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Photoprotector Effect of Emulsions with Yerba-Mate (*Ilex paraguariensis*) Extract

Juliana Andriolli Ribeiro [1], Ederlan Magri [2], Itamar Luís Gonçalves [1], Karina Paese [3], Juliana Roman [1] and Alice Teresa Valduga [2,*]

[1] Department of Health Sciences, Universidade Regional Integrada do Alto Uruguai e das Missões—URI, Sete de Setembro Avenue, 1621, Erechim 99700-000, RS, Brazil; itamar3141@yahoo.com.br (I.L.G.)
[2] Postgraduate Program in Ecology, Universidade Regional Integrada do Alto Uruguai e das Missões—URI, Sete de Setembro Avenue, 1621, Erechim 99700-000, RS, Brazil; ederlan.magri@gmail.com
[3] Faculty of Pharmacy, Universidade Federal do Rio Grande do Sul, Avenida Ipiranga, Porto Alegre 90040-60, RS, Brazil; karinapaese@gmail.com
* Correspondence: valice@uricer.edu.br

Abstract: Yerba-mate contains in its composition a high concentration of phenolic compounds. This class of secondary metabolites exhibits strong values of molar absorptivity on ultraviolet and visible wavelengths. This study evaluated the effect of yerba-mate extracts on the in vitro solar protection factor (SPF) value of sunscreen formulations. The sunscreen formulations were prepared to have non-ionic lotion as a basis and yerba-mate extract and/or avobenzone as active agents. The SPF and resveratrol protective effect of the formulations were determined by UV-vis spectrometry. A synergic effect between the yerba-mate extract and avobenzone on the SPF was found. Yerba-mate extract at 5% improved the SPF of the avobenzone 5% formulation from 28.46 ± 5.45 to 40.48 ± 0.84. Yerba-mate extract at 5% avoided resveratrol degradation by ultraviolet radiation. At this same concentration, avobenzone produced a smaller effect than yerba-mate extracts in resveratrol protection. The formulations with yerba-mate + avobenzone presented smaller changes in pH values during 12 days of storage. The spreadability profile of yerba-mate and avobenzone formulations was similar to the profile of avobenzone formulations. The results reported here show the suitability of the yerba-mate extract use in photoprotective formulations, highlighting their in vitro effect and opening possibilities for new investigations exploring this property.

Keywords: biological activity; biologically active molecules; photochemistry; phytochemistry

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1. Introduction

Plant biodiversity is a source of phytochemical compounds with a considerable potential for technological applications, mainly focusing on nutraceuticals, cosmetics and health [1]. Yerba-mate (*Ilex paraguariensis* St. Hil) is a plant with a high concentration of phenolic compounds, having in its composition chlorogenic and cinnamic acids and flavonoids [2]. An investigation identified that yerba-mate had the highest content of total chlorogenic acid (91.886 mg·1000 g^{-1}) among 100 plants commercialized in Brazil, approximately 5.5 times higher than the value found in the white tea (16.401 mg·1000 g^{-1}), which had the second highest content [3]. In some South American countries, processed yerba-mate leaves are used for the preparation of beverages widely consumed [4–6]. The use of yerba-mate extracts due to their antioxidant properties is well consolidated in foods [7,8].

There are increasing efforts towards developing more efficient sunscreens as sun exposure is a cause of alterations in nucleic acids and is a source of oxidative stress linked with premature aging and skin cancer [9]. Vegetable sources have been used in sunscreen formulations aiming to improve their photoprotective effect. This strategy explores the photoprotective molecules produced by plants to guard their genetic material from ultraviolet radiation. [10]. Recently grape seed extract showed a protective effect on skin fibroblasts

exposed to ultraviolet light and was used in a sunscreen formulation [11]. Additionally, olive leaf extract showed in vivo photoprotective effect on yeasts and synergism with chemical filters [12]. Additionally, chlorogenic acids isolated from coffee were used as a preventive agent against premature skin aging induced by UV radiation [13].

Sunscreens contain in their composition physical filters able to increase the reflection and scattering of radiation or chemical filters. This last group is able to absorb the energy from radiation yielding an activated state, which, via chemical process, converts the photon energy to heat by returning the molecule to the initial electronic state [14]. Regarding the chemical filters, the presence of aromatic molecules with extensive conjugated π system may be highlighted in their chemical structures, as is depicted in Figure 1. Polyphenols found in yerba-mate also have this structural characteristic, as reported in Figure 2.

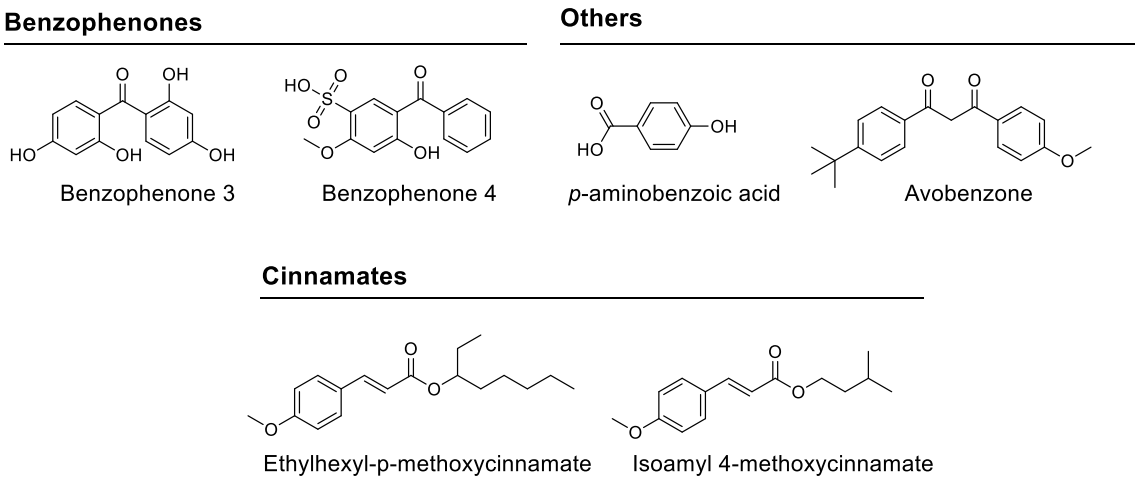

Figure 1. Chemical structures of the main chemical filters employed in sunscreens formulations.

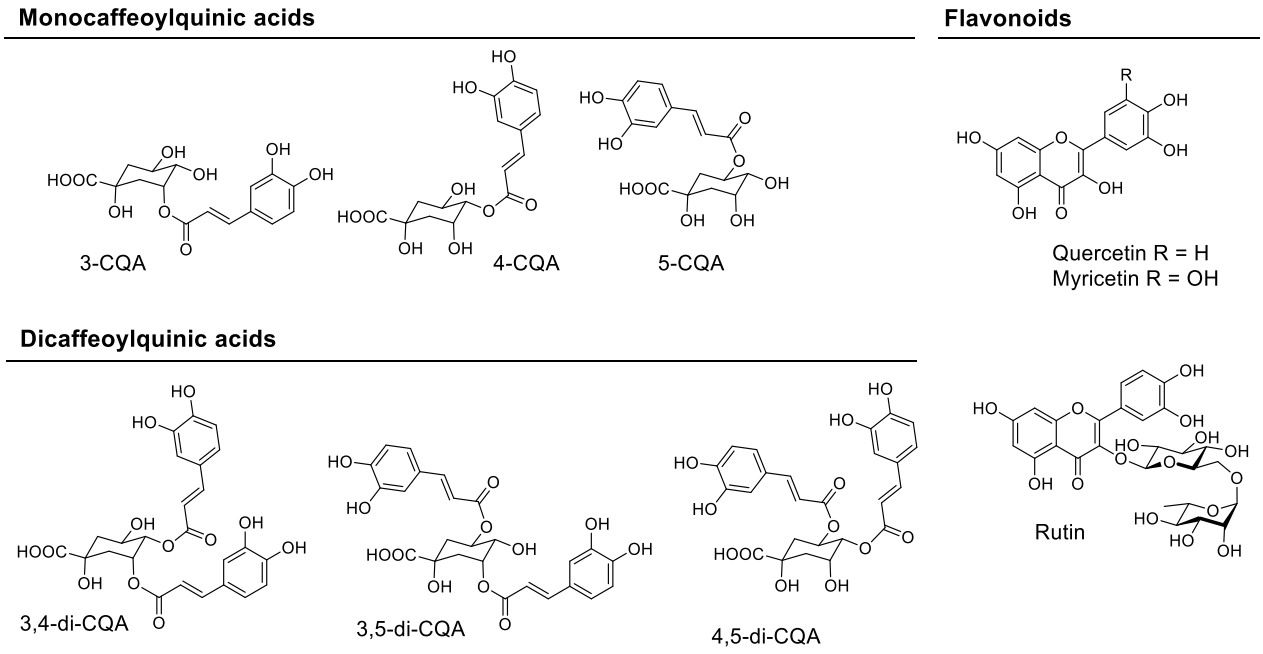

Figure 2. Chemical structures of the main polyphenols found in yerba-mate leaves.

Some drawbacks of current sunscreens make the development of natural products-based sunscreens attractive. Chemical ultraviolet filters, widely used in pharmaceutical formulations, are a cause of detrimental effects on marine ecosystems [15]. The use of natural products as

the active ingredient in sunscreens formulations is an ecofriendly strategy with the potential to reduce these impacts. Another worrying aspect linked to chemical filter use is their reactivity to skin and absorption dermic, with possible systemic toxicity [16]. In vivo investigations reported the toxicity absence of yerba-mate extracts [17,18].

The use of yerba-mate extracts in topic formulations aiming to provide photoprotection is poorly explored until now. Due to the chemical similarity among ultraviolet filters currently used in sunscreen formulations and metabolites present in yerba-mate, this research explored the use of hydroethanolic extract of yerba-mate on emulsions which have their photoprotective effect investigated.

2. Materials and Methods

2.1. Extracts Preparation

Leaves of yerba-mate were collected at Pinhão city under the coordinates 25°54′17″ S e 51°35′14″ W. The collection was performed at the median part of the plant and 20 plants were used as a representative sample of the area. The estimated age of leaves was 18 months. The leaves (1 kg) were dried at 35 °C in an oven with air circulation to constant weight and crushed in a knife mill (0.85 mm). The material was submitted to maceration with ethanol: water 1:1 for 24 h. The extract was filtered and dried under reduced pressure in a rotative evaporator and lyophilized.

2.2. Formulations Preparations

Nine formulations were obtained with increasing concentrations of yerba-mate extracts and/or avobenzone. The basis used was the oil/water (O/W) non-ionic emulsion (Table 1) at 11.15/88.85 O/W ratio, prepared as follows: both phases A (oil phase) and B (aqueous phase) were heated separately to 75 °C. Next, the aqueous phase was added to the oil phase at a stirring rate of 500 rpm and mixing was maintained until it formed emulsion and kept under stirring until cooling to room temperature. Phase C was added at the end when the temperature was within 40 °C. Stirring was, then, maintained for 5 more min. The avobenzone insertion involved its levigation with propylene glycol while yerba-mate extracts were directly mixed into the emulsion [19].

Table 1. Composition of basis emulsion.

	Component	**Amount (%)**
Phase A	Polawax	6.0
	Propylparaben	0.1
	Butyl hydroxytoluene	0.05
	Octyl stearate	5.0
Phase B	Propylene glycol	5.0
	Methylparaben	0.2
	Water	up to 100
Phase C	Imidazolidinyl urea	0.6

2.3. Formulation Characterization

A preliminary rheological investigation was performed by spreadability quantification [20]. For this purpose, the parallel-plate method was used. This method used plates of glass (20 × 20 cm) with defined mass which are disposed on the amount of formulation under assessment. After 1 min, the diameter reached by the formulation was quantified and expressed in square millimeters, by the circle-area calculation. A total of ten glass plates were used in this experiment, producing an increase in the mass on the formulation. Values of spreadability were plotted against the mass of plates.

2.4. Stability Investigation

The preliminary stability was assessed according to tests defined by ANVISA and widely used for stability investigation [21,22]. The samples were submitted to freeze–thaw cycles for 12 days and storing conditions defined by 24 h at 40 ± 2 °C and 24 h at 4 ± 2 °C. At the initial time and t = 12 days pH, organoleptic characteristics and stability after centrifugation were evaluated. A set of samples was kept under environmental conditions and submitted to the same tests. Color and flavor changes were monitored visually and macroscopic changes were analyzed by comparing with and standard formulation. The pH was measured in an aqueous solution at 10%, using a pH meter previously calibrated with buffer solutions with pH 4.01 and 7.01. The phases separation was monitored after the centrifugation under 3.000 r.p.m for 30 min.

2.5. SPF Determination

SPF was determined according to the method developed by Sayre 1978 [23] and modified by Mansur 1986 [24]. The formulations were dissolved in ethanol at the concentration of 0.2 mg/mL and the absorbance was measured from 290 to 320 nm with 5 nm of resolution. The SPF was calculated according to Equation (1), where FC is a correction factor = 10; EE is the erythemal efficiency spectrum, I is the solar simulator intensity spectrum as measured with a calibrated spectroradiometer and A is the absorbance 290 to 320 nm measured in 5 nm increments. The values of EE and I were previously determined by Sayre 1978 [23].

$$\mathrm{SPF} = \mathrm{FC} \cdot \sum_{290}^{320} \mathrm{EE}(\lambda) \cdot \mathrm{I}(\lambda) \cdot \mathrm{A}(\lambda) \quad (1)$$

2.6. Photoprotective Investigation

The effect of formulations on resveratrol stability was investigated according to protocols previously defined [25]. This experiment involved the use of a small chamber recovered with mirrors and with ultraviolet light. Resveratrol (15 mL) in acetonitrile 8 μg/mL was added to Petri dishes that were exposed to the ultraviolet radiation in a chamber. Each dish was covered by a film of 300 mg of each formulation before exposure to an ultraviolet lamp emitting UVA 2% and UVB 0.5%. Samples were collected at 15, 30, 45, 60, 120 and 180 min for absorbance monitoring at 306 nm and resveratrol quantification. This experiment used a positive control of a Petri dish with a cover impermeable to the ultraviolet light and a negative control of a Petri dish without any protection and covered with a lotion without any active agent.

2.7. Statistical Analysis

Normality of data distribution was tested with Shapiro–Wilk test. The SPF and pH values were compared by ANOVA followed by Tukey test. Was considered as significative p values lower than 0.05. All the analyses were performed using the GraphPad Prism 9.3.

3. Results and Discussion

3.1. Extraction and SPF Determination

The extraction of soluble from yerba-mate leaves yielded 9.0 % (*w/w*), after solvent removal by lyophilization. Studies with exhaustive extraction in yerba-mate leaves showed a yield of 50.7% [26].

The efficiency of sunscreens in protecting the skin against the dangers of sun radiation is quantified through the solar protection factor measurement. The effect of yerba-mate extracts (YM), avobenzone (A) or their combination (YM + A) on SPF was assessed using an in vitro protocol. The most efficient formulation presented was yerba-mate extract 5% with avobenzone 5%, which showed SPF 40.48 ± 0.84. Otherwise, the formulation with only avobenzone 5% presented 28.46 ± 5.45 as SPF and the formulation with only yerba-mate extract showed SPF = 12.03 ± 0.01 (Table 2). These results have shown a synergic effect of yerba-mate extracts on the improvement of SPF of avobenzone formulations. A linear positive relationship between the concentrations of active agents and the SPF may be

observed. The increase in SPF was more expressive when the yerba-mate extract was used together with avobenzone, as depicted in the red line of Figure 3.

Table 2. SPF determination of formulations with yerba-mate extracts, avobenzone and both.

Formulations	SPF
YM 1%	2.05± 0.04 ^{e}
YM 2%	4.35 ± 0.07 ^{de}
YM 5%	12.03 ± 0.01 ^{c}
A1%	3.35 ± 0.10 ^{de}
A2%	7.53 ± 0.05 ^{cd}
A5%	28.46 ± 5.45 ^{b}
YM1% + A1%	4.22 ± 0.25 ^{de}
YM2% + A2%	12.32 ± 0.07 ^{c}
YM5% + A5%	40.48 ± 0.84 ^{a}
Control	0.01 ± 0.04 ^{e}

Means with the same letter are not significantly different, according to the ANOVA followed by Tukey test.

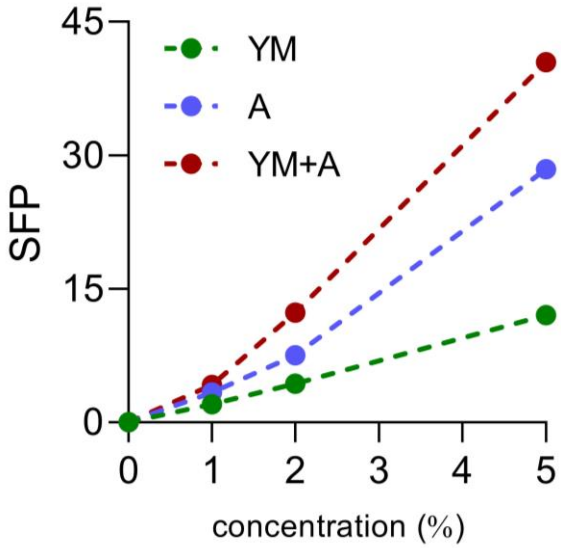

Figure 3. Relation between concentration and SPF.

The synergic effect among extracts of natural products and chemical or physical sun blockers with or without nanotechnological basis is a strategy widely explored, aiming to improve the SPF [10]. Through this approach, high SPF values were reached, such as the example of formulations with grape pomace extract at 10% in association with chemical filters which yielded an SPF of 76.67 [27]. Despite of the possibilities of increasing the extract concentrations, it may be highlighted that the SPF value reported here with yerba-mate extract was only 5%.

These results are the first reports about the in vitro photoprotective activity of yerba-mate extracts, with the experimental determination of SPF. Previously, it was identified that yerba-mate extracts by oral or topical administration were able to avoid the lipidic peroxidation and nucleic acids and proteins damage in rats exposed to ultraviolet radiation [28,29].

Despite of facility of the in vitro SFP measurement, some authors have not found a good level of correlation between in vitro and in vivo SFP values [30,31]. Some investigations reported r^2 values ranging from 0.26 to 0.72 for the relationship between in vitro and in vivo SPF values [31]. The clinical concept of SPF is the ratio of erythematous minimum radiation dose on unprotected skin and this same dose on the skin with a photoprotector agent [24].

3.2. Photoprotective Effect on Resveratrol Degradation

Aiming to prove our results, the photoprotective activity of the formulations was investigated by the quantification of their ability in protecting a solution of resveratrol 8 µg/mL of the degradation produced by UVA and UVB radiation. At 1%, neither yerba-mate extract nor avobenzone were able to avoid the resveratrol degradation (Figure 4a,d). At 2% and 5% yerba-mate, extract showed a higher photoprotective effect than avobenzone, as may be observed in Figure 4b,c,e,f. In the formulations with yerba-mate extract 5%, with and without avobenzone, the totality of initial resveratrol amount remained unchanged at the end of monitoring time (Figure 4c,i). In this concentration, the profile of resveratrol against the time overlapped with the positive control (plate covered with impermeable to ultraviolet radiation material, represented in graphs by black circles). The formulations with yerba-mate and avobenzone both at 1% and 2%, kept resveratrol levels higher than the formulations with only avobenzone, as may be observed in Figure 4d,e,g,h. Additionally, it may be observed that, in the absence of photoprotective agent, only 44% of the initial resveratrol remained after 180 min of exposure to ultraviolet light. This value was obtained in plates covered by a lotion film (orange circles in the graphs of the Figure 4) and in the negative control (white circles). These results shown that yerba-mate extract at 2% and 5% was effective in resveratrol protection against the ultraviolet radiation.

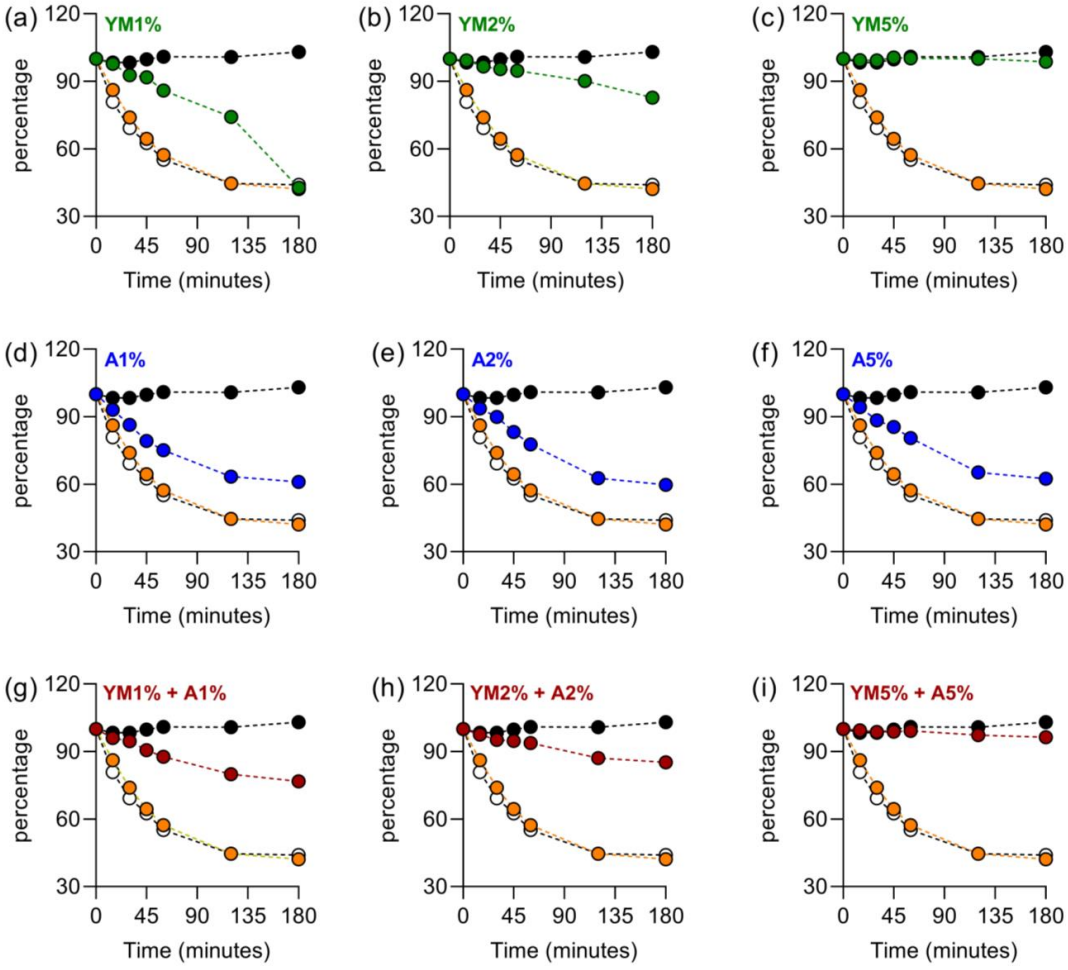

Figure 4. Effect of formulations investigated on resveratrol protection against UV light. In (**a**–**c**) formulations presented yerba-mate extracts in increasing concentrations; in (**d**–**f**) avobenzone and in (**g**–**i**) the combination of both. In all the figures black circles are the positive control, the white circles are the negative control and the orange circles are the lotion without any photoprotective agent. YM: yerba-mate extract; A: avobenzone.

The pronounced effect of yerba-mate extracts on protection of resveratrol against ultraviolet radiation may be linked with the high level of chlorogenic acids present in yerba-mate [3]. The three position isomers of chlorogenic acid have a strong absorption on UVA and UVB regions of the electromagnetic spectrum, mainly above 280 nm. The maximum absorption value of these isomers occurs at 326 nm with a shoulder at 296 nm [32].

3.3. Characterization and Stability

The formulations with avobenzone were white (Figure 5a), while the formulations with the association of yerba-mate extract and avobenzone were pale yellow (Figure 5b). The color and the flavor were not changed during 12 days of storing on environmental conditions and on freeze–thaw cycles. Regarding the mechanical resistance against centrifugation, phase separation occurred only at the highest concentrations of all the formulations. This aspect was observed under environmental conditions at the end of storing period. Phase separation may be associated with the density difference between the two phases under the influence of gravity, defined by Stokes' law [33].

The pH of formulations was monitored at the times 0 and 12 days under environmental and stress conditions. The initial formulation pH values were acid, a condition that is compatible with the slightly acidic pH of skin [34]. pH changes in cosmetical products usually are linked with the occurrence of chemical reactions, and is a parameter easily monitored as a stability indicator. In addition, this parameter may be a useful indicator of the final product quality [35]. The most expressive pH changes were identified in formulations with only avobenzone, as shown in Figure 6d–f, in which a significant pH decrease was observed at t = 12 days under environmental and stress conditions. The formulations with yerba-mate extract and avobenzone had smaller pH alterations, as depicted in Figure 6g–i. Minor changes in the pH values of skin formulations usually occur and, when ranging within of physiological limits, they are acceptable.

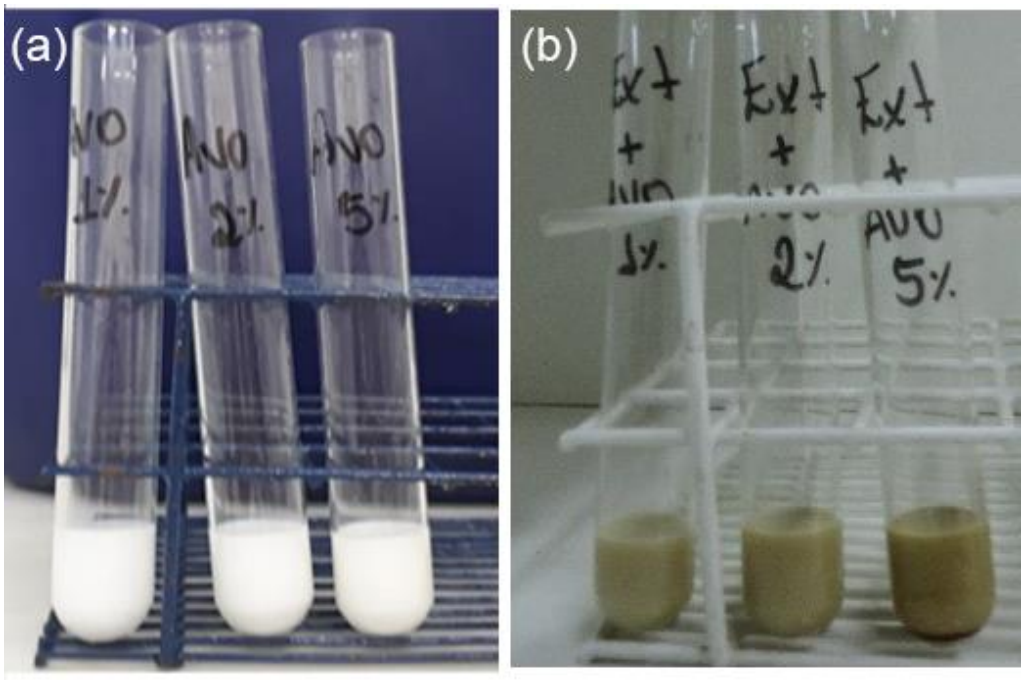

Figure 5. Physical aspect of avobenzone (**a**) and yerba-mate + avobenzone (**b**) photoprotective emulsions in increasing concentrations.

The spreadability is an important feature of topical pharmaceutical formulations, in order to provide the formation of an evenly distributed film [20]. This parameter was investigated using the parallel-plate method. The formulations with yerba-mate extracts were those that showed a spreadability more similar to the control. A presence of

yerba-mate extract in a dose-dependent manner decreased the spreadability (Figure 7a). The avobenzone at the same concentrations of yerba-mate extract produced a higher impact on spreadability (Figure 7b). The effect of combination of yerba-mate extract at 5% with increasing concentrations of avobenzone on the spreadability is depicted in Figure 7c. Regarding this experiment, a very similar spreadability profile to the reported in the Figure 7b may be observed, showing that the yerba-mate extract addiction was not able to produce the spreadability loss if compared to avobenzone. By comparing Figure 7b with Figure 7c, may be noticed that yerba-mate extract did not produce a synergic effect in the spreadability reduction, and it did not produce a decrease in spreadability of avobenzone formulations. YM5% + A5% and A5% were the formulations that showed lower spreadability.

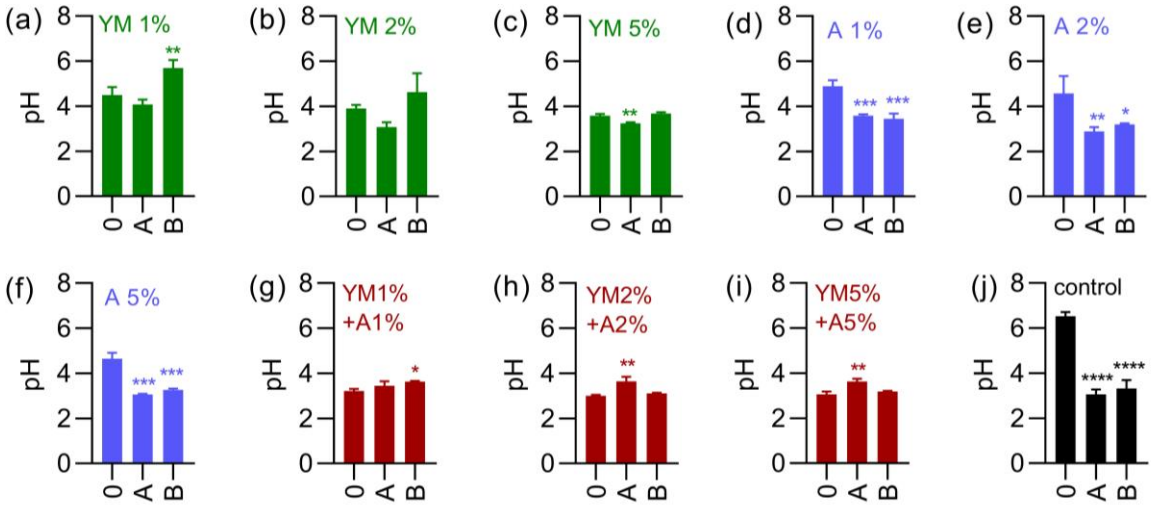

Figure 6. Changes in pH of formulations investigated during 12 days of storing under environmental conditions (A) and under stress conditions defined by freeze–thaw cycles during 12 days and storing conditions defined by 24 h at 40 ± 2 °C and 24 h at 4 ± 2 °C (B). In (**a**–**c**) formulations presented yerba-mate extracts in increasing concentrations; in (**d**–**f**) avobenzone; in (**g**–**i**) the combination of both and in (**j**) is depicted the control behavior. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$ according to ANOVA followed by Tukey test.

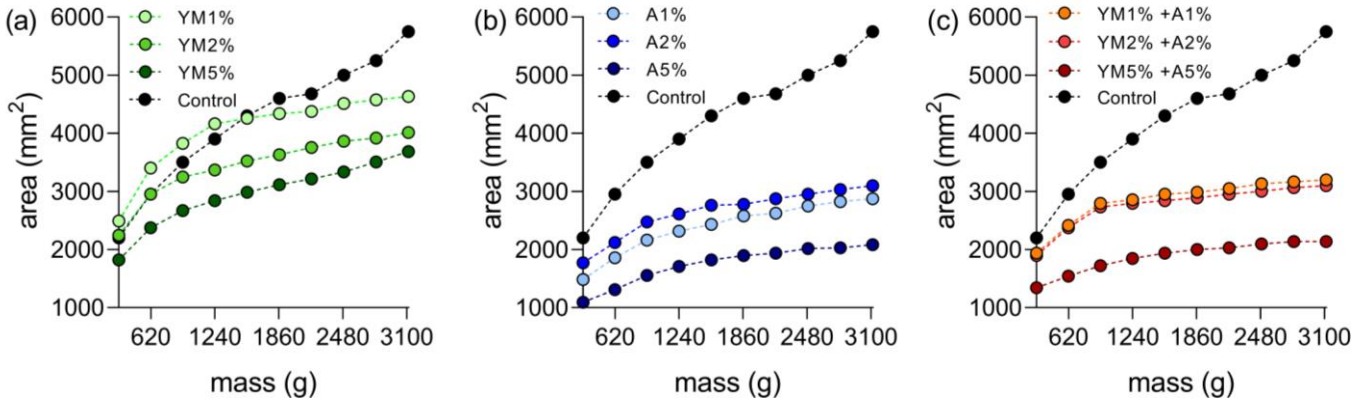

Figure 7. Effect of yerba-mate extract and avobenzone on the spreadability of the developed formulation. In (**a**) formulations presented yerba-mate extracts in increasing concentrations; in (**b**) avobenzone; and in (**c**) the combination of both. YM: yerba-mate extract; A: avobenzone.

4. Conclusions

In this investigation, topic formulations with yerba-mate extract and avobenzone were investigated aiming to determine their in vitro photoprotective effect. A synergic effect of

yerba-mate and avobenzone on SPF of the formulations was identified. A high SPF value of 40.48 ± 0.84 was found for the formulation with yerba-mate 5% and avobenzone 5%. Yerba-mate extracts at 5% with or without avobenzone avoided the resveratrol degradation produced by ultraviolet light. The formulations with yerba-mate + avobenzone showed changes in pH values in a lesser extension and no changes in flavor and color were identified during 12 days of storing. The presence of yerba-mate did not produce a decrease in the spreadability, if compared to the avobenzone formulation. In summary, this investigation obtained topic formulations with a good stability profile and highlight the potential use of yerba-mate extracts on sunscreen formulations. The advances in this field involves pre-clinical and clinical trials, aiming to improve the in vivo photoprotective effect of yerba-mate extracts and their synergism with avobenzone.

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Conflicts of Interest: The authors declare no conflict of interests.

References

1. Valduga, A.T.; Gonçalves, I.L.; Magri, E.; Delalibera Finzer, J.R. Chemistry, pharmacology and new trends in traditional functional and medicinal beverages. *Food Res. Int.* **2019**, *120*, 478–503. [CrossRef] [PubMed]
2. Heck, C.I.; De Mejia, E.G. Yerba Mate Tea (*Ilex paraguariensis*): A Comprehensive Review on Chemistry, Health Implications, and Technological Considerations. *J. Food Sci.* **2007**, *72*, R138–R151. [CrossRef] [PubMed]
3. Meinhart, A.D.; Damin, F.M.; Caldeirão, L.; da Silveira, T.F.F.; Filho, J.T.; Godoy, H.T. Chlorogenic acid isomer contents in 100 plants commercialized in Brazil. *Food Res. Int.* **2017**, *99*, 522–530. [CrossRef] [PubMed]
4. Gonçalves, I.L.; Dartora, N.; Piovezan Borges, A.C.; Picolo, A.P.; Dallago, R.M.; Mera de Souza, L.; Valduga, A.T. Accelerated maturation of processed yerba-mate under the controlled conditions of temperature and humidity. *Nutr. Food Sci.* **2015**, *45*, 564–573. [CrossRef]
5. Lewinski, C.S.; Gonçalves, I.L.; Piovezan Borges, A.C.; Dartora, N.; de Souza, L.M.; Valduga, A.T. Effects of UV light on the physic-chemical properties of yerba-mate. *Nutr. Food Sci.* **2015**, *45*, 221–228. [CrossRef]
6. Magri, E.; Valduga, A.T.; Gonçalves, I.L.; Barbosa, J.Z.; Rabel, D.d.O.; Menezes, I.M.N.R.; Nascimento, P.d.A.; Oliveira, A.; Corrêa, R.S.; Motta, A.C.V. Cadmium and lead concentrations in yerba mate leaves from agroforestry and plantation systems: An international survey in South America. *J. Food Compos. Anal.* **2021**, *96*, 103702. [CrossRef]
7. Faion, A.M.; Beal, P.; Ril, F.T.; Cichoski, A.J.; Cansian, R.L.; Valduga, A.T.; de Oliveira, D.; Valduga, E. Influence of the addition of natural antioxidant from mate leaves (Ilex paraguariensis St. Hill) on the chemical, microbiological and sensory characteristics of different formulations of Prato cheese. *J. Food Sci. Technol.* **2015**, *52*, 1516–1524. [CrossRef]
8. Beal, P.; Faion, A.M.; Cichoski, A.J.; Cansian, R.L.; Valduga, A.T.; de Oliveira, D.; Valduga, E. Oxidative stability of fermented Italian-type sausages using mate leaves (Ilex paraguariensis St. Hil) extract as natural antioxidant. *Int. J. Food Sci. Nutr.* **2011**, *62*, 703–710. [CrossRef]
9. Saguie, B.O.; Martins, R.L.; Fonseca, A.d.S.d.; Romana-Souza, B.; Monte-Alto-Costa, A. An ex vivo model of human skin photoaging induced by uva radiation compatible with summer exposure in Brazil. *J. Photochem. Photobiol. B Biol.* **2021**, *221*, 112255. [CrossRef]
10. He, H.; Li, A.; Li, S.; Tang, J.; Li, L.; Xiong, L. Natural components in sunscreens: Topical formulations with sun protection factor (spf). *Biomed. Pharmacother.* **2021**, *134*, 111161. [CrossRef]
11. Yarovaya, L.; Waranuch, N.; Wisuitiprot, W.; Khunkitti, W. Effect of grape seed extract on skin fibroblasts exposed to uva light and its photostability in sunscreen formulation. *J. Cosmet. Dermatol.* **2021**, *20*, 1271–1282. [CrossRef]
12. da Silva, A.C.P.; Paiva, J.P.; Diniz, R.R.; dos Anjos, V.M.; Silva, A.B.S.M.; Pinto, A.V.; dos Santos, E.P.; Leitão, A.C.; Cabral, L.M.; Rodrigues, C.R.; et al. Photoprotection assessment of olive (*Olea europaea* L.) leaves extract standardized to oleuropein: In vitro and in silico approach for improved sunscreens. *J. Photochem. Photobiol. B Biol.* **2019**, *193*, 162–171. [CrossRef]
13. Cho, Y.-H.; Bahuguna, A.; Kim, H.-H.; Kim, D.-I.; Kim, H.-J.; Yu, J.-M.; Jung, H.-G.; Jang, J.-Y.; Kwak, J.-H.; Park, G.-H.; et al. Potential effect of compounds isolated from Coffea arabica against UV-B induced skin damage by protecting fibroblast cells. *J. Photochem. Photobiol. B Biol.* **2017**, *174*, 323–332. [CrossRef]

14. Chiari-Andréo, B.G.; Almeida, F.B.d.; Yamasaki, P.R.; Santos, J.L.d.; Corrêa, M.A.; Chin, C.M.; Isaac, V.L.B. Can natural products improve skin photoprotection? *Rodriguésia* **2020**, *71*, 1–14. [CrossRef]
15. Amador-Castro, F.; Rodriguez-Martinez, V.; Carrillo-Nieves, D. Robust natural ultraviolet filters from marine ecosystems for the formulation of environmental friendlier bio-sunscreens. *Sci. Total Environ.* **2020**, *749*, 141576. [CrossRef]
16. DiNardo, J.C.; Downs, C.A. Dermatological and environmental toxicological impact of the sunscreen ingredient oxybenzone/benzophenone-3. *J. Cosmet. Dermatol.* **2018**, *17*, 15–19. [CrossRef]
17. Piovezan-Borges, A.C.; Valério-Júnior, C.; Gonçalves, I.L.; Mielniczki-Pereira, A.A.; Valduga, A.T. Antioxidant potential of yerba mate (Ilex paraguariensis St. Hil.) extracts in Saccharomyces cerevisae deficient in oxidant defense genes. *Braz. J. Biol.* **2016**, *76*, 539–544. [CrossRef]
18. Alice Teresa, V.; Itamar Luís, G.; Ana Cláudia Piovezan, B.; Albanin Aparecida, M.-P.; Ana Paula, P. Cytotoxic/antioxidant activity and sensorial acceptance of yerba-mate development by oxidation process. *Acta Scientiarum. Technol.* **2016**, *38*, 115–121. [CrossRef]
19. Aulton, M.E.; Taylor, K. *Aulton's Pharmaceutics: The Design and Manufacture of Medicines*; Elsevier Health Sciences: Amsterdam, The Netherlands, 2013.
20. Borghetti, G.S.; Knorst, M.T. Development and evaluation of physical stability from O/W lotions containing sunscreens. *Rev. Bras. De Ciências Farm.* **2006**, *42*, 531–537. [CrossRef]
21. ANVISA. *Guia de Estabilidade de Produtos Cosméticos*; ANVISA: Brasília, Brazil, 2004; p. 54.
22. Tozetto, J.T.; Tozetto, A.T.; Hoshino, B.T.; Andrighetti, C.R.; Ribeiro, E.B.; Cavalheiro, L.; Ferrarini, S.R. Extract of *Punica granatum* L.: An alternative to BHT as an antioxidant in semissolid emulsified systems. *Química Nova* **2017**, *40*, 97–104.
23. Sayre, R.M.; Agin, P.P.; LeVee, G.J.; Marlowe, E. A comparison of in vivo and in vitro testing of sunscreening formulas. *Photochem. Photobiol.* **1979**, *29*, 559–566. [CrossRef] [PubMed]
24. de Souza Mansur, J.; Breder, M.N.R.; D' Ascensão Mansur, M.C.; Azulay, R.D. Correlação entre a determinação do fator de proteção solar em seres humanos e por espectrofotometria. *An. Bras. De Dermatol.* **1986**, *61*, 167–172.
25. Allan, K.E.; Lenehan, C.E.; Ellis, A.V. UV light stability of α-cyclodextrin/resveratrol host–guest complexes and isomer stability at varying pH. *Aust. J. Chem.* **2009**, *62*, 921–926. [CrossRef]
26. Valduga, A.T.; Finzer, J.R.D.; Mosele, S.H. *Processamento de Erva-Mate*; EdiFAPES: Erechim, Brazil, 2003.
27. Hubner, A.; Sobreira, F.; Vetore Neto, A.; Pinto, C.A.S.d.O.; Dario, M.F.; Díaz, I.E.C.; Lourenço, F.R.; Rosado, C.; Baby, A.R.; Bacchi, E.M. The Synergistic behavior of antioxidant phenolic compounds obtained from winemaking waste's valorization, increased the efficacy of a sunscreen system. *Antioxidants* **2019**, *8*, 530. [CrossRef] [PubMed]
28. Barg, M.; Rezin, G.T.; Leffa, D.D.; Balbinot, F.; Gomes, L.M.; Carvalho-Silva, M.; Vuolo, F.; Petronilho, F.; Dal-Pizzol, F.; Streck, E.L.; et al. Evaluation of the protective effect of Ilex paraguariensis and Camellia sinensis extracts on the prevention of oxidative damage caused by ultraviolet radiation. *Environ. Toxicol. Pharmacol.* **2014**, *37*, 195–201. [CrossRef] [PubMed]
29. Cuelho, C.H.F.; Alves, G.d.A.D.; Lovatto, M.O.; Bonilha, I.F.; Barbisan, F.; da Cruz, I.B.M.; Oliveira, S.M.; Fachinetto, R.; do Canto, G.S.; Manfron, M.P. Topical formulation containing Ilex Paraguariensis extract increases metalloproteinases and myeloperoxidase activities in mice exposed to UVB radiation. *J. Photochem. Photobiol. B Biol.* **2018**, *189*, 95–103. [CrossRef]
30. Sheu, M.-T.; Lin, C.-W.; Huang, M.-C.; Shen, C.-H.; Ho, H.-O. Correlation of in vivo and in vitro measurements of sun protection factor. *J. Food Drug Anal.* **2003**, *11*, 12. [CrossRef]
31. Bleasel, M.D.; Aldous, S. In vitro evaluation of sun protection factors of sunscreen agents using a novel UV spectrophotometric technique. *Int. J. Cosmet. Sci.* **2008**, *30*, 259–270. [CrossRef]
32. Butiuk, A.P.; Martos, M.A.; Adachi, O.; Hours, R.A. Study of the chlorogenic acid content in yerba mate (Ilex paraguariensis St. Hil.): Effect of plant fraction, processing step and harvesting season. *J. Appl. Res. Med. Aromat. Plants* **2016**, *3*, 27–33. [CrossRef]
33. Rousseau, D. Fat crystals and emulsion stability—A review. *Food Res. Int.* **2000**, *33*, 3–14. [CrossRef]
34. Finnegan, M.; Duffy, E.; Morrin, A. The determination of skin surface pH via the skin volatile emission using wearable colorimetric sensors. *Sens. Bio-Sens. Res.* **2022**, *35*, 100473. [CrossRef]
35. Some, I.T.; Bogaerts, P.; Hanus, R.; Hanocq, M.; Dubois, J. Improved kinetic parameter estimation in pH-profile data treatment. *Int. J. Pharm.* **2000**, *198*, 39–49. [CrossRef]