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# A thermogravimetric study of ascorbic acid and its excipients in pharmaceutical formulations[1]

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**Abstract**

The thermal decomposition of ascorbic acid and its excipients in tablet formulations was studied under an atmosphere of nitrogen using a thermogravimetric balance. To maximize the tendency of an interaction, binary mixtures (1:1 by weight) of drug and excipient and between excipients were utilized. Two new methods were employed to assess the change in reactivities, and the thermal behavior of the materials under investigation. In the first method, named the $\alpha_s - \alpha_r$ method, the solid state reactivity of the sample was compared to that of a reference. The term $\alpha$ refers to the extent of the reaction. The second method is called the $W_p/W_t$ method. In this method, the effect of the excipients on the decomposition pattern of ascorbic acid can be shown. The terms $W_p$ and $W_t$ refer to the percentage of residual solid material obtained experimentally ($W_p$) and theoretically ($W_t$). The ratio $W_p/W_t$ is reported at various values of temperature.

*Keywords:* Thermal decomposition; Ascorbic acid; Interaction; $\alpha_s - \alpha_r$ method; $W_p/W_t$ method

## 1. Introduction

The objectives of this research study were: (1) to study the effect of excipients on the stability of ascorbic acid pharmaceutical tablet formulations, (2) to test for reactivity of ascorbic acid pharmaceutical formulation, and (3) to test reproducibility of the results.

In the presence of excipients the degradation of ascorbic acid may be affected, and this initial study uses thermal analysis to study the effect of these excipients on the degradation pattern at an elevated temperature in an atmosphere of nitrogen. In commercial tablets, a variety of excipients may be present. In this study, the

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degradation process of ascorbic acid with its excipients is expressed by thermogravimetric plots showing the percentage mass loss against temperature in degrees Celsius. In this project, the behavior of binary mixtures in nitrogen is studied. It was felt that the study of ternary mixtures and more complex mixtures would involve complications that should be left to a further study. The thermal analysis was not repeated in air as this would have led to the extra difficulty of coping with combustion processes.

## 2. Experimental

### 2.1. Materials

The materials studied were ascorbic acid, dibasic calcium phosphate, microcrystalline cellulose (Avicel® PH 101), stearic acid, magnesium stearate, and silicon dioxide.

### 2.2. Instrumentation

The equipment employed was a TA Instruments, SDT 2960 Simultaneous TGA–DTA with The Thermal Analyst 2000 using TA Operating System version 1.0B.

### 2.3. Procedure

In single-component decomposition, ascorbic acid and its excipients used in the formulation of vitamin C tablets were employed without any further treatment. In order to obtain obvious results of the interactions of these solid materials, the combinations of an equivalent ratio (w/w) binary mixtures were prepared instead of an actual ratio as in a commercial formulation. The binary mixtures (1 : 1 by weight) were mixed in a porcelain mortar. The density and particle size of the materials were taken into consideration before arriving at the order of mixing for the solids in the mortar. In these two-component systems, the low-density material was placed in the mortar first, followed by the component of higher density. This was done in order to avoid the settling of the denser solids to the bottom of the mixture [1]. The experiments were carried out in an atmosphere of dry nitrogen at the flow rate of 50 mL $min^{-1}$. The rising temperature experimetns were set between 25 and 700°C at the heating rate of 10°C $min^{-1}$. Sample weight was varied between 5 and 16 mg depending on the nature of each material. The sample was placed in an alumina crucible while an empty alumina crucible of the same size was utilized as a reference.

## 3. Results

### 3.1. Single-component results

The TG/DTG plots for ascorbic acid and excipients show the following changes.

(a) Ascorbic acid ——→ Carbon [2] (Fig. 1)

(b) Dibasic calcium phosphate undergoes dehydration [3].

$$2CaHPO_4 \xrightarrow{-H_2O} Ca_2P_2O_4 \text{ (Fig. 2)}$$

(c) Microcrystalline Cellulose ——→ Carbon [4] (Fig. 3)

(d) Stearic acid. The TG/DTA plots is shown in Fig. 4. The DTA shows a melting point at 71°C and boiling point at around 290°C. The loss of mass from 150 to 300°C shown on the TG plot is therefore due to the increased volatility of the material and the material eventually boiling.

(e) Magnesium stearate. Magnesium stearate as supplied in the pharmaceutical industry is a mixture of magnesium stearate and magnesium palmitate. It also exists in different polymorphic forms [5]. The TG and DTG plot (Fig. 5) shows an overlapping two-step degradation due to either the presence of these two fatty salts or different polymorphs. The end product is magnesium oxide.

(f) Silicon dioxide. Fumed silica shows no weight loss in the temperature range studied. It may be concluded that it is $SiO_2$ and stable.

### 3.2. Binary mixture results

Typical results on the binary mixtures are shown in Tables 1–5. The peak temperatures were taken from the DTG plots. A detailed comment on these results is to found in the discussion.

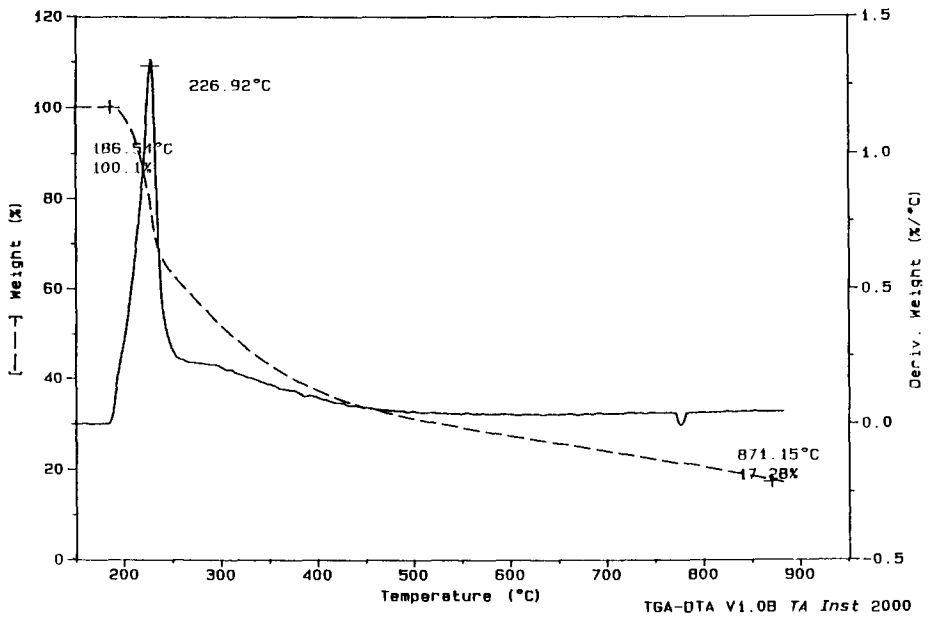


Fig. 1. TG/DTG plot for ascorbic acid under an atmosphere of dry nitrogen.

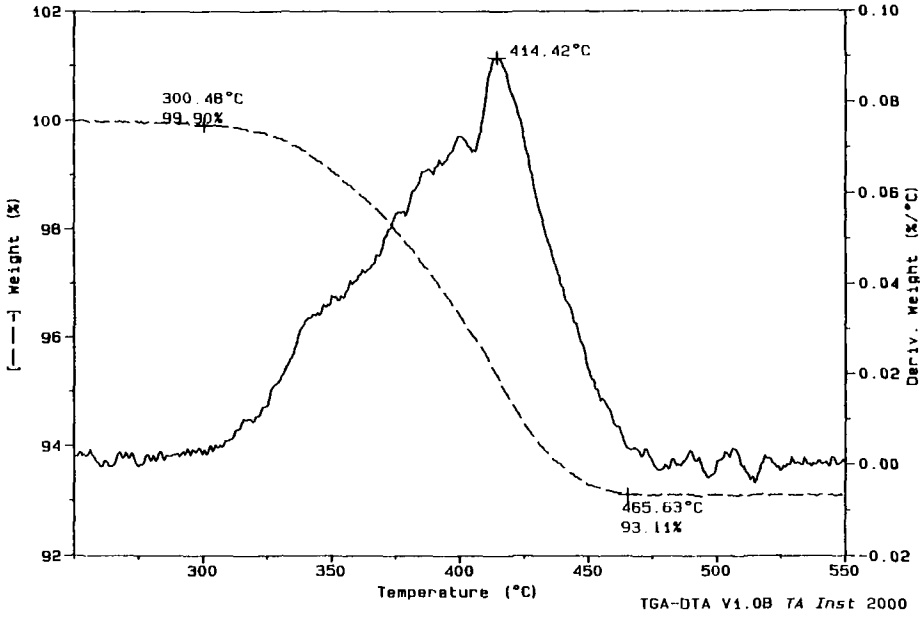


Fig. 2. TG/DTG plot for dibasic calcium phosphate under an atmosphere of dry nitrogen.

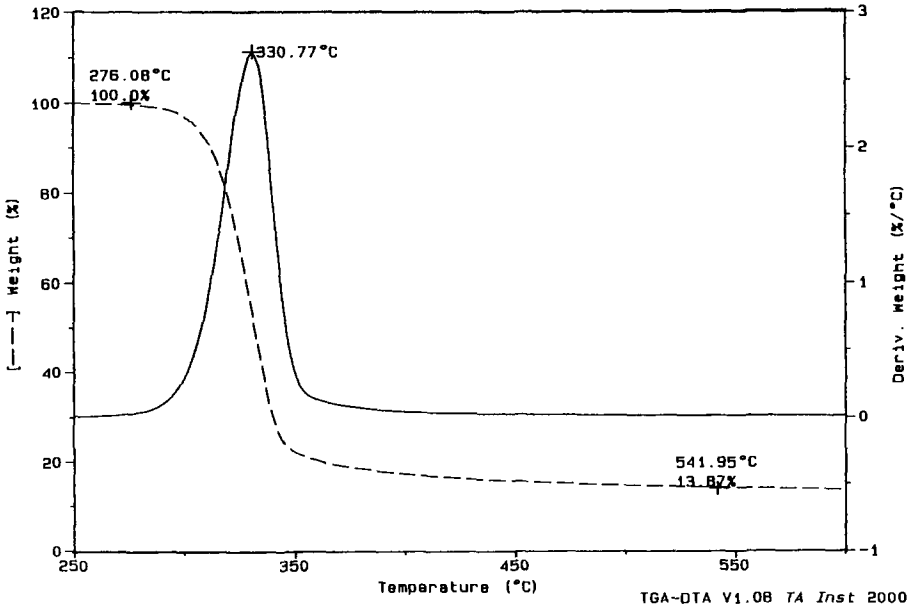


Fig. 3. TG/DTG plot for Avicel PH 101 under an atmosphere of dry nitrogen.

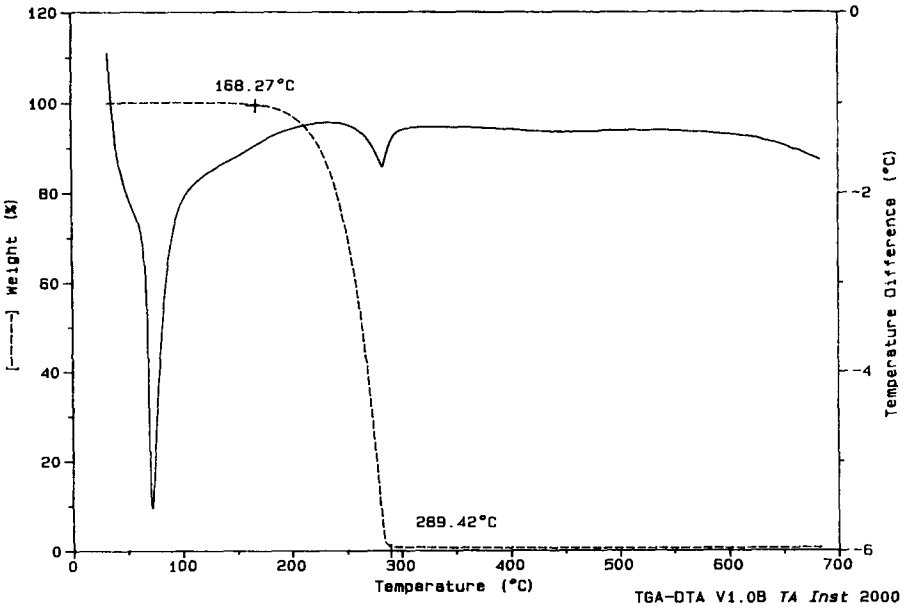


Fig. 4. TG/DTA plot for stearic acid under an atmosphere of dry nitrogen.

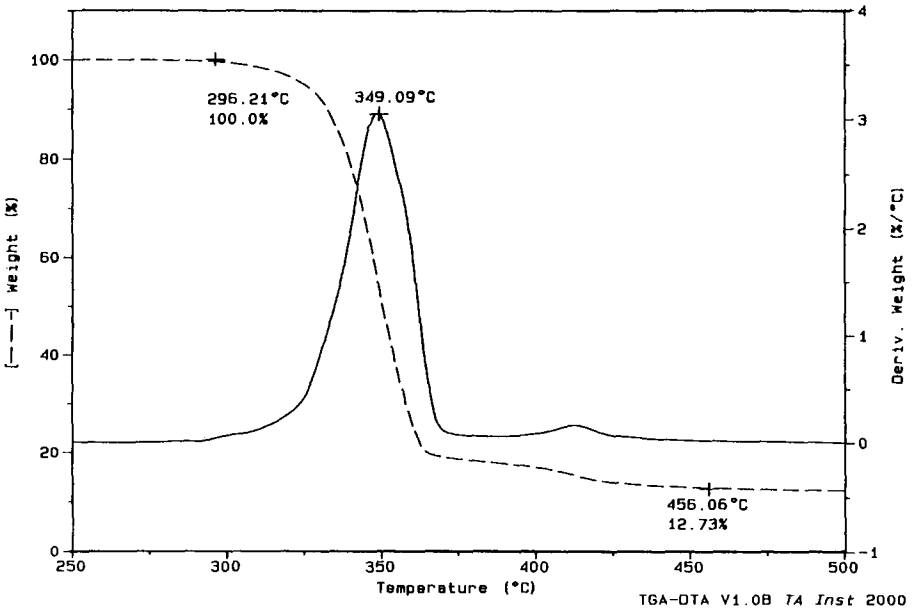


Fig. 5. TG/DTG plot for magnesium stearate under an atmosphere of dry nitrogen.

## 4. Discussion

### 4.1. $\alpha_s$–$\alpha_r$ Method [6]

In this method, thermogravimetric runs were carried out under identical conditions as for microcrystalline cellulose. The first run was conducted without any pretreatment and the thermogravimetric result was considered as a reference. The same material was kept in a dry atmosphere at room temperature for 30 days and 5 consecutive runs were carried out in the same day. The solid state reactivities of these six runs were assessed from the plots of $\alpha_{sample}$ (the extent of decomposition of the sample) which were calculated from runs # 2–6, against the value of $\alpha_{reference}$ (that of the reference) which was calculated from run # 1. Corresponding values of $\alpha_s$ and $\alpha_r$ at various temperatures taken from the TG plots allow for the construction of an $\alpha_s$ versus $\alpha_r$ plot. If the solid state reactivities of the sample coincide with that of the reference, then the plot of corresponding values of $\alpha_s$ versus $\alpha_r$ should be linear over the entire temperature range. If the solid state reactivity of the sample exceeds that of the reference then the $\alpha_s$ will lie above the "coincident line" and vice versa.

Fig. 6 and 7 show the $\alpha_s$–$\alpha_r$ plots for six runs of Avicel® PH 101 and for the binary mixture of Avicel with silicon dioxide, respectively. Figure 6 shows that the "comparative reactivity" of the cellulose altered significantly over the thirty-day period of storage. The close proximity of all the curves labeled 2–6 is almost certainly due to the effect of absorbed water promoting sintering (probably in the form of coalescence of the crystals) and thereby reducing the reactivity of these samples in comparison to the reference. The presence of silica, however showed no alteration in the reactivity of the cellulose (see Fig. 7) indicating that it almost certainly acted simply as a spacer separating the crystals of Avicel® PH 101.

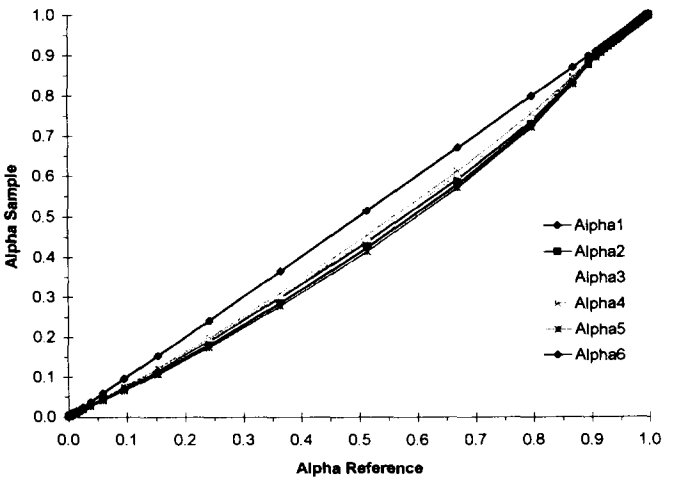


Fig. 6. $\alpha_s$–$\alpha_r$ plot for six experiments of Avicel PH 101 using $\alpha_1$ as a reference.

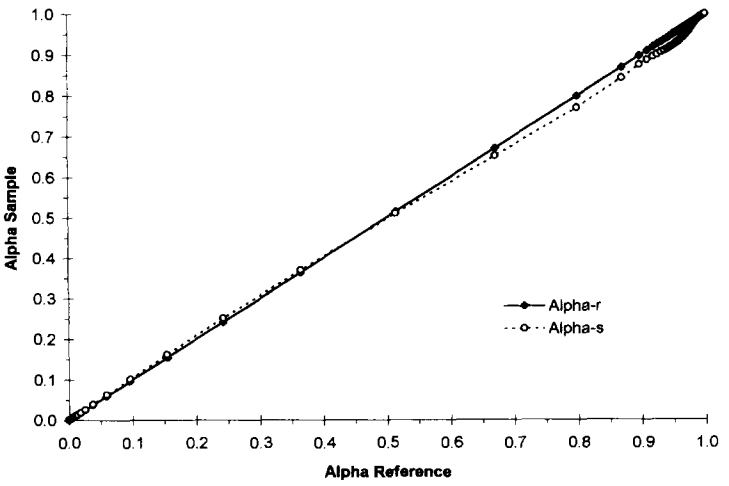


Fig. 7. $\alpha_s$–$\alpha_r$ plot for the binary mixture of Avicel PH 101 with silicon dioxide using Avicel as a reference.

### 4.2. $W_p/W_t$ Method of analysis for assessing the effects of excipients on the thermal decomposition of ascorbic acid [7]

The thermogravimetric runs were carried out under identical conditions on the binary mixtures of ascorbic acid with the excipients as well as on the single components. The data obtained from the TG analysis of the individual components of the mixture are "added" and then divided by two to produce a theoretical TG plot for the mixture. The ratio of the percentage weight loss of the experimental 1 : 1 binary mixture to that of the theoretical values give a straight line, having a value of 1 if the reactivity has not been altered.

The $W_p/W_t$ plot for the binary mixture of dibasic calcium phosphate with Avicel which shows deviations from the horizontal line in both directions is displayed in Fig. 8. This indicates that in the initial experimental decomposition of the binary mixture, the process is taking place at a slightly higher temperature than that predicted from a simple theoretical consideration. The position is reversed as the reaction proceeds to completion. The explanation must be kinetic in origin. In the early period (275–325°C), process of nucleation and initial growth of reaction interfaces are involved, whilst in the latter period (325–375°C) there must be a diminution of the reaction interface.

In Fig. 9, the $W_p/W_t$ plot for the binary mixture of dibasic calcium phosphate with magnesium stearate shows a deviation only in an upward direction, in other words the experimental results occur at a higher temperature than that theoretically predicted. The explanation is kinetic in origin probably because of an increase in the activation energy for the mixture.

In Fig. 10, the $W_p/W_t$ plot for the binary mixture of ascorbic acid with stearic acid shows the experimental result occurring at a lower temperature than that theoretically predicted. In this case, this would be associated with a possible lowering of the activation energy in the binary mixture.

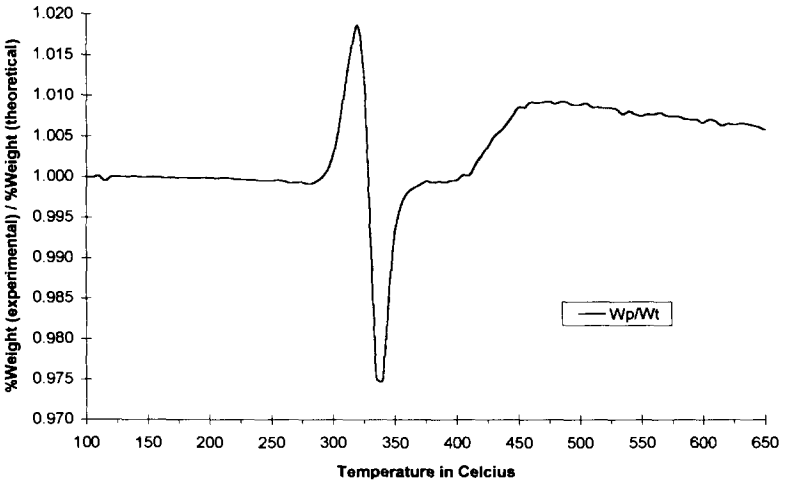


Fig. 8. $W_p/W_t$ plot for the binary mixture of dibasic calcium phosphate with Avicel PH 101.

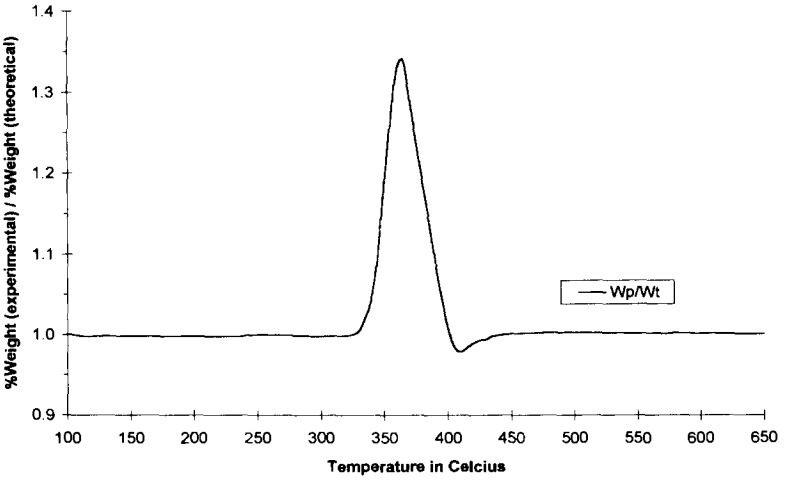


Fig. 9. $W_p/W_t$ plot for the binary mixture of dibasic calcium phosphate with magnesium stearate.

The $W_p/W_t$ plots for six identical experiments with Avicel® PH 101 are shown in Fig. 11. These results should be identical and it would be difficult to see differences in a TG plot. An individual kinetic analysis would reveal no significant difference. The results plotted as a $W_p/W_t$ graph establish a range of insignificant variation. This variation is due to instrumental error.

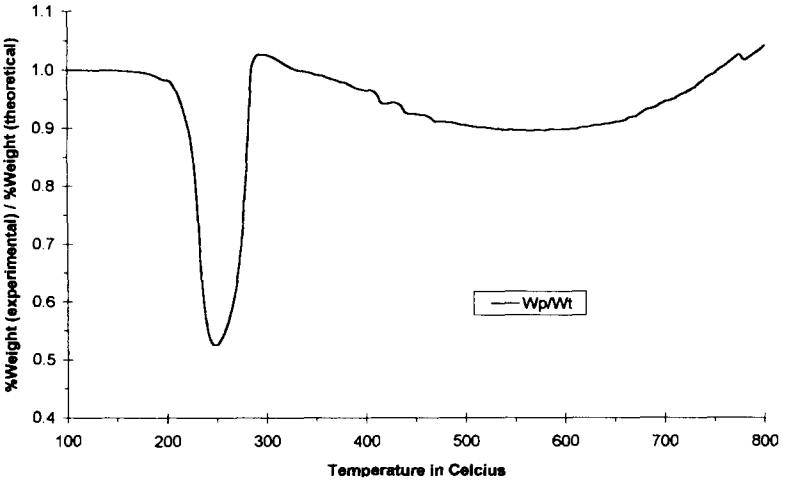


Fig. 10. $W_p/W_t$ plot for the binary mixture of ascorbic acid with stearic acid.

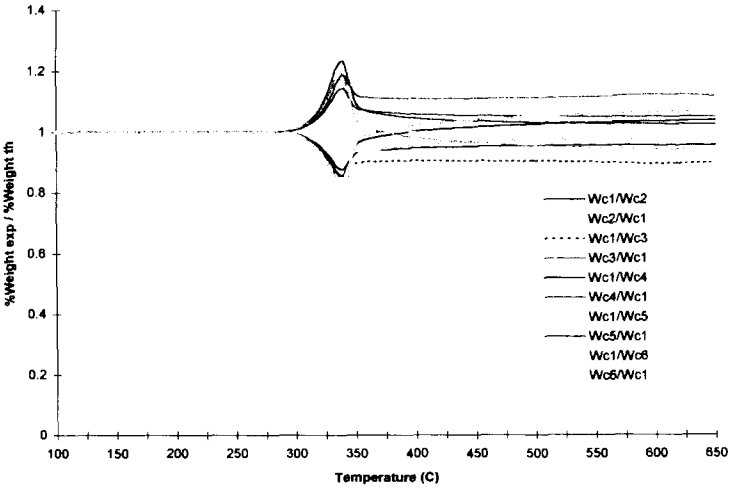


Fig. 11. $W_p/W_t$ plot for six experiments with Avicel PH 101.

### 4.3. Tables 1–5

Tables 1–5 show data cited in the Figures and in additional DTG curves not shown. With reference to Table 1, it should first be noted that the presence of excipients alters the DTG decomposition peak for ascorbic acid over a range of 80°C. The binary mixture of ascorbic acid with silica produced two peaks. It is thought that this

Table 1
Binary mixture results based on ascorbic acid

| | Compound | 1st Peak Temp./°C | 2nd Peak Temp./°C | Comment |
|---|---|---|---|---|
| Single component | A | 226.9 | | |
| binary mixture | A + B | 214.4 | | |
| | A + C | 222.8 | | |
| | A + D | 231.3 | | |
| | A + E | 242.0 | | Complex peak |
| | A + F | 219.0 | 293.0 | Additional peak |

Key: A, ascorbic acid; B, dibasic calcium phosphate; C, Avicel PH 101; D, stearic acid; E, magnesium stearate; F, silicon dioxide.

Table 2
Binary mixture results based on dibasic calcium phosphate

| | Compound | Peak Temp./°C |
|---|---|---|
| Single component | B | 414.42 (only 7% weight loss) |
| Binary mixture | B + A | Shoulder observed but no peak |
| | B + C | No peak discerned |
| | B + D | No peak discerned |
| | B + E | 420.0 |
| | B + F | 408.0 |

Key: A, ascorbic acid; B, dibasic calcium phosphate; C, Avicel PH 101; D, stearic acid; E, magnesium stearate; F, silicon dioxide.

Table 3
Binary mixture results based on Avicel PH 101

| | Compound | Peak Temp./°C |
|---|---|---|
| Single component | C | 330.77 |
| Binary mixture | C + A | 287.48 |
| | C + B | 330.77 |
| | C + D | 330.77 |
| | C + E | 344.71 |
| | C + F | 313.13 |

Key: A, ascorbic acid; B, dibasic calcium phosphate; C, Avicel PH 101; D, stearic acid; E, magnesium stearate; F, silicon dioxide.

represents a typical thermal desorption phenomenon in which material is absorbed onto the silica surface and then thermally desorbed as two separate components.

Table 2 shows that the dehydration of calcium phosphate involved only a small percentage of mass loss and is not discernible in most of the binary mixtures.

Table 4
Binary mixture results based on stearic acid

| | Compound | 1st Peak Temp./°C | 2nd Peak Temp./°C |
|---|---|---|---|
| Single component | D | 278.85 | |
| Binary mixture | D + A | 231.30 | |
| | D + B | 259.01 | |
| | D + C | 255.05 | |
| | D + E | 255.77 | |
| | D + F | 243.03 | 416.23 |

Key: A, ascorbic acid; B, dibasic calcium phosphate; C, Avicel PH 101; D, stearic acid; E, magnesium stearate; F, silicon dioxide.

Table 5
Binary mixture results based on magnesium stearate

| | Compound | 1st Peak Temp./°C | 2nd Peak Temp./°C |
|---|---|---|---|
| Single component | E | 349.09 | |
| Binary mixture | E + A | No peak observed | |
| | E + B | 345.91 | |
| | E + C | Overlapping peaks | |
| | E + D | 353.13 | |
| | E + F | 357.69 | 435.58 |

Key: A, ascorbic acid; B, dibasic calcium phosphate; C, Avicel PH 101; D, stearic acid; E, magnesium stearate; F, silicon dioxide.

The data shown in Table 3 for binary mixtures incorporating Avicel shows a lowering of the peak temperature due to the Avicel degradation in the presence of ascorbic acid but a marked rise in the peak temperature when magnesium stearate is present. No clear reason can be given for this.

Table 4 shows that the peaks for stearic acid are lowered in the binary mixtures but the occurrence of a second higher temperature peak in the presence of silica must be ascribed to thermal desorption of surface species.

The same point has to made for the second peak in the magnesium stearate–silica mixture shown in Table 5. The complexity of the peaks shown in the magnesium stearate binary mixtures would indicate various reactions between the two components which need further studies, probably involving techniques other than thermal analysis.

## 5. Conclusion

The thermal decomposition behavior of ascorbic acid was more or less influenced by other excipients in the Vitamin C tablet formulations. Among various excipients in this

study, only microcrystalline cellulose was not affected by the presence of calcium phosphate, stearic acid, or silicon dioxide. Employing the $W_p/W_t$ method to study the reproducibility of the results as shown in Fig. 11 using microcrystalline cellulose as a model, we found that this material gave good reproducibility with insignificant variation in the percentage weight loss of $\pm 0.2$. This value may be due to instrumental error and/or incorporated with other factors. The advantage of the $\alpha_s - \alpha_r$ analysis is that it enables the reactivity of similar samples, e.g., differently aged cellulose, or the same kind of samples in a different environment, e.g., cellulose in the presence of silica, to be compared without recourse to the complete kinetic description involving the Arrhenius parameters, $A$ and $E$, and the reaction rate equation. However, the comparison between any solid mixture and its single components can be possible only if the mixture gives distinctive steps over the decomposition region. This method only provides the reactivity information for substances being compared in terms of "more reactive" and "less reactive" than the reference material. The $W_p/W_t$ method is more flexible in assessing the solid state reactivities for both single components and the binary mixtures. However, an area of insignificance as mentioned above should be determined for each material in identical experimental conditions. For binary mixtures in which both compounds degrade in the same temperature range, the influence of compounds toward each other cannot be defined. Instead, the $W_p/W_t$ method lends a vivid picture of comparison for the experimental TG signal to the theoretical one. To conclude that the experimental binary mixture is "more" or "less" reactive than its theoretical value would be more reliable when the area of insignificance is designated for a given mixture.

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