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# Determination of ascorbyl dipalmitate in cosmetic whitening powders by differential scanning calorimetry

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**Synopsis**

A fast and simple method has been developed to quantitate ascorbyl dipalmitate ADP in cosmetic whitening powders. The method involves obtaining a differential scanning calorimetry DSC thermograms of the product, integrating an endotherm due to a phase transition of ADP, and comparing the area of the endotherm to that obtained from a pure standard of ADP. The method has been applied to whitening powders produced by four different cosmetics companies. The resulting values are found to agree with those obtained by a previously published, more involved HPLC method.

## INTRODUCTION

Maintaining a pale, relatively unpigmented skin is important to a large segment of the Japanese market. Various cosmetic products have been developed (1) to aid in attaining this desired state, and they account for approximately six percent of Japanese cosmetic sales in recent years. These formulations are based on one of several active ingredients such as peroxides, ascorbic acid, and ascorbic acid derivatives (2). Their skin-whitening action is thought to be accomplished by the inactivation of tyrosinase, an enzyme that mediates the early steps of the melanin biosynthetic pathway (3).

Ascorbyl diplamitate is a more stable form of ascorbic acid and has been used successfully in several formulations (4). However, even the dipalmitate is not completely stable, and it is therefore imperative to be able to determine accurately the amount of the ingredient that is present in a formulation at a given time.

Literature references concerning the quantitative analysis of ADP are few. Several years ago, the analyses of ADP (5) and ascorbyl palmitate (6) in ointments, vegetable oil, and lard by high-performance liquid chromatography (HPLC) were reported. Initial attempts to apply an HPLC method to the whitening powders revealed two drawbacks: rather extensive sample preparation is necessary, and inconsistent results are obtained. We find that the results vary due to a stability problem with ADP in methanol solution when held for a period of a few hours, presumably due to transesterification. However, when the sample is injected immediately, the HPLC method gives results comparable to those obtained by DSC.

A gas chromatographic method for the determination of fatty acid esters of asco
(as the trimethylsilyl derivatives) has been described (7). However, the highe

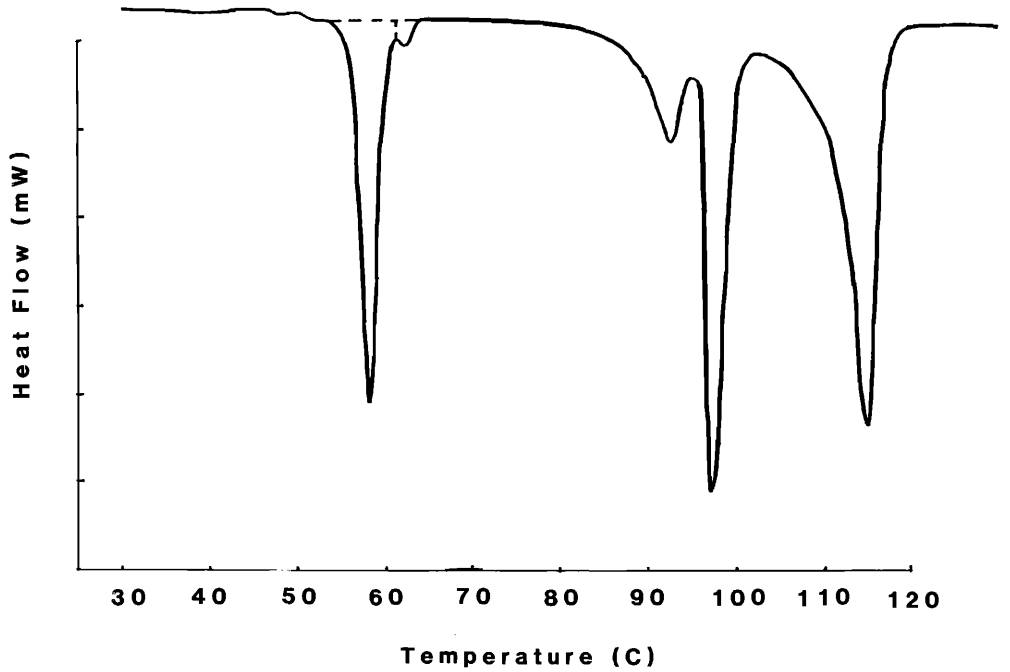


Figure 1a

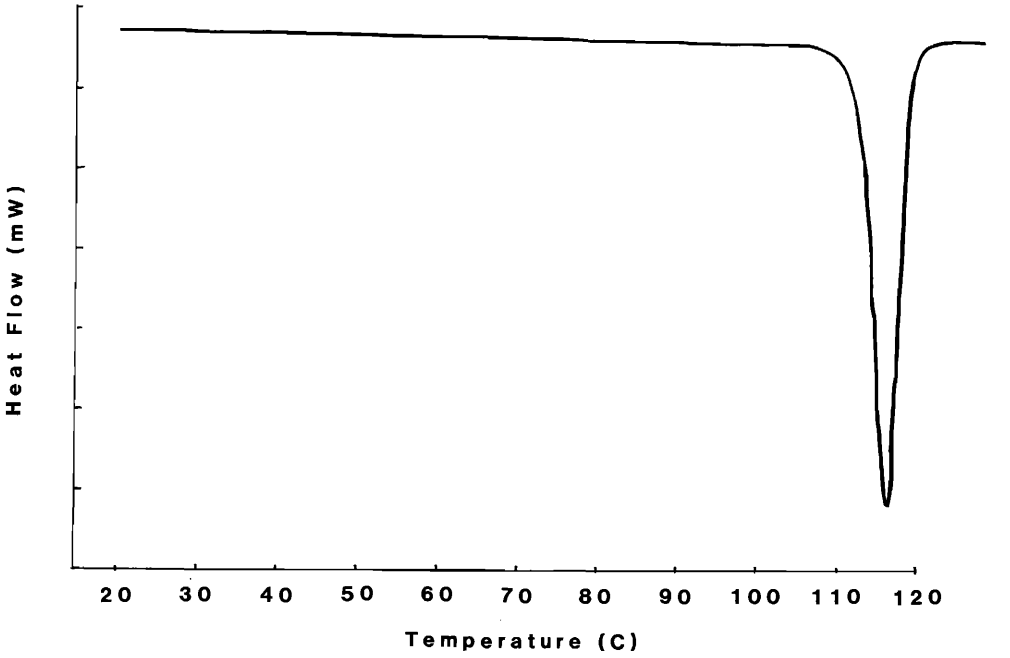


Figure 1b

**Figure 1.** DSC thermograms of ascorbyl compounds: 1a. Ascorbyl dipalmitate. 1b. Ascorbyl monopalmitate. 1c. Dehydroascorbic acid. 1d. Ascorbic acid.

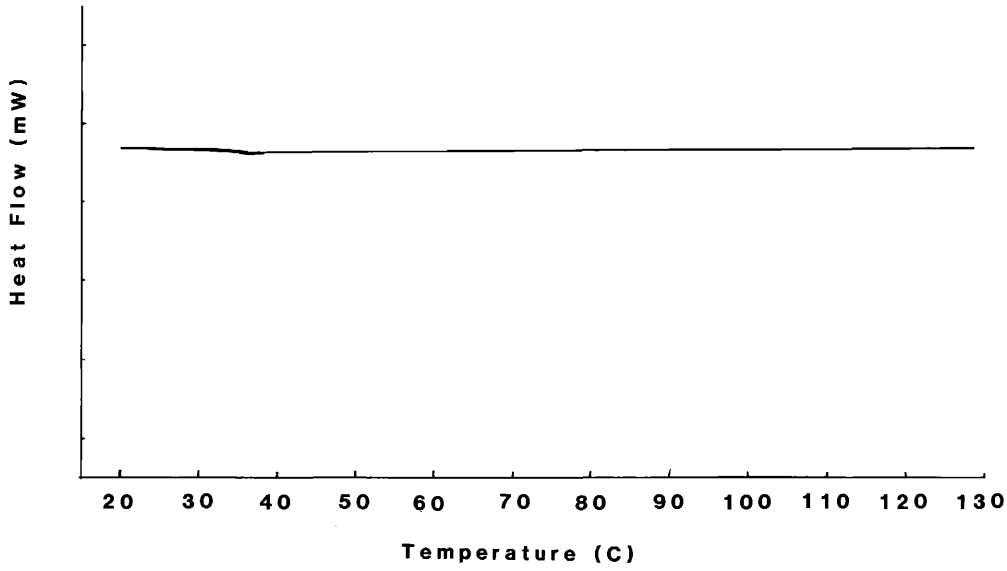


Figure 1c

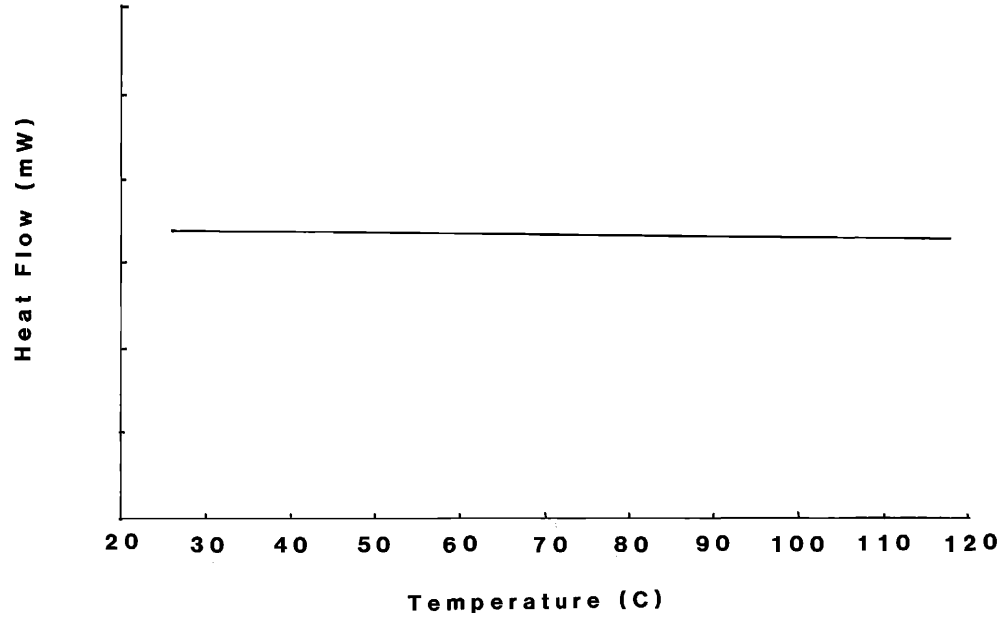


Figure 1d

Figure 1 (continued)

logue reported as successfully analyzed is the 2,6-dilauryl ester. We find that the method produces inconsistent results when applied to the dipalmitate, most likely due to thermal degradation. A thin-layer chromatographic (TLC) method for the determination of ascorbic acid esters has been described (9).

Cosmetic whitening powders are generally composed of inorganic materials such as talc, titanium doixide, sericite, and mica, and an organic active ingredient. Since the excipient materials generally will not have thermal transitions between 20° and 150°C, it was reasoned that perhaps ADP is amenable to quantitation by DSC in this inorganic matrix.

## REAGENTS AND APPARATUS

Ascorbyl dipalmitate was obtained from Nikko Chemicals, Ltd., Tokyo, Japan. Ascorbyl palmitate (NF-FCC grade) and ascorbic acid (USP grade) were obtained from Hoffman-La Roche, Inc. (Nutley, NJ). Dehydroascorbic acid was purchased from Pfaltz & Bauer, Inc. (Waterbury, CT). These compounds were used without further purification.

A DuPont Instruments Model 1090 Thermal Analyzer, Model 910 Differential Scanning Calorimeter Base, and a Model 1091 Disc Memory were used throughout this study. Standard aluminum DSC pans (DuPont Part No. 900786-901 and 900779-901) were used. The samples (approximately 10 mg, weighed accurately to $\pm 0.01$ mg) were weighed directly into the tared pans. The samples were then heated at a programmed rate of 5°/min. The Advanced DSC Data Analysis Program (DuPont Part No. 994485-901) was used for the integration of the areas of the endotherms.

A Spectra Physics Model SP-8000B HPLC was used for the chromatographic analyses, using Chromegabond Diamine (5 μm) and a UV detector at 255 nm (6).

## RESULTS AND DISCUSSION

As an initial approach to this problem, the thermograms of ascorbic acid, ascorbyl palmitate, and dehydroascorbic acid were obtained and compared to that of ADP. Dehydroascorbic acid is the reaction product that results when ascorbic acid undergoes oxidation. The free acid and the monoester are the products expected from hydrolysis of the diester.

As can be seen in Figure 1a, the thermogram of ADP consists of three major endotherms. The highest endotherm corresponds to the melting of ADP (8). This melting-point endotherm is of no value for quantitative purposes, because it occurs within one degree of the melting-point endotherm of ascorbyl monopalmitate (Figure 1b). Dehydroascorbic acid and ascorbic acid exhibit no thermal transitions between 30° and 130°C (Figures 1c and 1d).

The endotherm of ADP that occurs between 56° and 58°C is suitable for quantitation because it does not coincide with any thermal transitions from any of the expected degradation products. This permits determinations on a particular sample, since the manufacture of the products is dry blending at ambient temperature.

Quantitation of ADP is accomplished by use of the DuPont Advanced DSC Data Analysis Program, which is used to integrate the endotherm that occurs between 56° and 58°C. The energy that is absorbed during this transition is integrated and displayed in Joules per gram of sample.

The weight percent ADP can be calculated manually by a ratio of the endotherm of the sample to the endotherm of a pure standard of ADP according to the following [c = ascorbyl dipalmitate in the sample (%); U = sample endotherm (Joules/g); and S = ascorbyl dipalmitate standard endotherm (Joules/g)]:

$$c = \frac{100\ U}{S}$$

The enthalpy in Joules/g of pure ADP of the endotherm between 56° and 58°C was determined to be 30.4 Joules/g (RSD = ±0.7; N = 3).

Alternately, a calibration curve of enthalpy versus percent ADP in an inert medium such as talc can also be determined and plotted. The percent ADP in an unknown whitening powder can then be determined directly from the graph (Figure 2).

Figures 3 a–d show the thermograms of whitening powders produced by four cosmetic companies. It is interesting to note that in these commercially available mixtures, the endotherm that corresponds to the melting point of ADP is lowered to approximately

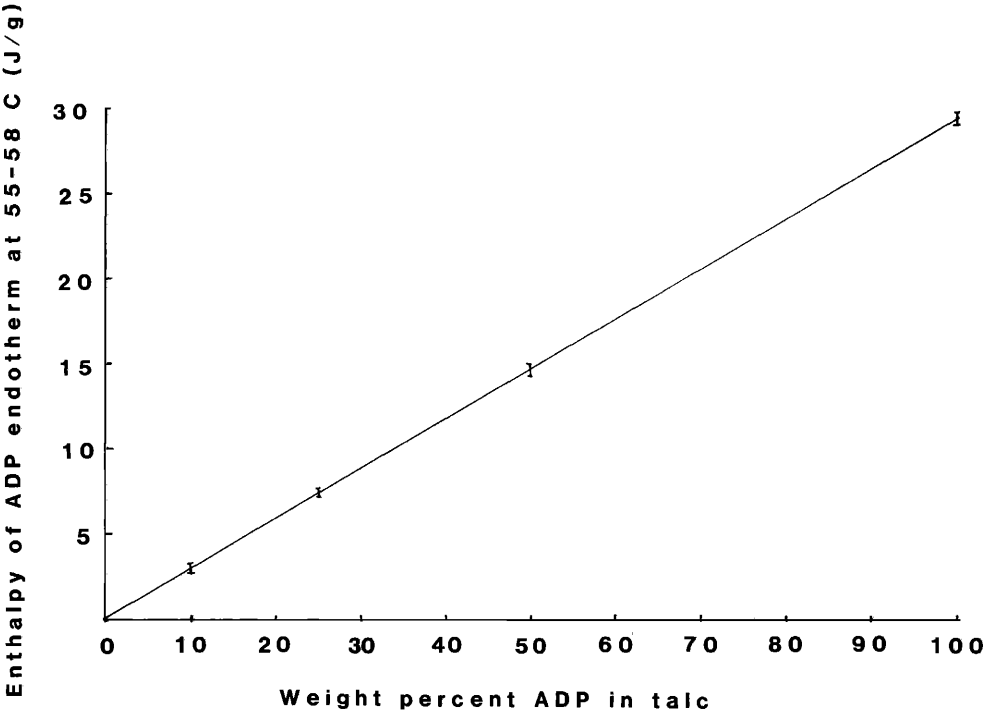


**Figure 2.** Plot of enthalpy versus weight percent ADP in talc.

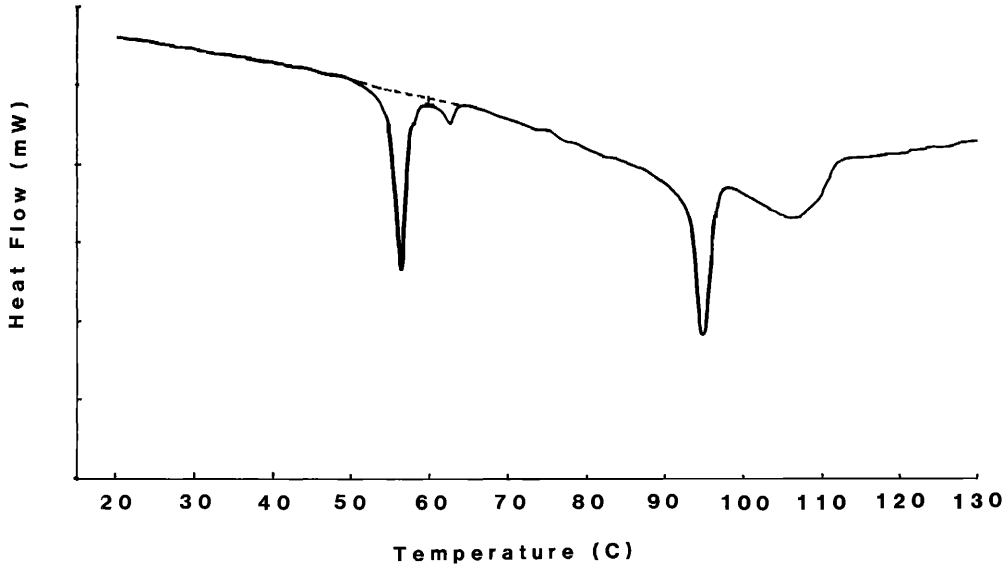


Figure3a

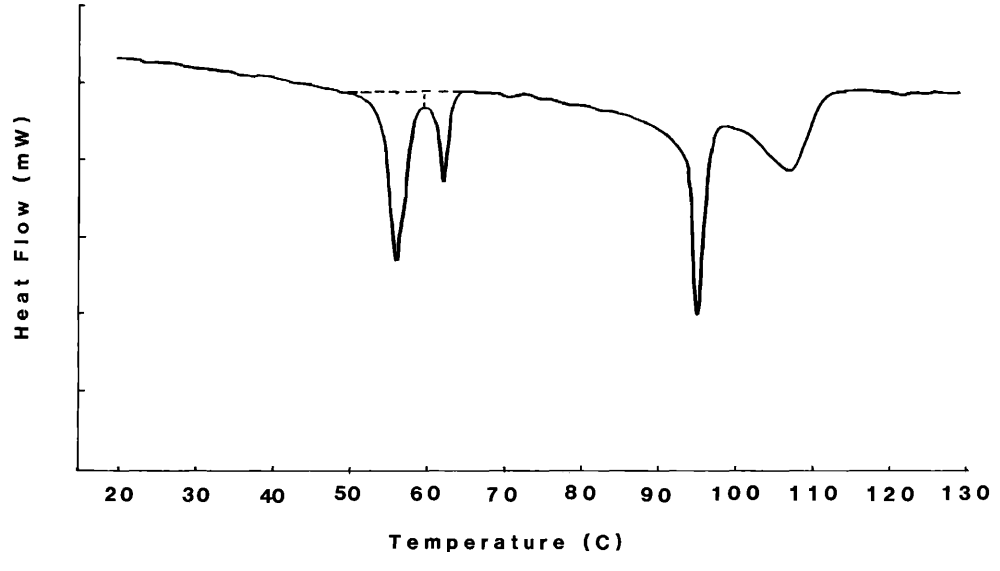


Figure3b

**Figure 3.** DSC thermograms of commercially available whitening powders: 3a: Company A. 3b: Company B. 3c: Company C. 3d: Company D.

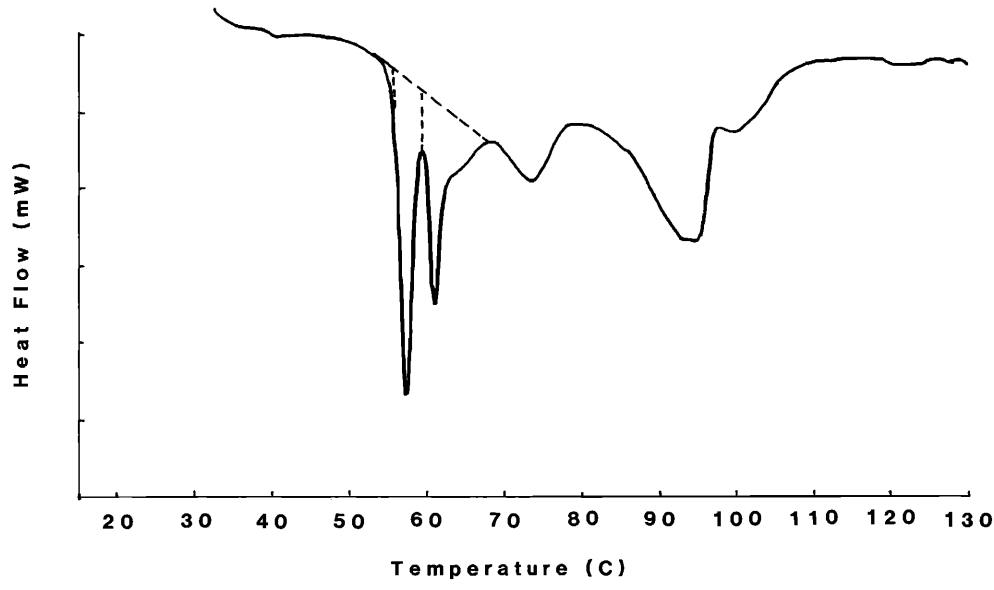


Figure 3c

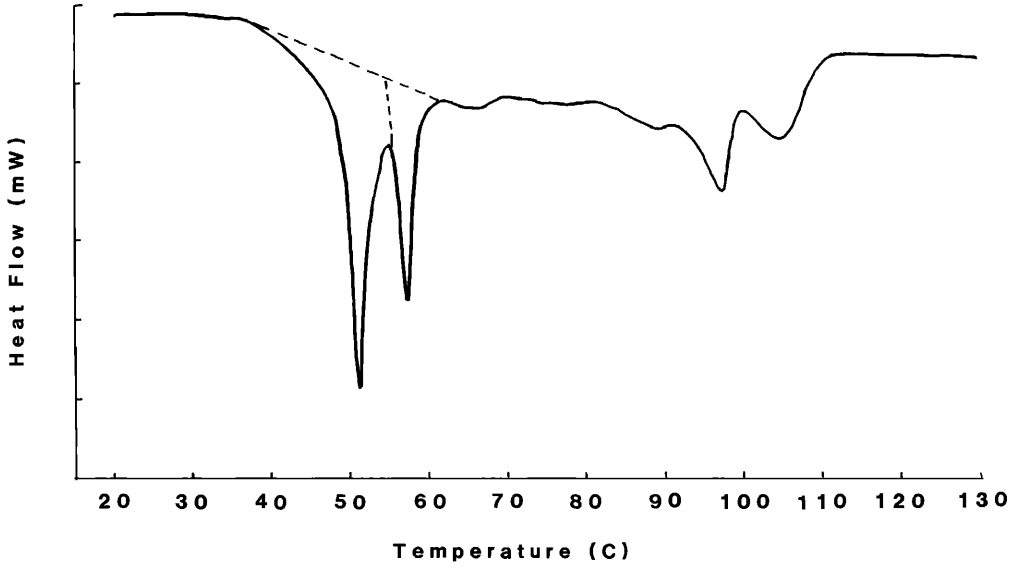


Figure 3d

Figure 3 (continued)

**Table I**
Ascorbyl Dipamitate Content of Commercially Available Cosmetic Whitening Powders: A Comparison of the DSC and HPLC Methods

| | DSC Method | | HPLC Method | | |
|---|---|---|---|---|---|
| | Weight (%) | RSD | Weight (%) | RSD | |
| Company A | 18.2 | 2.88 | 20.4 | 2.80 | |
| Company B | 20.4 | 0.83 | 19.9 | 1.85 | |
| Company C | 14.5 | 1.72 | 14.7 | 1.60 | |
| Company D | 22.7 | 2.60 | 23.9 | 0.20 | (N = 3) |

| Known amounts of ADP DSC Method | | | |
|---|---|---|---|
| Weight (%) | RSD | % Recovery | |
| 9.8 | 2.9 | 98 | |
| 24.2 | 2.9 | 97 | |
| 49.7 | 0.7 | 99 | (N = 3) |

108°C and is broadened to the extent that it is not suitable for quantitative purposes. However, the endotherm that occurs between 56° and 58°C remains unaffected, so it is useful for quantitation. Known amounts of ADP were dry-blended with talc, and the quantitative results are indicated in Table I. The quantitative results from the DSC method are compared in Table I to results obtained by the published HPLC method (6). It can be seen that the two methods give comparable values.

## CONCLUSION

A fast, easy, and reproducible quantitative DSC method has been developed to determine the concentration of ADP in cosmetic whitening powders. The 56°–58°C endothermic peak was used for the quantitation. The method is simple compared to GC and HPLC, requires no sample preparation, and is independent of the stability of ADP in solution.

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