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THE THERMAL ANALYSIS OF SOME NON-PRESCRIPTION VITAMIN PREPARATIONS

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ABSTRACT

DTA (DSC) and TG curves of fourteen commercial, non-prescription vitamin preparations are presented. Although each vitamin preparation gave a unique DTA or TG curve, thermal analysis proved to be unsatisfactory for most qualitative purposes other than the recognition of the gross curve features. Most of the significant features of the curves are related to the binder or filler material since this constituted the bulk of the samples. The complexity of the mixtures made it difficult to assign specific DTA curve peaks to a given vitamin.

INTRODUCTION

The application of modern thermoanalytical techniques to the analysis of some common non-prescription pharmaceutical products has recently been reported in a series of papers by Wendlandt and co-workers[1,2]. These studies have now been expanded to include thermal analysis data for some non-prescription commercial vitamin preparations. These vitamin preparations are reported to be of dubious health value in all except the most extreme cases of malnutrition and vitamin deficiency but nevertheless are subject to high consumer demand and are sold in vast quantities[3]. The investigation of the thermal properties of these products was deemed worthwhile even though the chemical complexity of vitamin molecules combined with small quantities present in standard dosage forms makes interpretation of the curves exceedingly difficult. This study is concerned with the gross observations of the thermal behavior of the total vitamin product, i.e., the vitamins plus binders, and seeks to identify similarities and differences between the formulations of similar products by different manufacturers.

EXPERIMENTAL

The non-prescription vitamin preparations used and their commercial sources are given in Table 1. The compositional data, when known, is that given by the supplier and is only approximate.

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TABLE 1

COMPOSITIONAL DATA AND SOURCES OF VITAMINS
Quantities given in weight per tablet or capsule.

Product	*Vit. B_1 (mg)*	*Ascorbic acid (mg)*	*Vit. B_6 (mg)*	*Riboflavin (mg)*	*Pantothenic acid (mg)*	*Niacinamide (mg)*	*Vit. A (mg)*	*Vit. B_{12} (μg)*	*Vit. D (μg)*	*Other*
Lilly Cevalin		100								
Lilly Riboflavin				10						
Lilly Betalin S	50									
Lilly Becotin	10		4.1	10	25	50		1		
Lilly Betalin	1		0.4	2	3.333	10		1		
Lilly Alphalin							3			
Rexall Niacin										nicotinic acid 100 mg
Lilly En-Cebrin	3	50	1.7	2	5	10	1.2	5	10	calcium carbonate 250 mg; iron(II) fumarate 30 mg; KI 0.15 mg; $CuSO_4$ 1 mg; MgO 5 mg; Mn 1 mg; $ZnCl_2$ 1.5 mg
Lilly Novacebrin	1.5	60	1	2	2.5	12	1.2	3	10	NaF 1 mg
Rexall Chewable Vit. C		100								
Rexall Vit. B_6			50							
Rexall B+C	15	300	5	10		50				calcium pantothenate 10 mg
Upjohn ascorbic acid		250								
Upjohn Unicap	2.5	50	0.5	2.5		20	1.5	2	10	calcium pantothenate 5 mg; vit. E 10 I.U.

Thermobalance

A DuPont Model 950 thermobalance was used to record the TG curves. Sample sizes ranged in mass from 5 to 10 mg and were run under a dynamic nitrogen atmosphere at a heating rate of 10°C min^{-1}.

DTA (DSC) apparatus

A DuPont DSC cell (which is actually a DTA cell) was used in conjunction with the Model 900 DTA console. It was found that very non-reproducible curves were obtained if 5–10 mg of the pure vitamin preparation was run, due to the large volume expansion and evolution of gaseous decomposition products. To prevent, or at least reduce this problem, a KBr sample pelletizing technique was employed. The pellet consisted of a "sandwich" of 5–10 mg of vitamin pressed between two 40 mg layers of KBr. After pressing in a simple home-built die at a pressure of 7,500 psi, the pellet had the approximate dimensions of 5 mm in diameter by 1–2 mm thick. It was placed in an aluminum sample container using a pure KBr pellet as the reference material. A comparison between the DTA curves for the pure sample and a KBr sandwich

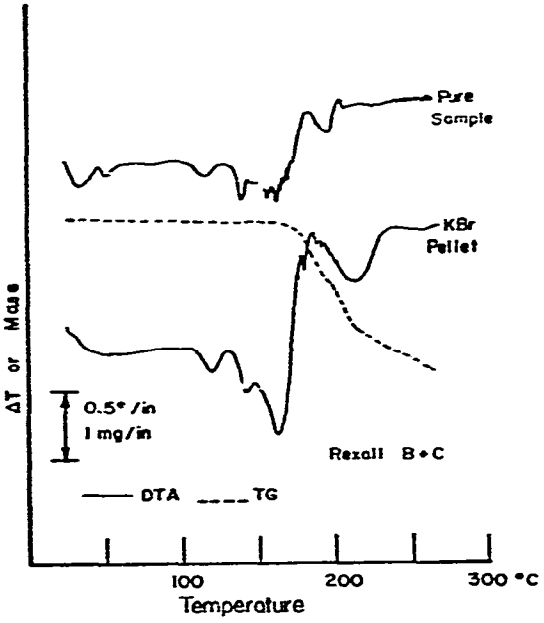

Fig. 1. Comparison between DTA curves of pure sample and a KBr pellet of Rexall B+C vitamins (TG curve also illustrated).

pellet of Rexall B+C vitamins is shown in Fig. 1. Both curves show the small endothermic peaks characteristic of the sample but the pellet sample yielded more reproducible results. All samples were run in duplicate or triplicate using the KBr pellet technique. The heating rate used was 10°C min^{-1} in a dynamic nitrogen atmosphere.

RESULTS AND DISCUSSION

Thermogravimetric and DTA curves were obtained for fourteen commercial non-prescription vitamin preparations to determine if qualitative recognition of vitamin components is feasible through standard thermoanalytical techniques. These curves are presented in Figs. 2–5.

The primary problem encountered in the thermal analysis of the samples was the excessive expansion during decomposition. The magnitude of this process in relation to the reported composition of the samples suggests that the binder or filler agent is responsible for this effect. The swelling not only reduces peak resolution through loss of thermal contact with the pan, but also gives spurious peaks due to released gases bubbling through the viscous liquid formed at elevated temperatures. These problems were partially negated through the use of the KBr pellet technique which improved thermal contact and minimized sample expansion.

The variety of compounding techniques and choice of binder materials used in the various commercial vitamin products also limits the quality of data obtained by thermal analysis. Preparations containing the same vitamin usually gave different thermal data for tablets from each commercial source. Thus, the qualitative identification of specific vitamins by thermal analysis consists of comparing curves obtained for an unknown with standard curves obtained for different brands of vitamins and noting similarities or, in some cases, treating the occurrence of a peak within a specified temperature range as an indication of the presence of a specific vitamin. Also, since most vitamins are present only in very minute quantities, i.e., in the microgram range for sample sizes commonly used with commercial thermal analysis instrumentation, the absence of a peak in the characteristic temperature range for a vitamin cannot be construed as implying that the vitamin is absent from the sample. The extremely minute concentrations present in most products is probably the most serious limitation hindering the application of thermal analysis to vitamin assay.

The DTA and TG curves for the three vitamin C preparations (Rexall Chewable, Lilly Cevalin, and Upjohn ascorbic acid) presented in Fig. 2 illustrate the diversity which is common in the thermal analysis curves of similar commercial preparations. Although a cursory inspection reveals few correlations between the curves, a detailed examination exposes certain similarities which may be characteristic of vitamin C preparations. All three curves have endothermic peaks with a procedural peak minimum temperature, $\Delta T_{min.}$, occurring at about 135–140°C. The shape and magnitude of these peaks vary considerably but this is probably related to the quantity and type of filler material present in the sample. This peak also occurs in the DTA curves of multiple vitamin preparations which contain vitamin C. However, the origin of this peak is unknown since the melting point of ascorbic acid (DL-racemic mixture) is reported as 168–169°C and the decomposition temperature[4] as 190°C. Even this peak cannot be used as an absolute indicator of the presence of vitamin C since thiamine hydrochloride also gives an endothermic peak near this temperature interval. The Upjohn ascorbic acid tablets gave a substantial endothermic peak at $\Delta T_{min}=$

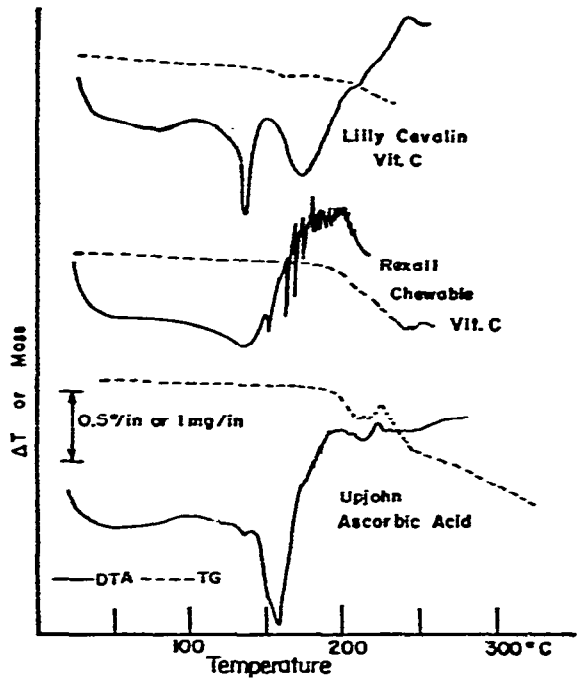

Fig. 2. DTA and TG curves of some commercial vitamin preparations.

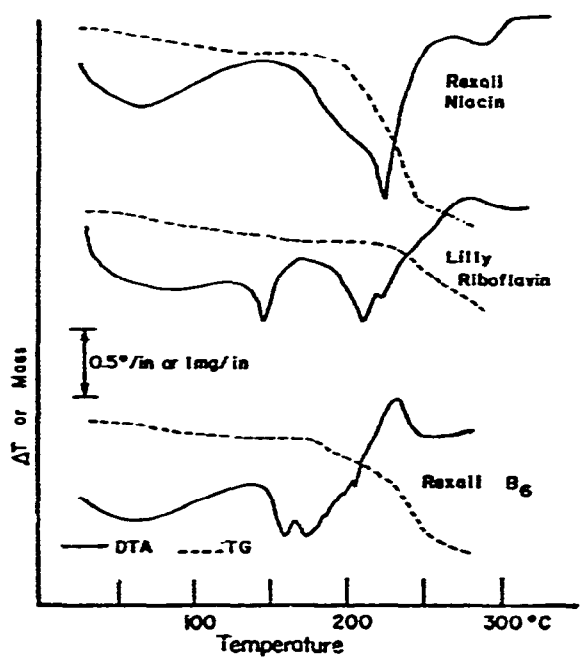

Fig. 3. DTA and TG curves of some commercial vitamin preparations.

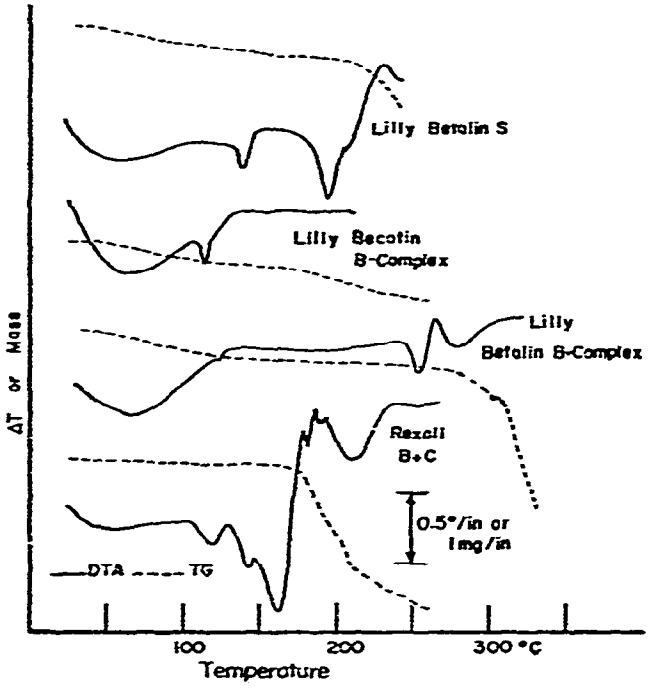

Fig. 4. DTA and TG curves of some commercial vitamin preparations.

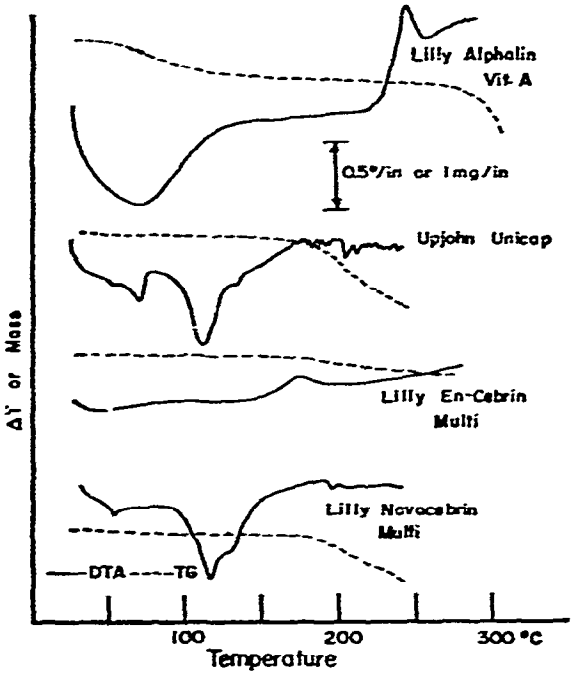

Fig. 5. DTA and TG curves of some commercial vitamin preparations.

160 °C, which probably represents the melting of the ascorbic acid. The TG curves show that mass-loss was initiated at a procedural decomposition temperature, T_i, of about 180 °C which coincides with the appearance of the series of small endothermic peaks in the Upjohn DTA curve. The Rexall Chewable and Lilly Cevalin TG curves also show a mass-loss beginning at about 180 °C but the Lilly product also sustained a slight mass-loss prior to this large mass-loss. All decomposition reactions above 180 °C were exothermic and resulted in a residue of a black carboneous material.

The fusion peak was also absent in the DTA curve for Rexall niacin. Although four peaks can be resolved, none occur at the reported melting point temperature[4] of 124–125 °C. The first broad endothermic peak appears to be a dehydration process as confirmed by the TG curve. The actual decomposition is initiated at about 160 °C and seems to occur in at least two reaction steps. A slight endothermic shoulder peak is resolvable in the DTA curve at 185 °C which is followed by a larger narrow peak with a $\Delta T_{min.} = 225$ °C. The second stage of decomposition begins at 245 °C (as indicated by the TG curve) which produces a small, broad endothermic peak with a $\Delta T_{min.} =$ 287 °C.

The DTA and TG curves for the Lilly riboflavin tablets (vitamin B_2) show an initial dehydration between 50 and 160 °C with a narrow endothermic peak occurring near the end of this process. Although the shape of this peak suggests that it results from a fusion process, the component involved cannot be identified since the $\Delta T_{min.}$ does not correlate with the reported melting point for riboflavin[4]. The large endotherm at 215 °C and the shoulder peak at 225 °C result from the decomposition of the binder, as indicated by the TG curves. The small exothermic peak at 290 °C corresponds, however, to the reported decomposition temperature of riboflavin[4].

The thermal curves for Rexall vitamin B_6 tablets illustrate one of the rare cases where the fusion peak of the vitamin is adequately resolved for identification purposes. The endothermic peak occurring at 160 °C correlates with the reported melting point of vitamin B_6 while the following peaks result from a decomposition process, as shown by the TG curve. The DTA curves for the other B group vitamin preparation, Lilly Betalin S thiamine hydrochloride (vitamin B_1), contained a narrow peak at 140 °C followed by a broad endothermic decomposition peak at 195 °C. A broad dehydration peak was also observed between room temperature and 110 °C.

The B complex vitamins, Lilly Becotin and Lilly Betalin, gave DTA curves with few peaks, none of which correspond to peaks observed for the single B vitamin tablets. Lilly Becotin tablets give a small, narrow endothermic peak with a $\Delta T_{min.} =$ 115 °C, while Lilly Betalin tablets gave a very small endothermic shoulder peak at about 125 °C; both peaks occur at the end of a dehydration process. No further peaks were observed until an endothermic peak, followed by an exothermic peak, occurred between 245 and 300 °C. The endothermic peak, with a procedural deviation temperature of 245 °C, could be due to thiamine hydrochloride which has a reported decomposition temperature[4] of 248 °C.

The DTA curve for Rexall B+C vitamin capsules shows characteristics which are a composite of the curves for the individual vitamins. The initial small endothermic

peak at 120°C can probably be attributed to a B group vitamin since a similar peak appears in the DTA curves of B complex vitamins but not in the curves for vitamin C. The second endothermic peak at about 140°C seems to be characteristic of vitamin C preparations and the following peak is probably the initial portion of the fusion peak for ascorbic acid which is superimposed on a decomposition process as shown by the TG curve.

The thermal data for Lilly Alphalin vitamin A shows an initial dehydration process followed by an exothermic decomposition initiated at about 225°C.

The thermal data for the multi-vitamin products show some features which are not present in the single vitamin curves. The small endothermic peak at about 60°C in the DTA curves of Upjohn Unicap and Lilly Novacebrin corresponds to the reported melting point[4] of vitamin A. This peak was not resolved in the single vitamin A product since it was obscured by the dehydration process. Additional features in the DTA curves include a large endothermic peak at about 110°C which is present for all of the products except Lilly En-Cebrin and an unidentified peak at 70°C for the Upjohn Unicap.

GENERAL

Although each commercial vitamin preparation gives a unique set of thermal curves, standard thermoanalytical techniques generally prove to be unsatisfactory for most qualitative purposes other than the recognition of the gross features of the curves. Most of the significant features of the curves are related to the binder or filler material, since this constitutes the bulk of the sample. This means that the subtle effects due to the minute quantities of the actual vitamin are often obscured. Also, the complexity of the mixture makes it difficult to attribute specific peaks to a specific material or specific effect. Catalogues of thermal data for every commercial vitamin preparation could probably be used effectively to identify a particular brand of vitamin tablet through a matching concept but this would be of little practical value. Perhaps a better use of thermal analysis would be in quality control by comparing the peaks due to the filler with the small peaks attributed to the actual vitamin to determine relative concentrations. Also, gross changes in the composition of the product, such as absorption of water, can be detected by the appearance of new peaks, shifts in existing peaks, or significant changes in the size of peaks in the thermal curves.

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