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Structural characterization and stability of dimethylaminoethanol and dimethylaminoethanol bitartrate for possible use in cosmetic firming

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Synopsis

2-Dimethylaminoethanol (DMAE) (also known as deanol) has been used as an ingredient in skin care, and in cognitive function- and mood-enhancing products. It is marketed as a free base or salt, and in theory, the two forms should be equally effective and able to substitute for each other in pharmaceutical formulations. Detecting possible alterations in the active principle is a basic part of preformulation studies. Accordingly, this study compared DMAE and DMAE bitartrate to identify potential alterations or differences between the free base and the salt that might compromise the long-term stability of cosmetic preparations at different temperatures, and also compared the behavior of the base substance and derivative alone and in solution. Samples were analyzed with different physicochemical methods such as differential scanning calorimetry, ultraviolet and infrared spectroscopy, and nuclear magnetic resonance spectroscopy.

INTRODUCTION

The search for new compounds to prevent or attenuate skin aging is a priority in current research on new active principles in cosmetics (1). Research in dermatology, neurology, and immunology has shown that the skin and brain are intimately related (2–4), and has given rise to a new discipline that combines neurology and cosmetic dermatology : "Neurocosmetic." In light of social issues surrounding the overlap between cosmetic and pharmacological applications of cosmetics, we have investigated treatments for drooping or flaccid skin.

Some morphological changes that appear as a consequence of skin aging result in almost complete detachment of the epidermis and empty spaces within the dermis. As a result, parts of the skin can hang loosely like empty bags, leading to flaccid skin (5). Developments at the interface between neurology and cosmetic dermatology have led to the use of dimethylaminoethanol (DMAE) as an ingredient in skin tensors (6).

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2-Dimethylaminoethanol is an acetylcholine precursor (7) that has been found effective in oral formulations to treat hyperactivity in children (8). In 2002 it began to be used in topical formulations of cosmetic skin tensors (9,10). The commercial availability of different derivatives of DMAE should in theory make it possible to substitute different products for each other in formulations without technological problems arising from structural changes that might affect the efficacy of the active principle. We therefore compared DMAE and DMAE bitartrate (Figure 1) to detect potential differences that might interfere with the long-term stability of different formulations under different conditions and storage temperatures. We also evaluated the behavior of DMAE and DMAE bitartrate alone and in solution.

Samples were analyzed with different physicochemical methods that included ultraviolet (UV) and infrared (IR) spectroscopy, differential scanning calorimetry (DSC) for DMAE bitartrate, and nuclear magnetic resonance spectroscopy (^{1}H-NMR). Because of its fluid nature, free-base DMAE was not analyzed by DSC.

MATERIALS AND METHODS

MATERIALS

The products used as ingredients in our formulations were: dimethylaminoethanol, a colorless liquid with a faint fish-like odor, supplied by Roig Farma-Grupo (Fagron, Barcelona,

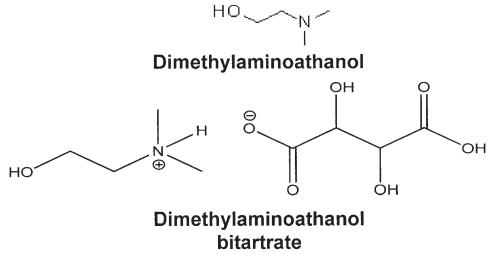

Figure 1. Molecular structure of DMAE.

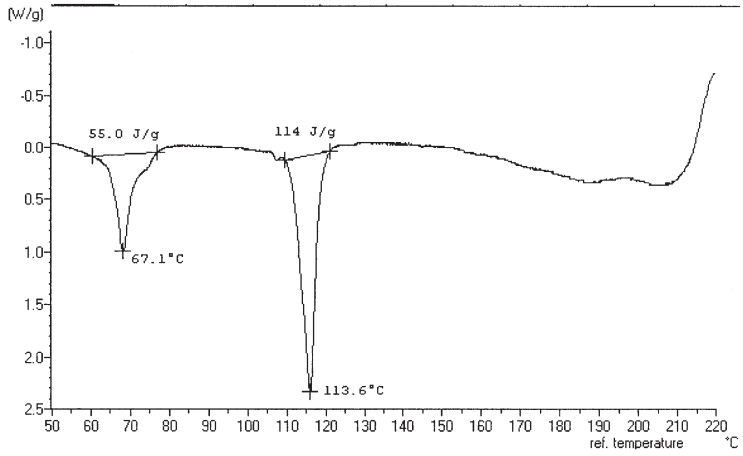

Figure 2. DSC thermogram of DMAE bitartrate at 25°C.

Spain), dimethylaminoethanol bitartrate, supplied as a white powder by Roig Farma-Grupo (Fagron), and deionized distilled water, supplied by Interapothek (Murcia, Spain).

METHODS

Three sets of samples were prepared. One set was stored at room temperature (20°–25°C), one at 40°C, and the third at 60°C. During the 30-day study period the molecular stability of the active principle was measured after the first 24 h and at seven-day intervals thereafter in samples kept at all three temperatures. The stability of free-base DMAE and DMAE bitartrate during a 30-day period was also studied in aqueous solutions at room temperature.

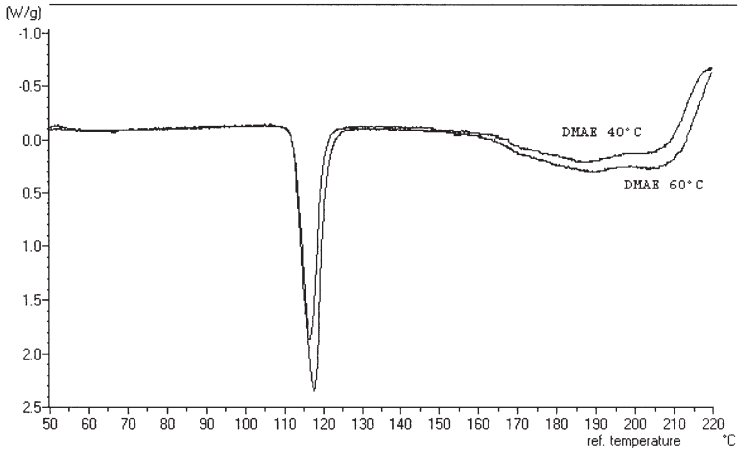

Figure 3. DSC thermograms of DMAE bitartrate at 40°C and 60°C.

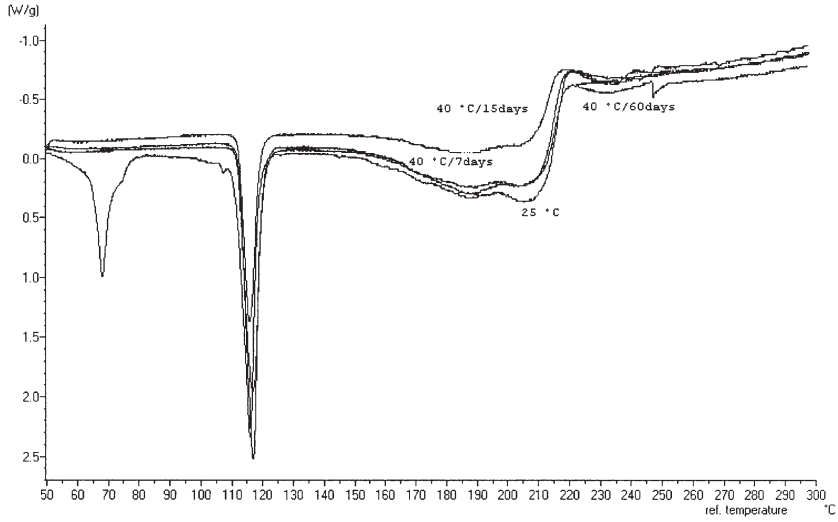

Figure 4. DSC thermograms of DMAE bitartrate during storage at 40°C (stability at different times).

Measurements were made in triplicate for each formula at each sampling time and storage temperature. The results are reported here as the mean of the three values ± standard deviation. All results were compared by analysis of variance (ANOVA) to identify significant differences.

Differential scanning calorimetry. The DSC thermograms of DMAE bitartrate were recorded with a Mettler FP80 differential scanning calorimeter, from 50°C to 300°C, at a rate of 5°C/min. Test samples weighing 5–6 mg were analyzed in crimped aluminium sample pans.

Ultraviolet spectroscopy. Ultraviolet spectra were recorded with a Perkin Elmer UV/Vis spectrometer. A precisely weighed amount of the active principle was dissolved as appropriate, and scans were obtained at wavelengths of 200–300 nm.

Infrared spectroscopy. Infrared spectra were recorded with a Perkin Elmer FT-IR Spectrum One instrument. Solid samples were analyzed with potassium bromide, and liquid samples were analyzed with sodium chloride disks.

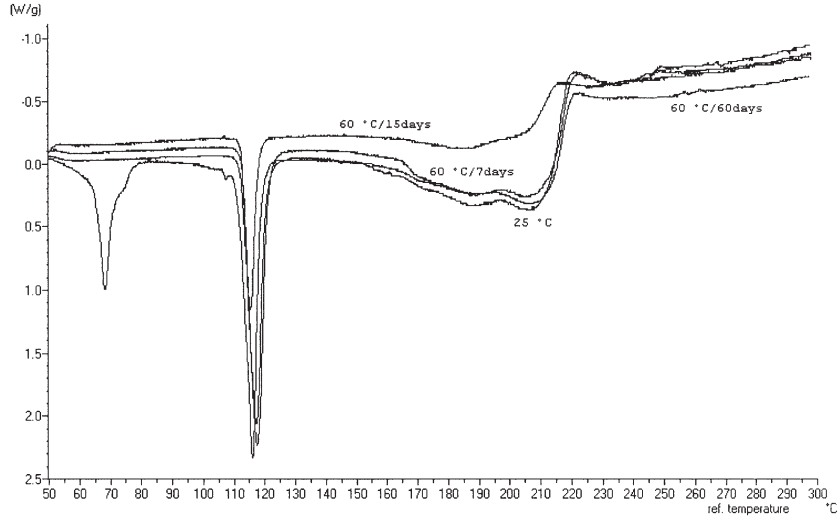

Figure 5. DSC thermograms of DMAE bitartrate during storage at 60°C (stability at different times).

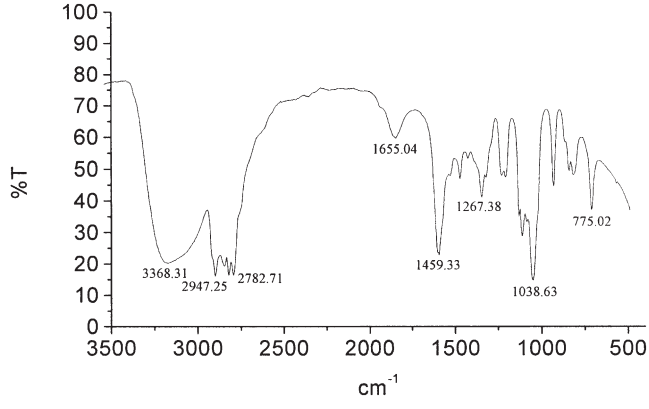

Figure 6. FTIR spectra of DMAE.

Nuclear magnetic resonance. The ^{1}H-NMR spectra were recorded with Varian Direct drive (400 MHz) spectrometers for solutions in D_2O.

RESULTS AND DISCUSSION

DIFFERENTIAL SCANNING CALORIMETRY

Figure 2 shows the thermogram of DMAE bitartrate at room temperature. Two endothermal peaks were evident: one at 67.1°C and a larger peak at 113.6°C that marked the melting point (melting range: 112.7°–118.2°C). The heat exchanges for these peaks were 55 J/g and 114 J/g. The basal heat curve showed signs of shift between 200°C and 212°C.

Stability was evaluated by comparing the DSC thermograms obtained at room temperature with those recorded at 40°C and 60°C. Figure 3 shows the results for DMAE bitartrate at each temperature. The endothermal peak at 67.1°C was no longer evident, although large peaks were seen at 114.5°C (40°C) and 115.1°C (60°C). Disappearance of the smaller endothermal peak may indicate loss of occluded water due to crystallization as a result of evaporation after storage of the samples at a the two higher temperatures.

Figures 4 and 5 compare the stability of DMAE bitartrate at different times in samples kept at room temperature versus 40°C or 60°C. The behavior at days 7, 14, and 30 was similar to that of the room-temperature samples, and the endothermal peak remained unchanged.

Calorimetric tests thus detected no changes in any of the samples kept at 25°C, 40°C, or 60°C for different periods. All curves showed the characteristic melting point for DMAE bitartrate.

ULTRAVIOLET SPECTROSCOPY

The spectra showed no clear peaks for maximal absorbance, and so the UV spectroscopy results were uninformative for the purposes of characterizing DMAE and DMAE bitartrate.

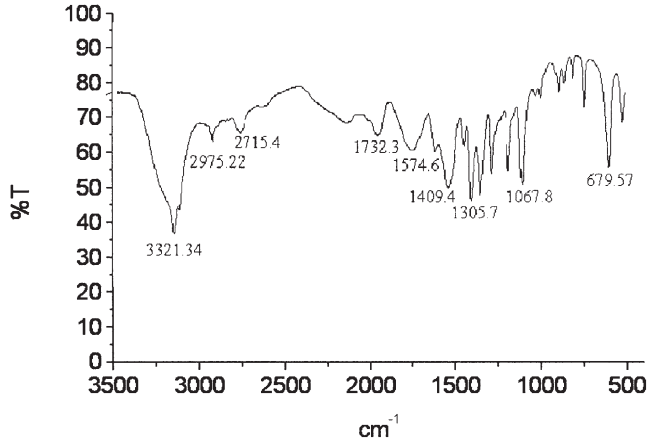

Figure 7. FTIR spectra of DMAE bitartrate.

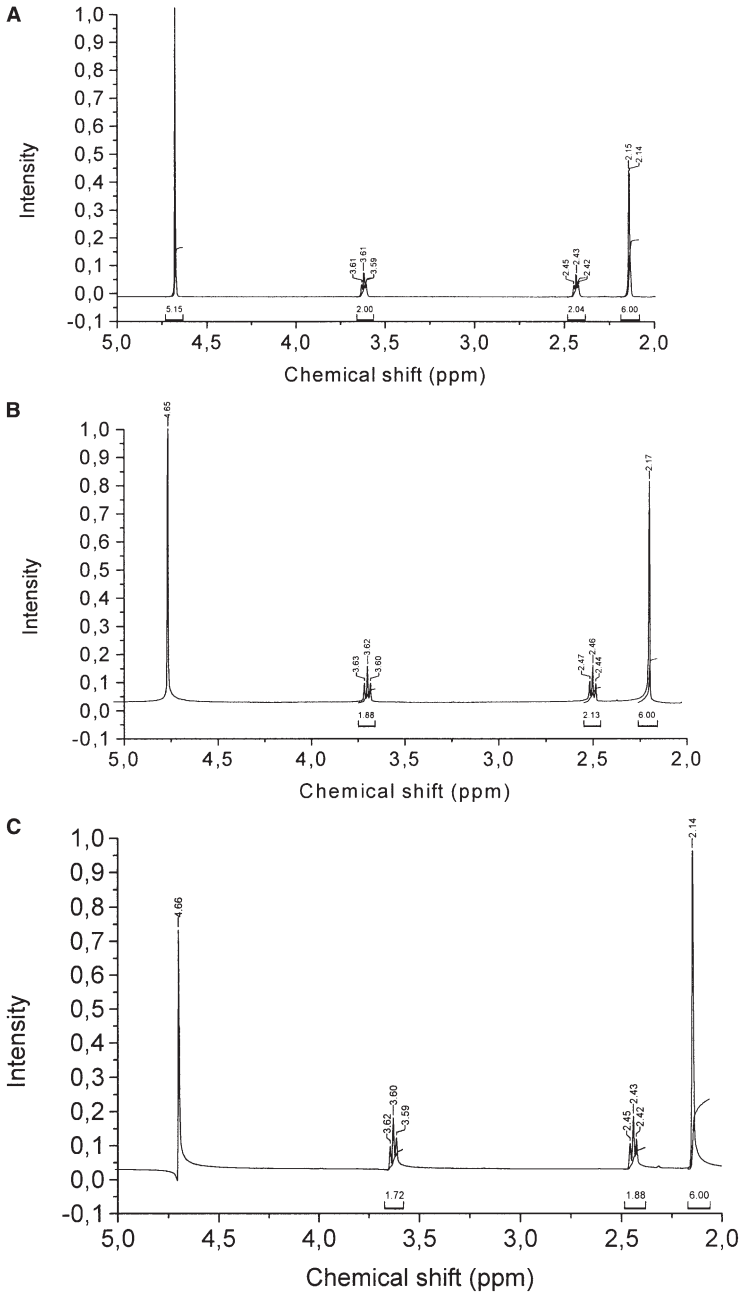

Figure 8. [1]HNMR spectra of DMAE at 25°C (A), 40°C (B), and 60°C (C).

INFRARED SPECTROSCOPY

We used IR spectroscopy to look for possible structural changes in DMAE and DMAE bitartrate after storage at different temperatures. Figures 6 and 7 show the positions of

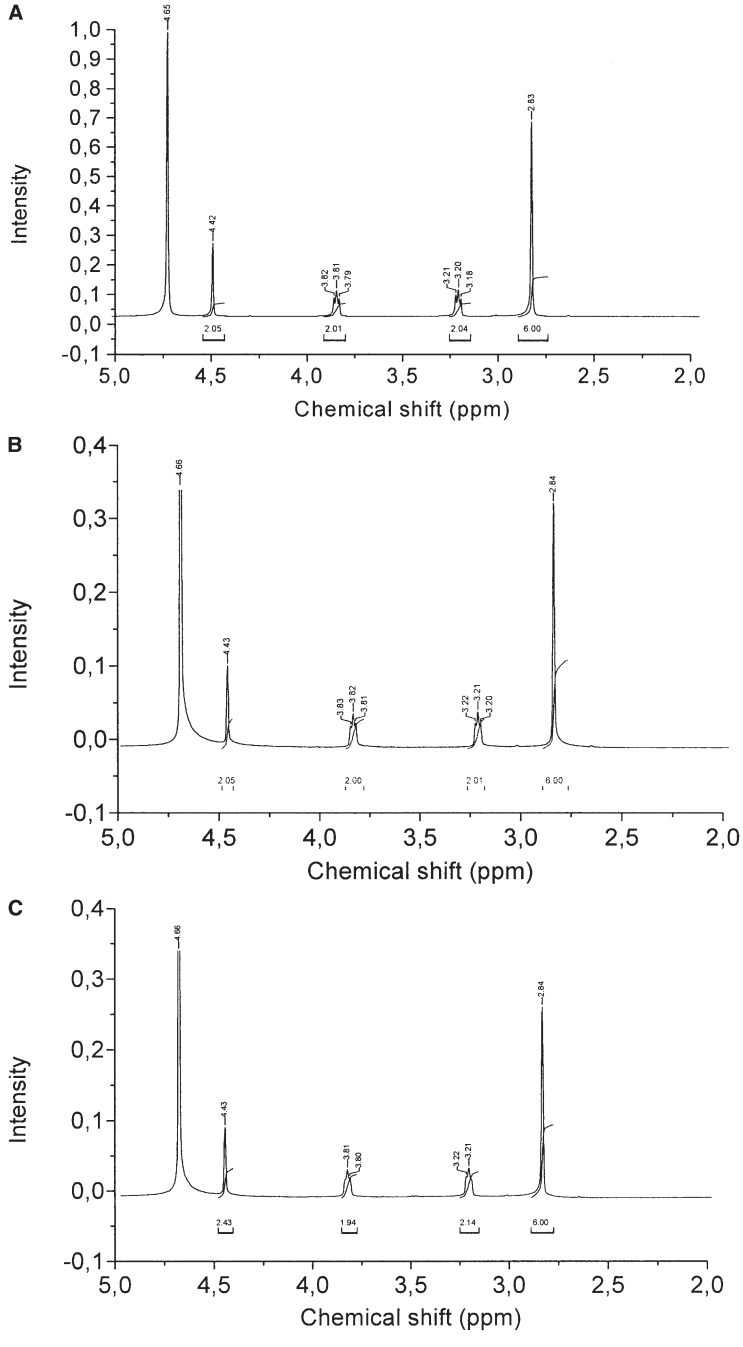

Figure 9. ^{1}HNMR spectra of DMAE bitartrate at 25°C (A), 40°C (B), and 60°C (C).

the main vibrational modes determined by analysis of the bands recorded from the samples. The IR spectrum for DMAE (Figure 6) was characterized by a large, intense band at 3368.31 cm^{-1} (O–H stretch) and by a series of absorbance bands between 2947

cm^{-1} and 2782 cm^{-1} (C–H aliphatic stretch). The IR spectrum for DMAE bitartrate (Figure 7) was characterized by an additional absorption peak at 1732.3 cm^{-1} (C=O stretch), a signal at 2975 cm^{-1}, and an intense band at 3321 cm^{-1}. The IR absorption bands for formulations kept at 25°C, 40°C, and 60°C were similar, as were the bands in the IR spectra for DMAE and DMAE bitartrate in aqueous solution after storage for 30 days.

The stability of the active principle is a determining factor for the success of pharmaceutical formulations. The samples of DMAE and DMAE bitartrate that we analyzed under different storage conditions showed a similar, stable behavior. However, to confirm the stability of these ingredients, we used further tests with a more specific analytical technique, i.e., ^{1}H-NMR spectroscopy.

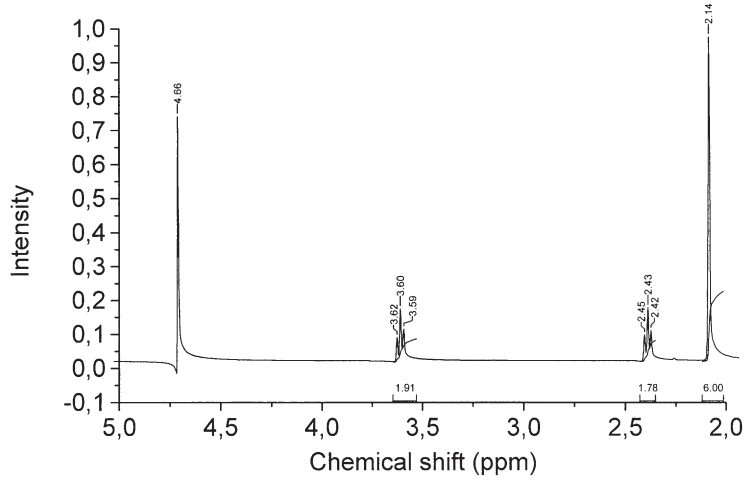

Figure 10. ^{1}HNMR spectra of DMAE in aqueous solution 30 days after preparation.

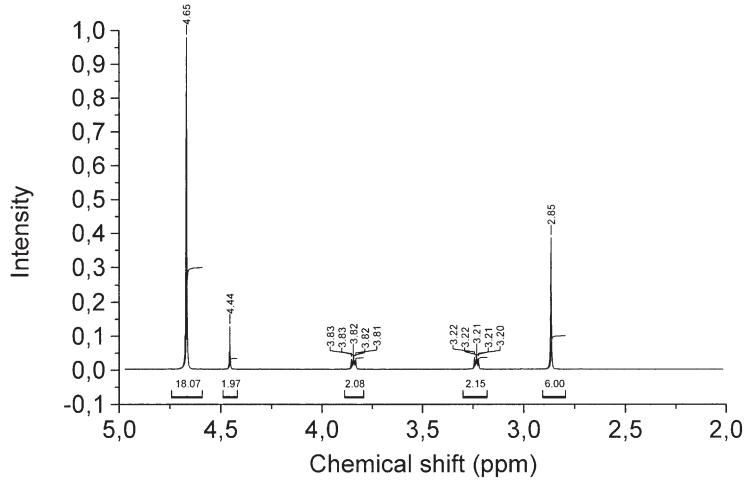

Figure 11. ^{1}HNMR spectra of DMAE bitartrate in aqueous solution after storage for 30 days.

NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

Nuclear magnetic resonance is one of the most specific methods for determining the structure of active principles. The ^{1}H-NMR spectra of DMAE and DMAE bitartrate alone are displayed in Figures 8 and 9 and the corresponding spectral data are given below.

Figure 8A shows signals for DMAE at 2.14, 2.4, and 3.61, which were assigned to $2CH_3$, CH_2–N and CH_2–O, respectively. Figures 8B and 8C illustrate the same signals for samples of DMAE heated to 40°C and 60°C.

Similarly, Figure 9A shows signals for DMAE bitartrate at 2.83 and 3.81, which were assigned to the same hydrogens as in the sample of free-base DMAE. An additional signal at 4.42 was assigned to the CH–COO. Heating the samples to higher temperatures did not affect the pattern of signals (Figures 9B and 9C).

When we compared the ^{1}H-NMR spectra for the DMAE alone and in aqueous solution after storage for 30 days (Figures 10,11) we found no differences. Identical results were also obtained in samples heated to 40°C and 60°C. Our ^{1}H-NMR results for DMAE and DMAE bitartrate were similar, and confirmed the IR spectroscopy and DSC findings.

CONCLUSION

We observed no changes in any of the physicochemical activities of DMAE and DMAE bitartrate with storage time or temperature. Our results show that both the free base and the bitartrate salt can be used in the preformulation stage to prepare liquid formulas containing this active principle.

ACKNOWLEDGMENTS

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