsulated extract; QCT: quercetin

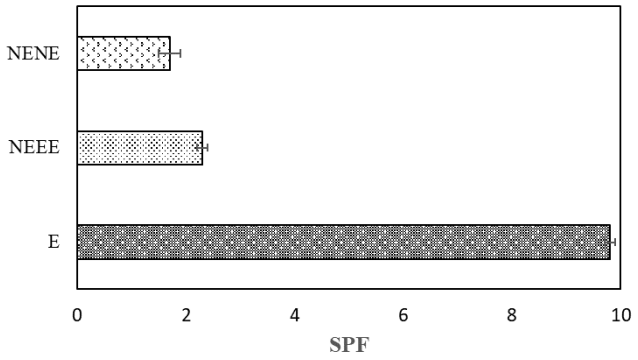

Figure 4: SPF value in the samples. E: extract; NENE: non-encapsulated extract based on nanoemulsion; NEEE:nanoemulsion based encapsulated extract

Table 3: Results of SPF determination of samples during the period of 15 days (n = 3).

Temperature	*25ºC*				*37ºC*			
Time (days)	*1st*		*15th*		*1st*		*15th*	
Sample	SPF	SD	SPF	SD	SPF	SD	SPF	SD
Extract	9.8	0.3	8.3	0.3	9.8	0.3	5.3	0.3
NEEE	2.3	0.1	2.3	0.0	2.3	0.1	2.2	0.2
NENE	1.6	0.2	1.2	0.1	1.6	0.2	0.9	0.1

SD: Stardard deviation; NENE: non-encapsulated extract based on nanoemulsion; NEEE: nanoemulsion-based encapsulated extract.

These results can be explained by the protection of extract substances that were solubilized in the oil. The oil was dispersed in the aqueous gel in the form of nanodroplets protected on their surfaces by Pluronic® F127 molecules.

A study of the photostability of active sunscreens such as avobenzone compared different vehicles, including solvent and emulsion. The results of this study showed that avobenzone in nanoemulsion is protected from degradation.[34]

Conclusion

The nanoemulgel containing *H. courbaril* extract protected and encapsulated in oil nanodroplets was successfully prepared, showing antioxidant and photoprotective potential, corroborating the high phenolic values found in the extract. The prepared nanoemulgel, at body temperature, appeared in a colloidal gel state, and at temperatures below 24°C it appeared as a liquid (sol colloidal state), facilitating its use as a spray in the sol condition and favoring spreadability at body temperature in the gel condition. In addition, the nanoemulgel formulation requires a smaller amount of synthetic photoprotective active to reach the desired SPF, presenting itself as a promising photoprotective cosmetic.

References

1. Fania L, Sampogna F, Ricci F, Hyeraci M, Paradisi A, Palese E, Di Lella G, Pallotta S, Panebianco A, Candi E, Dellambra E, Abeni D. Systemic Photoprotection in Skin Cancer Prevention: Knowledge among Dermatologists. Biomolecules. 2021;11(2):332-340. Available from: doi.org/10.3390/biom11020332
2. Thune P. Contact and photocontact allergy to sunscreens. Photodermatology. 1984;1(1):5-9. PMID: 6335754.
3. Rodrigues FA, Giffony P, dos Santos S, Guedes J, Ribeiro ME, de Araújo T, da Silva L, Zocolo G, Ricardo N. Spondias purpurea L. Stem Bark Extract: Antioxidant and in-vitro Photoprotective Activities. Journal of the Brazilian Chemical Society. 2021;32(10):1918-1930. Available from: doi.org/10.21577/0103-5053.20210082
4. Silva RV, Costa SC, Branco CR, Branco A. In-vitro photoprotective activity of the Spondias purpurea L. peel crude extract and its incorporation in a pharmaceutical formulation. Industrial Crops and Products. 2016;83:509-514. Available from: doi.org/10.1016/j.indcrop.2015.12.077
5. Paixão TP, Silva, MT, de Andrade MA, Barbosa NR & Raposo JLFV. (2023). Plants from Brazil with Potential Photoprotective Activity: A Review. Pharmacognosy Reviews. 17(33), 204-213. Available from: dx.doi.org/10.5530/097627870191
6. Costa SCC, Damasceno PKF, Lima RGG, Botura MB, Branco CRC, Silva TRS, Oliveira AP, Guimarães AL, Almeida JRGS, Branco A. Evaluation of antioxidant, photoprotective and antinociceptive activities of Marcetia macrophylla extract: potential for formulation of sunscreens. Brazilian Journal of Biology. 2021;83:e246312. Available from: doi.org/10.1590/1519-6984.246312
7. Bhatia N. Polypodium leucotomos: a potential new photoprotective agent. American Journal of Clinical Dermatology. 2015 ;16(2):73-79.Available from: doi.org/10.1007/s40257-015-0113-0
8. Ruth SL, David SM, Laan DC, Barbara JP, Larissa BB, Emerson SL, Hector HF, Dionatas UD, Ana FM, Romeu PM. Antioxidant effect of Hymenaea courbaril L (Jatob) sap on the healing of wounds on mice. Journal of Medicinal Plants Research. 2021;15(4):160-171. Available from: doi.org/10.5897/JMPR2021.7091
9. Matos JM, Costa ARC, Justino MN, Camara MBP, Vasconcelos OLS, Marques JC, Brandão CM, & de Carvalho Marques GE. Chemical prospection and antioxidant activity of Humiria balsamifera (Aubl.) A. St. Hil. and Hymenaea courbaril L. Natural Product Research. 2024;38(4), 614–618. Available from: doi.org/10.1080/14786419.2023.2189708
10. Mansur MC, Campos C, Vermelho AB, Nobrega J, da Cunha Boldrini L, Balottin L, Lage C, Rosado AS, Ricci-Júnior E, dos Santos EP. Photoprotective nanoemulsions containing microbial carotenoids and buriti oil: Efficacy and safety study. Arabian Journal of Chemistry. 2020;13(8):6741-6752. Available from: doi.org/10.1016/j.arabjc.2020.06.028
11. Martins RM, Martins SD, Barbosa GL, Silva EG, Fonseca MJ & Freitas LA. Natural component and solid lipid microparticles of solar filter in sunscreen: Photoprotective and photostability effect enhancement. Journal of Drug Delivery Science and Technology.2023;88-99. Available from: doi.org/10.1016/j.jddst.2023.104860
12. Coelho EL, de França FCF, Rebouças LM, Uchoa AFJ, Semião LM, Maia DS, Moreira DR, Pinheiro DP, da Silva LMR, Pessoa CO, Ribeiro MENP, Ricardo NMPS. Application of Curcuminoids-loaded Nanoemulsion for Cancer Therapy. Journal of Applied Pharmaceutical Sciences and Research. 2022; 5(3):34-39. Available from: doi.org/10.31069/japsrv5i3.04
13. Rebouças L, Sousa A, Gramosa N, de Araújo T, de Oliveira FD, do Ó Pessoa C, Araújo R, Santos E, Ricardo N. Linseed Oil Nanoemulsion with Pluronic® F127 Loaded with Betulinic Acid: Preparation, Rheology, MTT Assay and in-vitro Release Kinetics. Journal of the Brazilian Chemical Society. 2022;33(11):1319-1331.Available from:doi.org/10.21577/0103-5053.20220063
14. Kant V, Gopal A, Kumar D, Gopalkrishnan A, Pathak NN, Kurade NP, Tandan SK, Kumar D. Topical pluronic F-127 gel application enhances cutaneous wound healing in rats. Acta Histochemica. 2014;116(1):5-13. Available from: doi.org/10.1016/j.acthis.2013.04.010
15. Jørgensen EB, Hvidt S, Brown W, Schillén K. Effects of Salts on the Micellization and Gelation of a Triblock Copolymer Studied by Rheology and Light Scattering. Macromolecules. 1997;30(8):2355-2364. Available from: dx.doi.org/10.1021/ma9616322
16. Mohanan A, Nickerson MT, Ghosh S. Oxidative stability of flaxseed oil: Effect of hydrophilic, hydrophobic and intermediate polarity antioxidants. Food Chemistry. 2018;266:524-533. Available from: dx.doi.org/10.1016/j.foodchem.2018.05.117
17. Rahiminezhad Z, Hashemi Gahruie H, Esteghlal S, Mesbahi GR, Golmakani MT, Hosseini SM. Oxidative stability of linseed oil nanoemulsions filled in calcium alginate hydrogels. LWT. 2020;127:109392. Available from: dx.doi.org/10.1016/j.lwt.2020.109392
18. Aithal GC, Narayan R, Nayak UY. Nanoemulgel: A Promising Phase in Drug Delivery. Current Pharmaceutical

Design. 2020;26(2):279-291.Available from: doi.org/10.2174/1381612826666191226100241
19. Jusril NA, Abu Bakar SI, Khalil KA, Md Saad WM, Wen NK, Adenan MI. Development and Optimization of Nanoemulsion from Ethanolic Extract of Centella asiatica (NanoSECA) Using D-Optimal Mixture Design to Improve Blood-Brain Barrier Permeability. Evidence-based Complementary and Alternative Medicine.2022;2022:3483511. Available from: doi.org/10.1155/2022/3483511
20. Seibert JB, Bautista-Silva JP, Amparo TR, Petit A, Pervier P, dos Santos Almeida JC, Azevedo MC, Silveira BM, Brandão GC, de Souza GH, de Medeiros Teixeira LF, dos Santos OD. Development of propolis nanoemulsion with antioxidant and antimicrobial activity for use as a potential natural preservative. Food Chemistry. 2019;287:61-67.Available from: https: doi.org/10.1016/j.foodchem.2019.02.078
21. Mariadi, Prasetyo BE, Adela H, Wiladatika W. Formulation and Characterization of Nanoemulsion of Tread leave Ethanol Extract (Catharanthus roseus (L.) G. Don) as Antihyperglycemic. Indonesian Journal of Pharmaceutical and Clinical Research. 2019;2(2):24-30. Available from: doi.org/10.32734/idjpcr.v2i2.3204
22. Mulia K, Ramadhan RM, Krisanti EA. Formulation and characterization of nanoemulgel mangosteen extract in virgin coconut oil for topical formulation. MATEC Web Conf. 2018;156:01013. Available from: doi.org/10.1051/matecconf/201815601013
23. Singleton VL, Rossi JA. Colorimetry of Total Phenolics with Phosphomolybdic-Phosphotungstic Acid Reagents. American Journal of Enology and Viticulture. 1965;16(3):144-158. Available from: doi.org/10.5344/ajev.1965.16.3.144
24. Gioffredi E, Boffito M, Calzone S, Giannitelli SM, Rainer A, Trombetta M, Mozetic P, Chiono V. Pluronic F127 Hydrogel Characterization and Biofabrication in Cellularized Constructs for Tissue Engineering Applications. Procedia CIRP. 2016;49:125-132. Available from: doi.org/10.1016/J.PROCIR.2015.11.001
25. Sayre, RM.; Agin, PP.; Levee, GJ.; Marlowe, E. Comparison of in-vivo and in-vitro testing of sunscreening formulas. Photochem. Photobiology. 1979;29(3):559-566. Available from: doi.org/10.1111/j.1751-1097.1979.tb07090.x
26. ANVISA. Agência Nacional de Vigilância Sanitária – Guia de estabilidade de produtos cosméticos. Brasília, 2004. v. 1. Available from: //www.gov.br/anvisa/pt-br/centraisdeconteudo/publicacoes/cosmeticos/manuais-e-guias/guia-de-estabilidade-de-cosmeticos.pdf/view
27. Santos WM, Menezes Filho AC, Castro CF, Teixeira MB, Soares FA, Porfiro CA. Chemical, physicochemical profile and dose-response effect of Hymenaea courbaril essential oil on bacteria. Brazilian Journal of Science. 2022;1(7):37-43. Available from: doi.org/10.14295/bjs.v1i7.154
28. Yakoubi S, Kobayashi I, Uemura K, Nakajima M, Isoda H, Ksouri R, Saidani-Tounsi M, Neves MA. Essential-Oil-Loaded Nanoemulsion Lipidic-Phase Optimization and Modeling by Response Surface Methodology (RSM): Enhancement of Their Antimicrobial Potential and Bioavailability in Nanoscale Food Delivery System. Foods. 2021;10(12):3149-3159. Available from: doi.org/10.3390/foods10123149
29. Veggi PC, Prado JM, Bataglion GA, Eberlin MN, Meireles MA. Obtaining phenolic compounds from jatoba (Hymenaea courbaril L.) bark by supercritical fluid extraction. Journal of Supercritical Fluids. 2014;89:68-77. Available from: doi.org/10.1016/j.supflu.2014.02.016
30. Yang SI, Liu S, Brooks GJ, Lanctot Y, Gruber JV. Reliable and simple spectrophotometric determination of sun protection factor: A case study using organic UV filter-based sunscreen products. Journal of Cosmetic Dermatology. 2017;17(3):518-522. Available from: doi.org/10.1111/jocd.12390
31. Ručová D, Vilková M, Sovová S. Photoprotective and antioxidant properties of scytonemin isolated from Antarctic cyanobacterium Nostoc commune Vaucher ex Bornet & Flahault and its potential as sunscreen ingredient. Journal of Applied Phycology. 2023;35:2839–2850. Available from: doi:10.1007/s10811-023-03109-6
32. ANVISA. Resolução RDC N°. 30, de 1 de junho de 2012. Aprova o Regulamento Técnico Mercosul sobre Protetores Solares em Cosméticos e dá outras Providências, Available in: http://bvsms.saude.gov.br/bvs/saudelegis/anvisa/2012/rdc0030_01_06_2012.html, accessed in May 2022.
33. Oliveira FG, Lima-Saraiva SR, Mélo BC, Silva RA, Santos MA, Félix WP, Almeida JR. Phytochemical screening, Sun Protection Factor (SPF) and sugar analysis of jatobá fruits (Hymenaea martiana Hayne): A native medicinal plant from the San Francisco Valley. Food Science and Technology. 2019;39(2):551-565. Available from: doi.org/10.1590/fst.18718
34. Marti-Mestres G, Fernandez C, Parsotam N, Nielloud F, Mestres JP, Maillols H. Stability of UV Filters in Different Vehicles: Solvents and Emulsions. Drug Development and Industrial Pharmacy. 1997;23(7):647-655.Available from: doi.org/10.3109/03639049709150765

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