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Development, physical-chemical stability and rheological behavior of silicones formulations containing Dimethylaminoethanol (DMAE)

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ABSTRACT

The aim of this paper was to develop formulations increased of DMAE and evaluate their physical-chemical stability and rheological behavior. Eleven formulations containing 3% DMAE pidolate or 3% DMAE acetamidobenzoate were developed and both preliminary stabilities tests and rheological measurements were carried out. They were considered stable during all period of study. The type of DMAE did not modify the viscosity of the emulsion and all presented pseudoplastic behavior with hysteresis area. An increase of hysteresis area could be observed with DMAE addition. The results point that the type of DMAE can influence the physical stability of the final product.

INTRODUCTION

DMAE (2-dimetilaminoetanol) is a substance which is found naturally in fish such as salmon, but it can also be found in small amount in the human brain. As it is a small molecule (PM=89.14 a.u.m.), it tends to penetrate easily into the skin (Zahniser *et al.*, 1978). This compound has been being used for years by the allopathic medicine for the improvement of the healthy patients' memory, and as well as of those with syndromes like Autism and Alzheimer. Unfortunately, doctors and patients had noticed a hardening of the cervical area when DMAE was introduced orally. Therefore, the scientists' interests were conducted to its dermatological application (Giannoccaro *et al.*, 2007). The mechanism of action of DMAE in the skin is not totally elucidated yet (Baumann, 2002; Morissette *et al.*, 2007; Deccache *et al.*, 2010). It is known that DMAE is similar to choline, being a precursor of a cetylcholine neurotransmitter(Baumann, 2002; Deccache *et al.*, 2010; Uhoda *et al.*, 2002; Grossman, 2005), which would stimulate the muscles of the face causing a tensor effect in the skin known as lifting effect (Perricone, 2001).

Besides the possible interference of the cholinergic neurotransmitter, there are also theories concerning the anti-inflammatory effects of DMAE, which are still not totally understood (Morissette, 2007; Grossman, 2005). Another mechanism would be acting on collagen synthesis in dermis, which has cholinergic receptors (Giannoccaro *et al.*, 2007). These cholinergic receptors present in the area of some cells modulate a wide variety of cellular activities such as proliferation, differentiation, migration and viability. The cholinergic fibroblasts receptors such as muscarinics and nicotinics in the presence of acetylcholine produce a transduction signal which mediate communications among different cellular types besides storing a significant amount of non-neural acetylcholine in the skin (Giannoccaro *et al.*, 2007; Uhoda *et al.*, 2002).

Thus, the role of acetylcholine and DMAE as modulators of the acetylcholine functions in the skin remains to be elucidated (Morissette, *et al.* 2007). Tadini and Maia Campos (2009) observed a significant increased in dermis thickness and also an improvement in collagen fiber thicknesses on hairless mice dermis, when formulations with 9.0% dimethyl-aminoethanol acetamidobenzoate were used. It can be noticed that studies must be accomplished in order to evaluate the effectiveness of topical products containing

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DMAE as a tensor agent on the face skin (Baumann, 2002; Grossman, 2005). The aim of this paper was to develop formulations containing DMAE. There were evaluated both the physical-chemical stability and the rheological behavior.

MATERIALS AND METHODS

Eleven formulations containing 3% of DMAE pidolate (liquid) or 3% of DMAE acetamidobenzoate (powder) were developed (from A to K, **Table I**). The visual and sensorial aspects were evaluated for each one. Unstable or disagreeable (to the skin) samples were discarded of the study, being selected the best ones for the accomplishment of the preliminary stability tests. The preliminary stability tests consisted on visual evaluation, centrifuge test and determination of the pH. For all tests the formulations were stored in 3 different temperatures over a period of 28 days, such as room temperature (25.0 ± 2.0 °C), refrigeration (5.0±2.0 °C) and hot oven (37.0± 2.0 °C) environments (ANVISA, 2004). For the visual evaluation, it was observed the stability of formulations regarding separation of the phases, homogeneity, odor and color changes. In the test of centrifuge, 5g of each formulation were submitted to centrifuga-tion (Excelsa II-Fanem) at 3000 rpm during 30 min. The pH determination was performed by using a digital pH-meter (Gehaka PG 2000) in samples diluted in deionized water (10% w/v) (Santos *et al.*, 2005).

Rheological measurements

The rheological evaluation was done by using a clone plate rotational type viscometer (DVII - Brookfield) with a spindle CP52. The viscosity values and flow index were obtained through the software Wingather V2.5, whereas the values of the histeresis area and rheological behavior were obtained from the software Origin 5.0 (Santos *et al.*, 2005; Gaspar and Maia Campos, 2003).

The analyses were accomplished in triplicate at 24 hours (T0), 15 days (T15) and 28 days (T28) for samples stored at room temperature (25.0 ± 2.0 ºC), refrigerator (5.0 ± 2.0 ºC) and hot oven (37.0 ± 2.0 ºC). The minimum apparent viscosity (cP) was calculated at the maximum point of shear rate (Gaspar and Maia Campos, 2003). The ascendant curve was constructed in a speed range from 5.0 to 60.0 r.p.m., being the descendent curve designed through the opposite, ranging between 60.0 and 5.0 r.p.m. The rheological behavior was obtained by rheograms which relate shear rate values (1/sec) with the shear stress (D/cm^2) (Htibl and Steinwendtner, 2000). The experimental data obtained from minimum apparent viscosity were submitted to statistical analysis by using the software GMC V. 7.6 (Maia Campos, 1999). Statistical analyzes of the apparently low viscosity data were performed by using Kruskal-Wallis and Freedman tests, considering significant $p \leq 0.05$.

RESULTS AND DISCUSSIONS

The formulation F (Table I) showed the best stability and skin sensory among all formulations increased with DMAE.

Furthermore, it was selected for the preliminary stability tests. Therefore, a base constituted of silicon was chosen (E) for the preliminary stability. Two types of DMAE were increased to that base, resulting in three formulations (Table II). Macroscopically, the formulations were stable during all the period of study. However, there were some changes in the color of the formulations E1 and E2 which were kept at room temperature and at hot oven. It indicates that formulations should be stored under refrigeration. The formulations submitted to the centrifuge test were stable as well no signs of instability were obtained. It was observed a decrease of the pH in emulsion (E) when different types of DMAE were added. Even when the formulations were stored under the 3 different temperatures for the whole experiment, the average pH for emulsion (E) was 7.88 ± 0.03. This value decreased to 7.37 ± 0.08 when the DMAE acetoamidobenzoate (E1) was incorporated and to 7.38 ± 0.02 when the DMAE pidolate (E2) was added.

Rheological measurements

The mean value results and standard deviation of the apparently low viscosity (cP) of the formulations studied are in Table III. Significant differences were not verified when the same sample was analyzed at the 3 times (T0, T15 and T28). Whereas for the independent factors (formulations and temperature), significant differences were observed (Table III). Comparing the formulations E (emulsion) x E1 (E + DMAE powder) x E2 (E + DMAE liquid) at room temperature, refrigerator and hot oven at T0 (24 hours), the result was that the addition of different types of DMAE has not significantly altered the viscosity of the emulsion. So, the type of DMAE does not modify the viscosity for the emulsion.

It was observed that all of the studied formulations, analyzed in the times T0, T15 and T28 at the three temperatures, obtained values of flow index below 1, which indicates them to be pseudoplastic samples. This behavior is suitable for cosmetic products with topical indication, because after the application of the tension, the emulsion presents easiness in flowing, reflecting good dispersal during the application and formation of uniform film in the skin (Gaspar and Maia Campos, 2003; Kortemeier and Leidreiter, 2006).

When DMAE was added to the formulations, an increase of the area of hysteresis could be observed. This approach could also be established for both types of DMAE, pidolate and acetoamidobenzoate. The average area of hysteresis for the emulsion (E) was 6.313 dyne/cm^2.s when stored under the three temperatures during 28 days. This area increased to 14.167 dyne/cm^2.s and to 18.430 dyne/cm^2.s when the DMAE acetoamidobenzoate (E1) and DMAE pidolate (E2) were respectively incorporated. The rheograms of the rheological behavior can be visualized in the Fig. 1-3, and all of them indicated that the analyzed samples present a non-Newtonian pseudoplastic behavior with a hysteresis area.

Table. 1: Description (%, w/w) of the components used in assessed formulations.

Components (INCI name)	Formulations										
	A	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**	**K**
Sodium Polyacrylate (and) Dimethicone (and) Cyclopentasiloxane (and) Trideceth-6 (and) PEG/PPG-18/18 Dimethicone.	3.0	6.0	-	-	6.0	-	-	10.0	6.0	6.0	-
Cyclopentasiloxane (and) Dimethicone Crosspolymer (and) Dimethicone (and) Laureth 23 (and) Laureth 4 (and) Acrylate Polymer (and) Mineral Oil (and) Water.	-	-	50.0	-	-	-	30.0	-	-	-	-
Cetoestearilic Alcohol 20 EO/ Sorbitol Monostearate (and) Berreniltrimônio Methosulfate and Cetoestearilic Alcohol (and) Isopropyl Palmitate (and) Cyclopentasiloxane (and) Dimethicone Crosspolymer.	-	-	-	50.0	-	80.0	-	-	-	-	-
Silicone glycol copolymer.	-	-	-	-	10.0	-	-	-	-	-	-
Divinyldimethicone / Dimethicone Copolymer (and) C12-13 Pareth-23 (and) C12-13 Pareth-3.	-	-	-	-	-	-	-	-	1.0	-	-
Dimethicone / Vinyl Dimethicone Crosspolymer (and) Silica.	-	-	-	-	-	-	-	-	-	3.0	-
Acrylate Polymer	-	-	-	-	-	-	-	-	-	-	2.0
Glycerin	-	-	-	-	-	-	-	-	-	-	5.0
Methyldibromo Glutaronitrile (and) Phenoxyethanol	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
2,2',2" nitrilotriethanol	-	-	-	-	-	-	-	-	-	-	*
Deionized Water (q.s.)	100	100	100	100	100	100	100	100	100	100	100

(*): until pH 6.0

Table. 2: Formulations selected for the preliminary stability effectiveness tests. Being E= emulsion; E1 = E + DMAE powder; E2 = E +DMAE liquid

Components		Composition (% w/w)		
INCI name	**Brand names**	**E**	**E1**	**E2**
Cetoestearilic Alcohol 20 EO / Sorbitol Monostearate (and) Berreniltrimônio Methosulfate and Cetoestearilic Alcohol (and) Isopropyl Palmitate (and) Cyclopentasiloxane (and) Dimethicone Crosspolymer	(DC*LC Blend ®)	80.0%	80.0%	80.0%
Dimethyl MEA Pidolate	(DMAE pidolato ®)	-	-	3.0%
Dimethyl MEA Acetoamidobenzoate	(DMAE acetoamidobenzoato ®)	-	3.0%	-
Methyldibromo Glutaronitrile (and) Phenoxyethanol	(Cosmoguard ®)	0.2%	0.2%	0.2%
Deionized Water	(Deionized Water)	qs 100	qs 100	qs 100

Table. 3: Mean value results (n=3) and standard deviation of the apparently low viscosity (cP) of the formulations studied in times T0, when stored at room temperature (25.0 ± 2.0 °C), T15 and T28 at room temperature (25.0 ± 2.0 °C), refrigeration (5.0 ± 2.0 °C) and hot oven (37.0 ± 2.0 °C). Values established at the maximum point of the shear rate. E = emulsion; E1= E + DMAE powder; E2= E + DMAE liquid.

	Room temperature			Refrigeration		Hot oven	
	T0	**T15**	**T28**	**T15**	**T28**	**T15**	**T28**
E	981 ± 47.29	966 ± 33.09	962 ± 24.26	884 ± 121.24	961 ± 16.28	911 ± 52.00	1003 ± 118.50
E1	1134 ± 22.24	1221 ± 10.25	1282 ± 112.30	994 ± 18.50	980 ± 16.62	988 ± 31.01	947 ± 31.13
E2	1004 ± 31.57	1128 ± 30.92	1062 ± 46.75	925 ± 26.50	879 ± 92.65	868 ± 3.47	882 ± 123.49

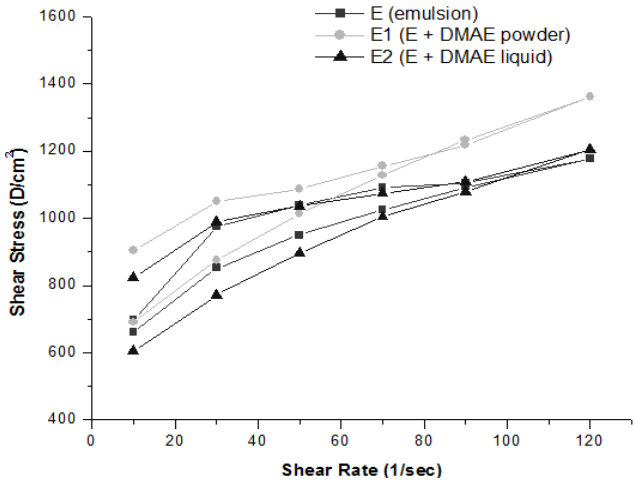

Fig. 1: Mean rheograms (n=3) of the values of shear rate (1/sec) and shear stress (D/cm^2) of the formulations E (emulsion), E1 (E + DMAE powder) and E2 (E + DMAE liquid) analyzed at T0, at room temperature (25.0 ± 2.0 °C).

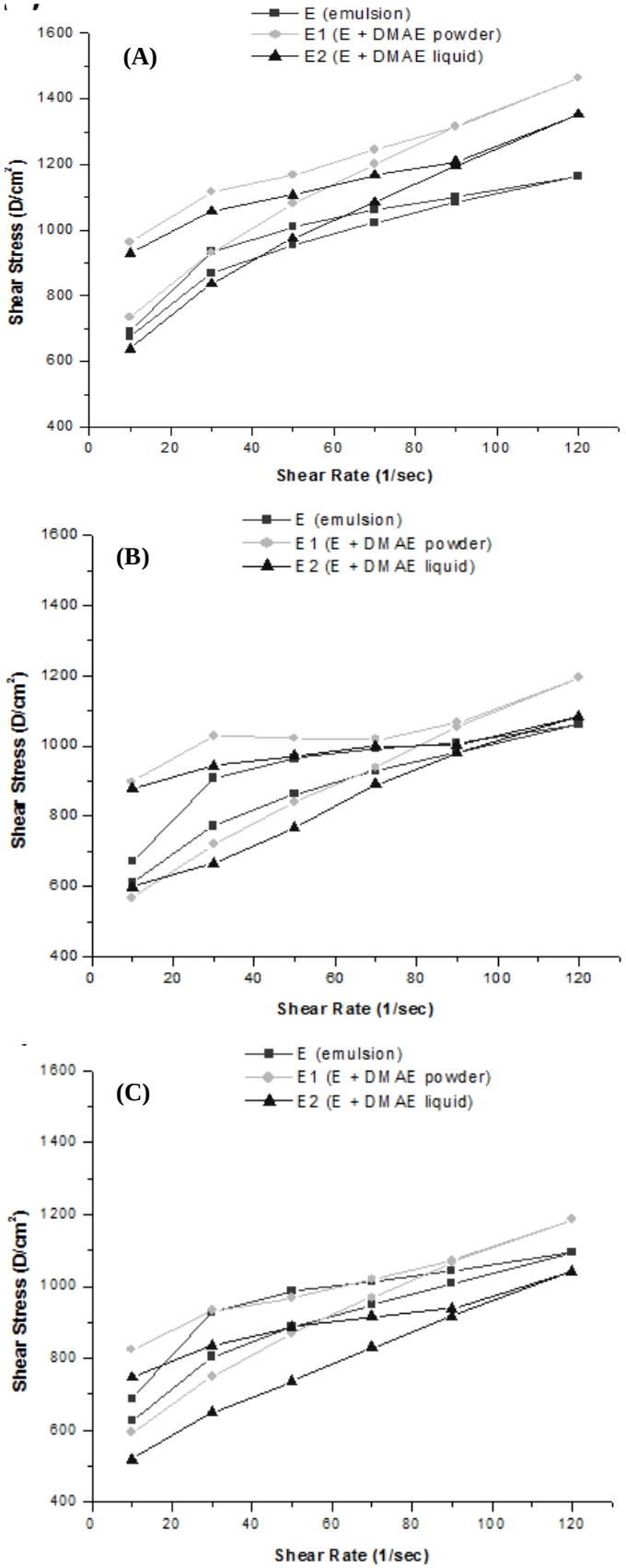

Fig. 2: Mean rheograms (n=3) of the values of shear rate (1/sec) and shear stress (D/cm^2) of the formulations E (emulsion), E1 (E + DMAE powder) and E2 (E + DMAE liquid) analyzed in S15: **(a)** at room temperature (25.0 ± 2.0 °C), **(b)** in refrigerator (5.0 ± 2.0 °C) and **(c)** in hot oven (37.0 ± 2.0 °C).

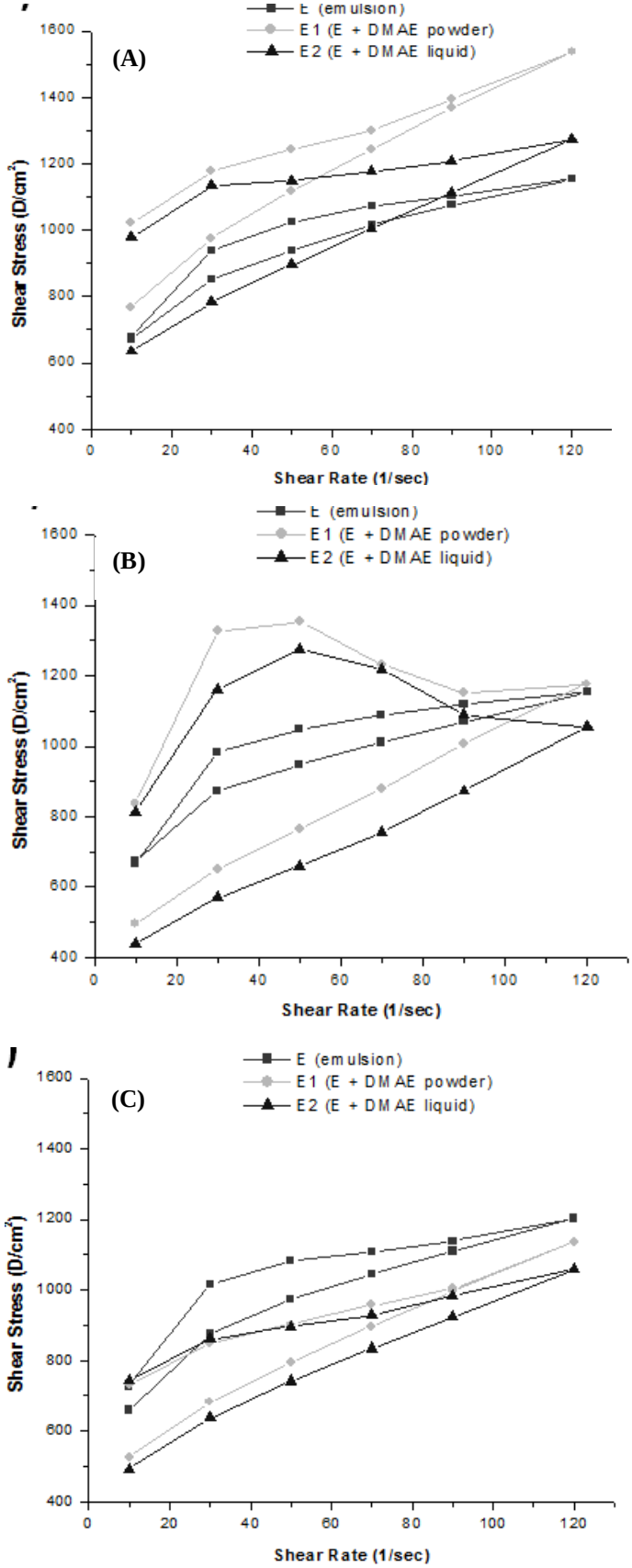

Fig. 3: Mean rheograms (n=3) of the values of shear rate (1/sec) and shear stress (D/cm^2) of the formulations E (emulsion), E1 (E + DMAE powder) and E2 (E + DMAE liquid) analyzed in T28: **(a)** at room temperature (25.0 ± 2.0 °C), **(b)** in refrigerator (5.0 ± 2.0 °C) and **(c)** in hot oven (37.0 ± 2.0 °C).

After these initial analyses, regarding the development and evaluation of stabilities tests and rheological behavior, new experiments concerning *in vivo* skin effects were carried out by our research group. Guimarães *et al.*. (2011) evaluated the effects of formulations containing DMAE pidolate and DMAE acetoamidobenzoate on the skin at male hybrid swines. It was observed, none of the formulations led to an increase of collagen fibers. The formulations containing DMAE pidolate increased the thickness of the stratum corneum, however, for the viable epidermis and dermis, both types of DMAE did not cause significant changes. The results point that the type of DMAE can influence the physical stability of the final product. Moreover, the formulations containing DMAE acetoamidobenzoate and pidolate showed hydrating effect on the epidermis without causing skin irritation, but did not produce a tensor effect on the skin in this experimental model.

CONCLUSIONS

The emulsions presented non-Newtonian pseudoplastic behavior with hysteresis area. Both DMAE acetoamidobenzoate and pidolate did not cause significant change in the emulsions' viscosity. The DMAE addition led to increase the emulsions' hysteresis area. It was found that the type of DMAE employed in the formulation can influence the physical stability of the final product and, through macroscopic analysis, the formulations should be stored under refrigeration.

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