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Original Article

SOLVENT EFFECT ON PHOTOSTABILITY OF BUTYL METHOXY DI BENZOYL METHANE FORMULATED IN SOLUTION AND EMULSION

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ABSTRACT

Objective: The current study was undertaken to correlate the impact of some cosmetics solvents in the photostability of butyl methoxy dibenzoyl methane (BMDBM) into systems with an increasing order of complexity, from simple solutions to emulsions.

Methods: Solutions and emulsions containing BMDBM in different solvents were prepared and evaluated using spectrophotometer or transmittance analyzer, respectively. Also, emulsions containing BMDBM in combination with octyl methoxycinnamate (OMC) in ratio 1:1 and 1: 2, and in the presence of octocrylene in the ratio 1:2:1 were prepared. The percentage of decay absorbance at 356 nm was measured before and after irradiation at 500 W/m^2 at intervals of 20 min until completing 100 min. Finally, a photolysis assay was carried to analyze deoxygenated and not BMDBM solutions.

Results: The absorbance decay of BMDBM in solution was higher in solvents such as mineral oil, isopropyl palmitate and isopropyl myristate. Also, it was observed that concentration and degassing had an effect on the decay kinetics. In emulsions containing only, BMDBM, the absorbance decay did not exceed 20% in all solvents, suggesting a protective effect of the matrix. In the contrary, a decay of 90% was observed in emulsion containing BMDBM and OMC in a 1:2 ratio. When Oct was added to that emulsion, stabilization on the absorbance decay of BMDBM was detected.

Conclusion: This study evidenced that the photochemistry of BMDBM is different in solutions and in emulsions. In solutions, the nature of solvents was important, while in emulsions the nature of UVB filters played a pivotal role in the stability of BMDBM.

Keywords: Butyl methoxy di benzoyl methane, Absorbance decay, Transmittance analysis.

INTRODUCTION

Skin cancer is one of most prevalent diseases in human adults over 50; the damage is caused by exposure to UV radiation. The disease's incidence is particularly high in tropical countries, where the radiation is most intense and year round, and has been demonstrated by high UV Indexes [1]. Besides cancer, exposure to UV radiation can also cause skin aging, immunosuppression and sunburns making it a serious public health problem. The best way to prevent these diseases is to avoid the direct exposures during peak irradiation times, and to preclude sunburn, but this is not always possible. An alternative is to use sunscreens; these are products that contain UV filters, which absorb, reflect or scatter the UV radiation on UVB region (290–320 nm) and UVA radiation (320–400 nm).

tert-Butyl methoxy di benzoyl methane (BMDBM) is the one of the filters most widely used in commercial sunscreens [2], because of its capacity to absorb UVA (ε<10000 L/mol cm at 358 nm) [3]. The photochemistry of BMDBM has been extensively studied and reported [4–6]. First at all, the BMDBM being a β-diketone suffers a keto-enol tautomerization in the ground state, where the equilibrium favors the enol form in the most of the media, because enol tautomer is able to make an intra-molecular hydrogen bond. The diketone and enol isomers exhibit different UV spectra, enol form exhibits a maximum of absorption at 355 nm while diketone tautomer absorbs at 260 nm, consequently only the first one is responsible for the UVA-protective capacity.

When a solution of BMDBM is irradiated, enol isomer is turned into diketone isomer by photo-isomerization process, and subsequently diketone form return to enol form through thermal equilibrium, in this way the photo-isomerization is a reversible process. Also, it has been observed, in the laser flash photolysis time scale, that enol isomer gives rise to enol rotamers, which are transient species, through an intramolecular hydrogen bond cleavage [7]. Furthermore, diketone isomer under irradiation is excited to triplet state, which can suffer two decay mechanisms: (a) photo-fragmentation by Norrish Type I process, (b) generation of singlet oxygen, some authors have suggested singlet oxygen may promotes the degradation of enol isomer, process known as self-degradation [8]. Both photo-fragmentation and photo-isomerization lead to loss of UVA-protective capacity, since only the enol tautomer is effective as UVA filter.

A large number of studies have been devoted to improve photo stability of BMDBM, using excited state quenchers such as octocrilene, diethylhexyl 2,6-naphthalate and ethyl hexyl methoxy crylene [9], and antioxidant agents such as vitamin C, vitamin E, and ubiquinone [10], as common strategies. Also BMDBM has been encapsulated into nanocarriers [11].

From another perspective, the solvent effect on photo-degradation and photo-isomerization of BMDBM has been extensively studied by photochemistry methods. The data in this field shows that solvent´s proticity and polarity are committed to the advancement of these reactions and therefore the stability of BMDBM depends mainly on the medium. Since BMDBM is one of the most effective and low-cost filters, the question that arises is whether the formulators can achieve stable and accessible preparations looking for suitable solvents to incorporate BMDBM. In a recent work, we found that some solvents commonly used in cosmetic formulations are able to stabilize BMDBM in solution [12]. Nevertheless, a sunscreen product is physically more complex than a simple solution, because it must have additional properties such as a specific rheological profile for uniform layer formation on the skin during the time of exposure to UV rays, which is easier with emulsified systems; moreover, they are more accepted by users [13, 14].

Some encouraging results have been found by Huong and coworkers, who studied the behavior of BMDBM both in dilute-concentrated solutions and in emulsions. They reveled interesting findings in the chemical behavior of BMDBM in diluted solutions compared to the concentrated solution, but no solvent effect was determined in emulsion because the samples analyzed corresponded to commercial products [15]. In 2005, two patents were published by Bonda and Dueva, and Sanogueira [16, 17] who reported a method that claims to protect BMDBM through controlling the polarity of the oil phase. Bonda found a parabolic relationship between polarity and the photostability of UV filters [18].

A wide variety of excipients are used in the formulation of sunscreens, which accomplish different functions within the preparation. Cosmetics solvents, such as dimethicone, hydrogenated polyisobutene, mineral oil, isopropyl myristate, isopropyl palmitate, dodecyl oleate and octyldodecanol are used as the oil phase of the emulsions; they allow solubilization of BMDBM and provide the product properties such as emollience, masking, coverage, spreadability, reduction of the feeling of oiliness, and others.

The concentration of these solvents is restricted according to Cosmetics Regulation (EC) Nº 1223/2009 of the European Parliament and of the Council [19].

The current study was undertaken to correlate the impact of these solvents in the photostability of BMDBM incorporated into systems with an increasing order of complexity, from simple solutions to O/W emulsions. Emulsions were prepared containing BMDBM alone and then in combination with UVB filters at concentrations similar to those use in commercial products. In this way, this study looks to contribute to the understanding of the complex stability of BMDBM and to provide new knowledge into the design of sunscreens.

MATERIALS AND METHODS

Materials

Butyl methoxy dibenzoyl methane (BMDBM) and octocrylene (Oct) were obtained from Merck (Darmstadt, Germany); octyl methoxycinnamate (OMC), isopropyl myristate, mineral oil, isopropyl palmitate, octyldodecanol and dimethicone were obtained from Dow Corning (Midland, United states); PPG-5-Laureth 5, cetearyl alcohol, stearyl alcohol and polysorbate 20 from Basf (Ludwigshafen, Germany), and water was purified by reverse osmosis.

Methods

Preparation of samples

BMDBM solutions were prepared using the solvents listed in table 1. The concentrations were different because the absorbance was adjusted to ca. 1 AU at absorption maximum, using a spectrophotometer Cary 50 Bio uv/vis (Varian, Palo Alto, California), and 1 mm quartz cells. The UV filter was solubilized using an ultrasonic bath.

Table 1: The solvents used in the performance test solution BMDBM and characteristics

Solvents	BMDBM Wavelength (nm)	BMDBM Concentration (M)	Absorbance (UA)
Isopropyl myristate	355.0	9.00×10^{-6}	1.15
Mineral oil	355.0	2.00×10^{-5}	1.02
Isopropyl palmitate	355.8	8.00×10^{-6}	0.88
Octyldodecanol	355.0	3.50×10^{-4}	1.29
Dimethicone	355.0	3.00×10^{-4}	0.99

Emulsions containing BMDBM as simple UV filter, were prepared according the composition described in table 2, where the nature of the solvent was changed in each sample: isopropyl myristate, mineral oil, isopropyl palmitate and octyldodecanol. O/W emulsions were prepared by standard emulsification method, the oil and aqueous phases were heated at 70±2 ° C, and then the oil phase was added to the aqueous phase slowly and was homogenized with an ultra-turrax T18BS1 (Ika, Staufen, Germany) at 3000 rpm for 10 min to room temperature. Additionally, three emulsions were prepared containing BMDBM in the presence of UVB filters: (1) BMDBM: OMC in a concentration ratio of 1:1, (2) BMDBM: OMC in a ratio (1:2) and (3) BMDBM: OMC: Oct in a ratio of 1:2:1. The excipients and the preparation method were the same used in emulsion comprising BMDBM alone, as is indicated in the table 2.

Table 2: Different behavioral tests of BMDBM emulsion

Ingredients	BMDBM emulsion	BMDBM: OMC (1:1)	BMDBM: OMC (1:2)	BMDBM: OMC: OCT (1:2:1)
	%			
PPG-5-laureth 5	3,6	3.6	3.6	3.6
Cetearyl alcohol	2.0	2.0	2.0	2.0
Stearyl alcohol	2.0	2.0	2.0	2.0
Polysorbate 20	2.0	2.0	2.0	2.0
SOLVENT	6.0	6.0	6.0	6.0*
Dimethicone	4.0	4.0	4.0	4.0
Butyl methoxy di benzoyl methane	5.2	5.2	5.2	5.2
Ethylhexylmethoxycinnamate	_	5.2	10.4	10.4
Octocrylene	_	_	_	5.0
Water	q. s. 100%			

*In these case only mineral oil was used as solvent.

Irradiation

BMDBM solutions were contained in quartz cells and emulsions were spread in polymethylmethacrylate (PMMA) plates, the amounts used were 1.3 mg/cm². The samples were irradiated at 500 W/m² using a solar simulator Solarbox 1500e (Co. fe. me. gra, Milano, Italy) equipped with xenon lamp and radiation in door filter. The total irradiation time was 100 min.

Absorbance decay measurement

A spectrophotometer Cary 50 Bio UV/vis was used to measure the decrease in absorbance of BMDBM in solutions, while a transmittance analyzer Labsphere 2000S (Labsphere, North Sutton, United States) was used to assess the emulsions. In both cases, the absorbances at 356 nm were registered before irradiation and every 20 min after irradiation, until 100 min. The percentage of absorbance decay for BMDBM at 356 nm was calculated using equation 1.

Equation 1.

$$\%Absorbance\ decay = \frac{AU_{t_0} - AU_{t_x}}{AU_{t_0}} \times 100$$

The absorbance decay for OMC at 309 nm was analyzed following the same process.

Photolysis assay

Photolysis was carried out in 10 mL portions of deoxygenated and not deoxygenates solutions of BMDBM (1.00x10^{-6} M) in palmitate and octyldodecanol. These solutions were irradiated in a photochemical multiarray reactor (Helios Italquartz, Milano, Italy) equipped with 16 phosphorus-coated low-pressure lamps, center of emission was 366 nm, during 3 hours. The light flux was measured by ferrioxalate actinometry (6.12x10^{-6} E/min). The deoxygenation of the solution was obtained by flushing for 15 min with nitrogen. The decay absorbance was followed using a 559 UV-visible spectrophotometer (PerkinElmer, Beaconsfield, UK).

Statistical analysis

All experiments were done in triplicate. The results are given as mean and standard deviation (SD). ANOVA tests were carried out to find the significant difference. The level of significance was 95% ($p<0.05$). All calculations were done using the statistical software Sigmaplot11.0

RESULTS AND DISCUSSION

The capacity of sunscreens to protect the skin from solar radiation is based on its capacity to absorb light. The UV spectra obtained from solutions with solvents used in cosmetic formulations did not show hipso or bathochromic shifts; however, hyperchromic effect was observed and it was necessary to adjust the concentration to achieve unify absorbance at 1 AU at 356 nm (table 1). This outcome suggested that solvents as octyldodecanol and dimethicone favored the diketo specie (260 nm) rather than enol (356 nm) form of BMDBM. In addition, when these solutions were irradiated under the conditions detailed in the methodology, it was found that the absorbance decay was greater in solvents such as mineral oil, isopropyl palmitate and isopropyl myristate and lower in dimethicone and octyldodecanol. This showed that decay was dependent on the solvent. Under the experimental conditions was not possible to distinguish if the absorbance decay obeyed to photo-fragmentation or enol-keto photo-tautomerization of BMDBM. Nevertheless, for the aim of this study, it was not decisive since both processes led to loss of UV-blocking efficacy. Surprisingly, the results described above were not consistent with those obtained in our laboratory and previously reported [12].

The discrepancy in results may be due to the existence of other variables in the degradation of BMDBM besides the solvent. Factors such as concentration, solvent purity, irradiation dose, among others have shown to play a vital role. Indeed, the data here showed a concentration effect, diluted solutions (isopropyl myristate, isopropyl palmitate and mineral oil) exhibited a higher decay that concentrated solutions, which were consistent with the data reported in the literature [17].

On the other hand, the results from the photolysis study at 366 nm showed that the degassing of solution affected the decay kinetics of BMDBM depending on the type of solvent used. For example, in octyldodecanol, the decay rate depended on degassing as illustrated in fig. 2a, while in isopropyl myristate (fig. 2b), the decay was not influenced by the degree of degassing.

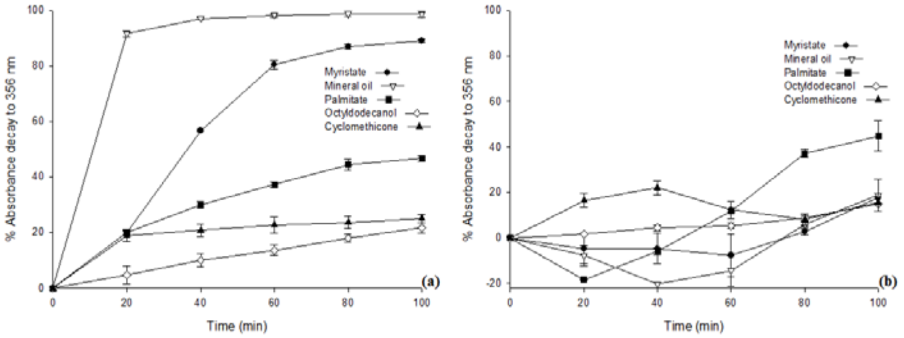

Fig. 1: Photostability assay of (a) BMDBM in solution and (b) BMDBM in emulsions varying the nature of solvent

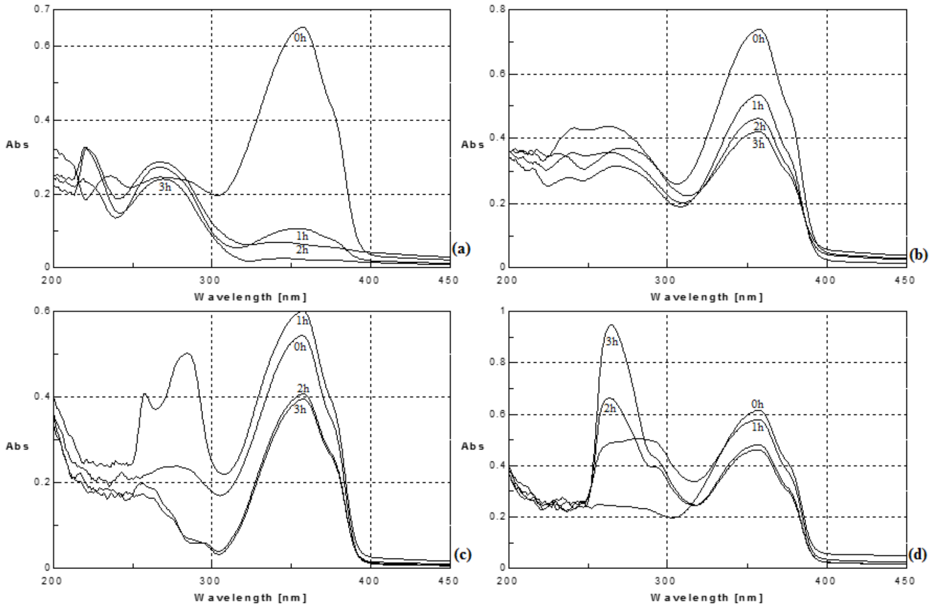

Fig. 2: UV absorbance evolution in photolysis study under irradiation at 366 nm of BMDBM in (a) degassed octyldodecanol, (b) not degassed octyldodecanol, (c) degassed palmitate, (d) not degassed palmitate

Also, some discrepancies concerning the BMDBM photo degradation in solutions were encountered when reviewed literature in the field. For instance, Schwack and Rudolph in 1995, and Mturi and Martincigh in 2008 reported in their publications that polar protic solvents as isopropanol and methanol stabilized the BMDBM. Polar aprotic solvents as dimethyl sulfoxide promoted the photo isomerization, whereas non-polar solvents as cyclohexane, isooctane favored the photo-fragmentation [5, 20]. The results obtained by Dubois´s team confirmed that the predominant reaction in polar aprotic solvents (acetonitrile) was the photo isomerization [21].

On the contrary, Huong *et al.,* in 2008 found that BMDBM diluted solutions were stable in dioxane, acetonitrile, ethyl acetate, THF, ethanol and isopropanol. However, BMDBM suffered photo isomerization in hexane, heptanes and cyclohexane; they also observed in their studies that aqueous solutions, containing more than 90% water promoted photo-fragmentation of BMDBM, while no solvent effect was observed in concentrated solution using non-volatile solvents [15].

This shows that there are additional factors, different to solvent that change the photochemical behavior of BMDBM. In fact, Nash & Tanner in their recent work recognized that differences are owing to slight alterations in the experimental conditions [9].

As alluded earlier, O/W emulsions are the wide spread vehicles for sunscreen. The BMDBM is dissolved into the oil phase. Technically, 40% is the maximum percentage of oil phase allowed to achieve emulsions with acceptable properties by the consumers.

In this work, the effect of solvent on the external phase was studied using a model O/W emulsion, the participation of the solvent was 30.3% of the total composition of the oil phase, following permissive levels established by Cosmetics Regulation (EC) Nº1223/2009. Moreover, in this study, the irradiation was performed after the product was spread on thin layer onto PMMA plates, trying to simulate the regular use conditions. The addition of fatty alcohols and dimethicone to the emulsions prepared was imperative in order to adequate the sample to an analysis method. Under these experimental conditions, it was observed that the absorbance decay did not exceed 20% in all emulsions, except in the case of isopropyl palmitate with a decay of 40 %, which showed that the nature of the solvent did not affect the loss of the absorption capacity, suggesting that the matrix may protect BMDBM. This may be explained by liquid emulsion droplets acting as light scatterer. A similar effect was noticed with UV filters as padimate-O and sulisobenzone, which were stabilized when they were incorporated into the internal phase of an emulsion. An opposite effect was observed when the filters were incorporated into the external phase [22]. In that study, however, the effect of emulsification of BMDBM could not be assessed.

Our findings evidence that BMDBM incorporated in O/W emulsions as the single filter is photostable. In addition, the results presented here reveal that the instability observed in commercial sunscreens from previous works, cannot be attributed merely to the excipients contribution as it is suggested in [23,24]. Contrary, stabilizer and synergistic effect of some excipients, such medium chain triglycerides waxes has been revealed as important contributors in microencapsulation studies [25].

During the first minutes of irradiation, an increased in absorption at 356 nm was observed from the absorbance spectrum in emulsions. This corresponds to the maximum absorbance of the enol form. This finding suggests a shift of the keto-enol equilibrium in the early stages. This phenomenon has been observed for other filters with isomeric character, such as isoamyl methoxi cinnamate, 4-methyl benzylidene camphor and octyl methoxy cinnamate (OMC) [26–28].

The sun screens should provide protection in the UVA and UVB range; therefore, the BMDBM must be associated with UVB filters, being the BMDBM: OMC mix the most widely used [29]. In this part of the study, both the effect of the solvent and the concentration of OMC in the stability of the BMDBM incorporated in emulsions was evaluated. The presence of OMC (fig. 3) increased dramatically the decay. The increase of photo reactivity of BMBDM in the presence of OMC is more remarkable in the 1:2 ratio. A 90% of absorbance decay was achieved in most of the solvents studied after 100 min of irradiation. Moreover, a similar profile was observed in all solvents. A notable difference regards to the behavior displayed by the emulsions containing only BMBDM (fig. 1b) is that here there was not increased in absorption at 356 nm in the first phase of the kinetics (fig. 3a-b).

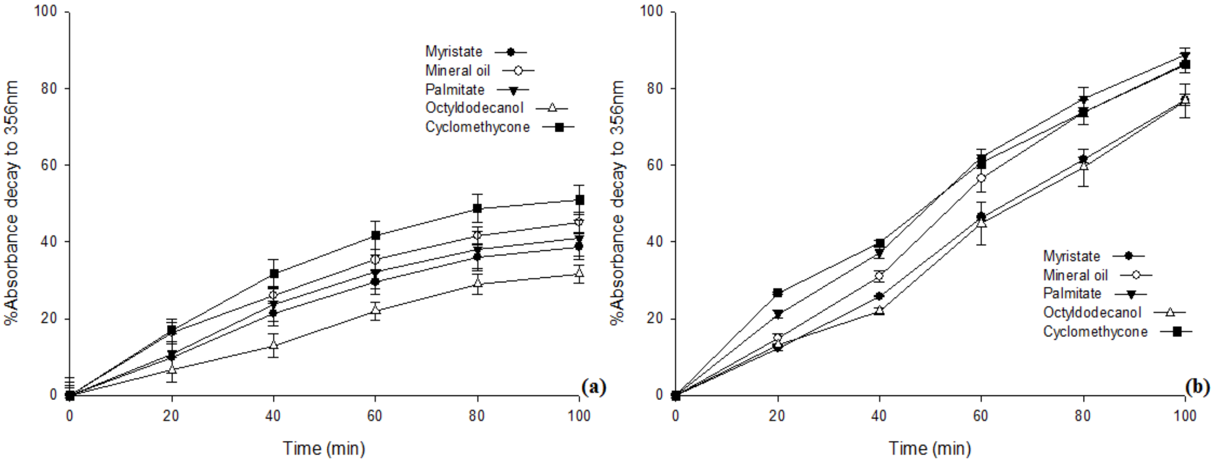

Fig. 3: Photostability assay of BMDBM in emulsions varying the nature of the solvents in presence of OMC (a) BMDBM: OMC with 1:1 ratio and (b) BMDBM: OMC with 1:2 ratio

A gradual increase in decay of absorption at 356 nm of BMDBM was observed with the concentration of OMC under the emulsified system, as it is depicted in fig. 4a.

In addition, the absorbance at 309 nm attributed to OMC was monitored in the same irradiated samples, and it was found that the degree of decay was different in the two types of emulsions studied, being higher with the ratio 1:2 (fig. 4b). The incompatibility between BMDBM and OMC has been previously reported [30]. It obeys to a [2+2] cyclo addition reaction leading to the formation of adducts, explaining the reason of the simultaneous reduction in OMC absorbance and the changes experienced by BMDBM.

Finally, the effect of Oct, other UVB filter, was assessed in the emulsion prepared with BMDBM and OMC at 1:2 ratio. Oct prevented the BMDBM filter from degradation, as is shown in fig. 4. The results were in accordance with earlier studies in the field [8, 16, 25].

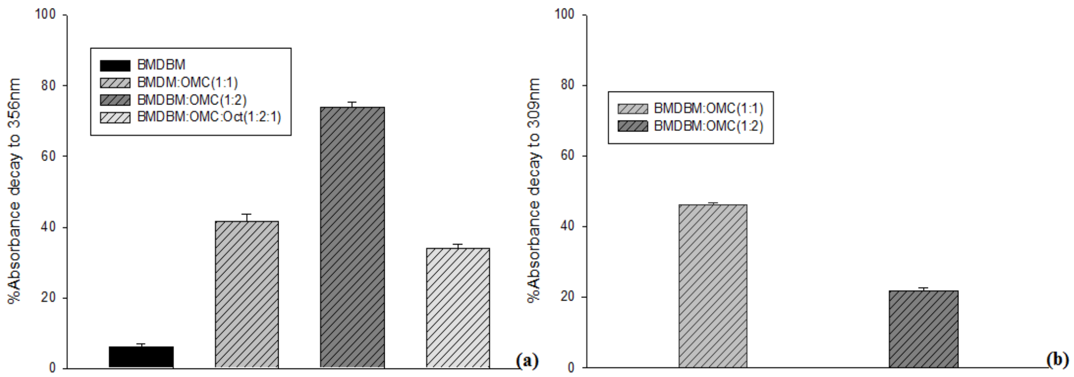

Fig. 4: Comparison of absorbance decay at (a) 356 nm (BMDBM) and (b) 309 nm (OMC), in emulsions using mineral oil as a solvent

The overall results presented here evidenced the existence of a second filter had more influence than the nature of solvents in the photostability of BMDBM in emulsified system. According to mechanisms previously proposed, the enol form of BMDBM interacts with OMC in the [2+2] reaction photo cyclo addition, and with Oct in the triplet-triplet energy transfer [26]; unlike photo-fragmentation reactions occurs through the diketone species of BMDBM [30]. Also, Dondi and coworkers, stated that the species diketone tends to accumulate in dilute solutions and nonpolar environments [26]. In light of this, it is not possible to expect high concentration of diketone species in the internal phase of the emulsions studied. This may shed light on the low reactivity of BMDBM towards photo-fragmentation in emulsions, and the high reactivity towards interaction with OMC and Oct.

CONCLUSION

In this study, it was showed that the degradation profiles of BMDBM solutions are not comparable to the profile in emulsions. The data revealed that the reactivity of BMDBM is dramatically altered by the presence of UVB filters in emulsions, where no solvent effect was observed. The results of this study indicated that the strategies of photo stabilization of BMDBM should be performed in the mixture of filters and not separately.

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CONFLICT OF INTERESTS

The authors have declared no conflict of interest

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