ELSEVIER

Thermochimica Acta 340–341 (1999) 131–138

thermochimica acta

www.elsevier.com/locate/tca

A thermal analysis study of ibuprofen and starch mixtures using simultaneous TG–DTA

Supaporn Lerdkanchanaporn

Department of Chemistry and College of Pharmacy, University of Toledo, Toledo, OH 43606, USA

Accepted 6 August 1999

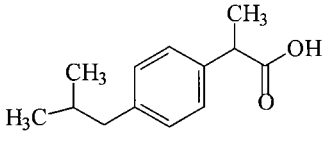
Abstract

Mixtures of ibuprofen and starch were examined in a flowing atmosphere of dry nitrogen using a simultaneous TG–DTA unit. This showed that the two main features of heat treatment of ibuprofen, namely melting and evaporation, were retained. The loss of water from the starch on heat treatment could be noticed in the mixtures, and the thermal degradation of the starch to carbon could also be observed as a separate step. The temperature for the evaporation of the ibuprofen increased and the starch degradation temperature also rose with increasing ibuprofen content in the binary mixtures. The separation of these two processes enabled the percentage of composition of the mixture to be established. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Ibuprofen; TG–DTA; Starch

1. Introduction

The previous work on ibuprofen which has the formula:



showed a zero order evaporation process occurring after melting with an E_{act} of 81.8 – 87.0 kJ mol^{-1} [1]. Other thermal analysis studies on ibuprofen involve DSC and show that the degree of crystallinity and the nature of the solvents used for crystallization have an effect on the melting point [2]. Labhasetwar et al. [3] also demonstrated, using a conventional melting point apparatus, that the ibuprofen crystallized from various solutions or dispersions, such as propylene glycol, diethylene glycol, polyethylene glycol (PEG) 3000, PEG 4000, glycerine, etc. showed variation in the melting point which could be related to crystal habit. Romero et al. [4,5] suggested that the stereochemical aspects of ibuprofen affect the properties of the samples and the crystal habit. The evaporation in nitrogen can be detected from around 120°C up to 240°C. Starch is a mixture of two biopolymers: amylose, a linear (1 → 4)-α-D-glucan and amylopectin, a branched D-glucan with mostly α-D-(1 → 4) and approximately 4% α-D-(1 → 6) linkages [6,7].

Simultaneous TG–DTA finds increasing use in the pharmaceutical industry to study compatibility in tablet formulations and to assess whether it can be used analytically [8] in mixtures. In the present study, the emphasis is on solid mixtures of ibuprofen [1] and

PII: S0040-6031(99)00259-2

starch [9]. The objectives of the present study were: (i) to study the effect of starch on the thermal treatment of ibuprofen, (ii) to see if there was any reactivity between the ibuprofen and the starch, (iii) to check on reproducibility of the results, and (iv) to see if TG–DTA could be used as an analytical tool in the binary mixtures of ibuprofen and starch.

In the presence of air, combustion of these organic materials would be expected, leading to strong exothermic effects and complete gasification. This might be deleterious to the possible use of TG as an analytical device. Accordingly, the present study is confined to thermal analysis of binary mixtures of ibuprofen and starch in nitrogen. The TG–DTA plot of racemic ibuprofen in these circumstances shows a melting point (DTA onset temperature) in the range of 73.5–74.8°C, followed by evaporation which is often completed before the boiling point is reached. Starch on the other hand degrades in nitrogen to leave a carbon residue [10–14]. Typically, the reaction appears as a single stage process in the temperature range 250–400°C depending on the nature of the starch [15]. The residue of carbon is around 14% of the total mass of starch, but again this depends on the source of the starch and the nature of the experiment (heating rate, initial sample mass, etc.). These would seem to indicate the possibility that TG–DTA studies in nitrogen could lead to the analysis of binary mixtures of ibuprofen and starch.

2. Experimental

2.1. Materials

The ibuprofen was supplied by Pharmacia & Upjohn. The material was described as a racemic compound [1]. The starch supplied was Starch 1500® (pregelatinized corn starch, lot # 4SE01OH) obtained from Chelsea Labs.

2.2. Equipment and procedure

The equipment used to study the behavior of ibuprofen, starch, and their mixtures was a simultaneous TG–DTA model no. SDT 2960 (TA Instruments). The thermal analysis experiments were performed between ambient and 600°C, and the thermogravimetric (TG), the derivative thermogravimetric (DTG), and the differential thermal analysis (DTA) data were collected. The temperature program was a heating rate of 10°C min^{-1} from ambient to 600°C. A purge gas was a flowing dry nitrogen (99% purity) at a rate of 200 mL min^{-1} measured by an electronic flowmeter from J & W Scientific, model no. ADM 1000. Nitrogen gas was dried by passing it through a cylinder containing Drierite®. The sample mass was kept in the range of 7.73–10.21 mg. Platinum crucibles were used with a capacity of 110 μl and the reference crucible was left empty. Each sample was subjected to the same heating program and conditions. All compounds were tested in triplicate, and the mean values and the greatest SD among a set of three runs were reported.

The mixing of the two components was achieved by grinding the binary mixture in a 5 dram glass bottle with the aid of grinding pebbles (Burundum®, cylindrical shape, $0.5'' \times 0.5''$ diameter) for 15 min using a roller mixing jar from Paul O. Abbe, NJ ($5.75''$ diameter, 1725 rpm).

3. Results and discussion

Typical TG, DTG, and DTA plots for ibuprofen in nitrogen are shown in Fig. 1. From the DTA plot, the melting of ibuprofen can be seen as the initial peak (T_i) at 74°C and the peak temperature (T_p) at 77°C. The evaporation of ibuprofen can be observed on all plots, and the DTA shows a T_i at 196°C, with a T_p at 232°C. However, the T_p does not portray the normal boiling point as the evaporation process had exhausted all the material before reaching the true boiling point.

Typical TG, DTG, and DTA plots for the starch in nitrogen are shown in Fig. 2. This shows the loss of water up to around 145°C, the degradation of the starch to carbon over the range 234 – 496°C followed by a slow loss of weight from the carbon residue beyond this temperature up to 600°C where the experiment was stopped. The moisture loss was around 4%, and the residue at 496°C was 14% of the original sample.

Mixtures of ibuprofen and starch were examined using the thermal analysis unit. Fig. 3 shows typical TG, DTG, and DTA plots for a (50 : 50% w/w) mixture in nitrogen. It can be seen that all the characteristics of the ibuprofen can be discerned, namely, the

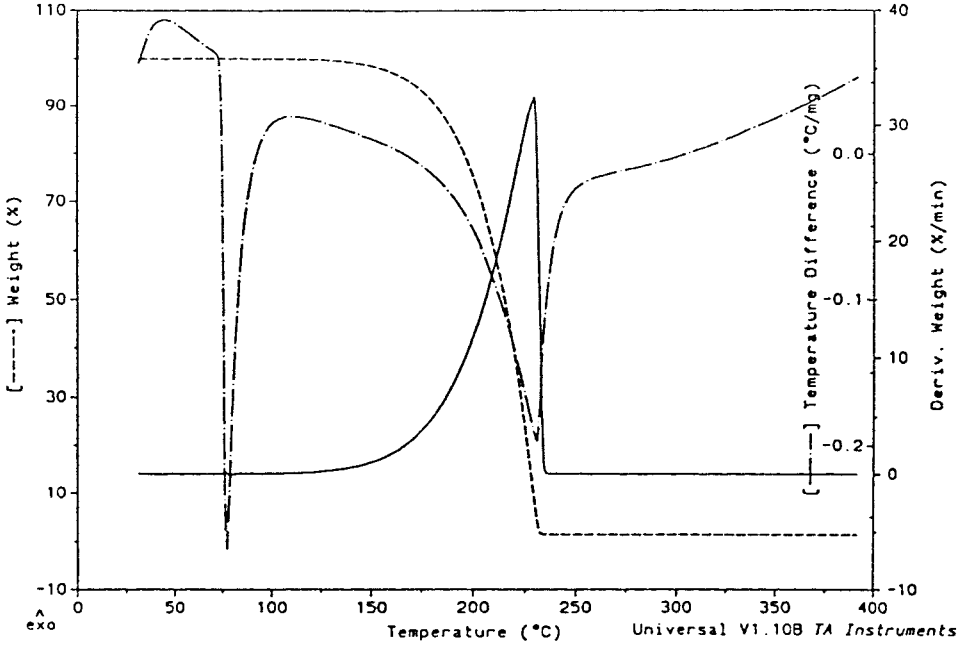


Fig. 1. A typical TG, DTG, and DTA plot for ibuprofen in a nitrogen atmosphere.

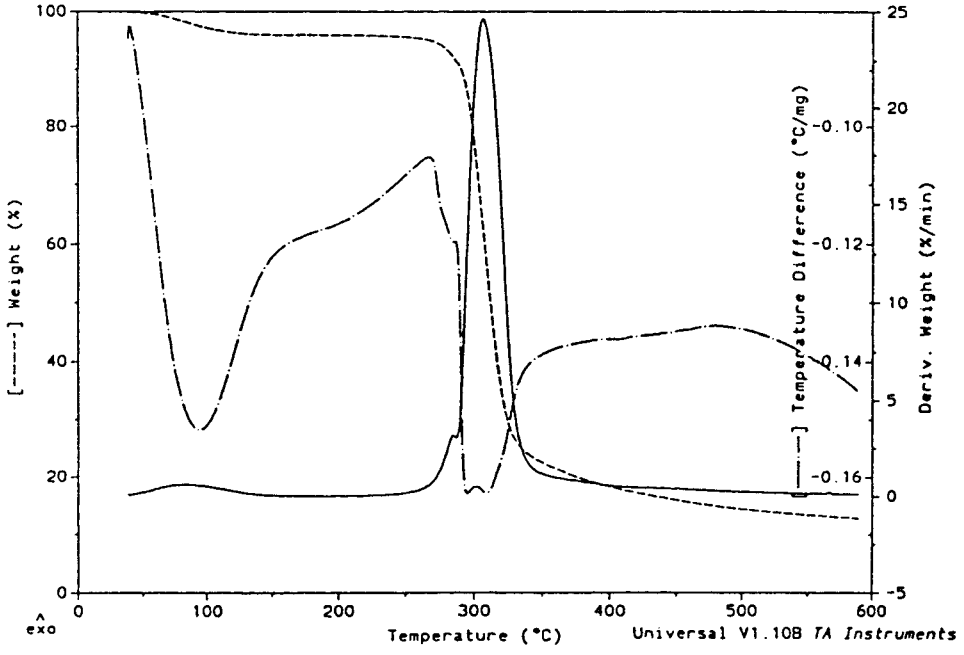


Fig. 2. A typical TG, DTG, and DTA plot for starch in a nitrogen atmosphere.

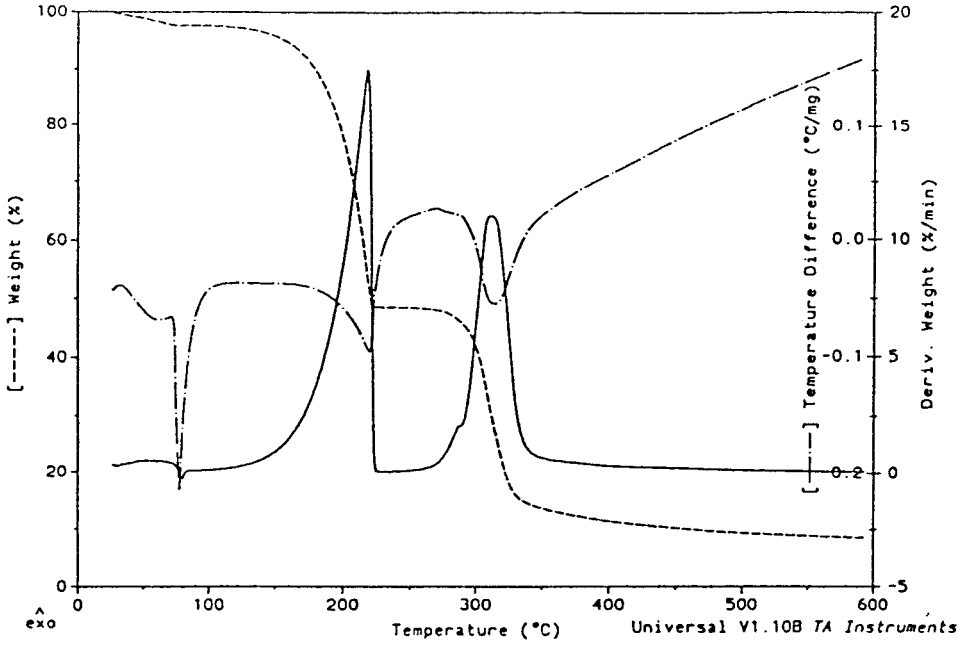


Fig. 3. A typical TG, DTG, and DTA plot for a 50 : 50 (% by mass) mixture of ibuprofen and starch in a nitrogen atmosphere.

melting (shown on the DTA plot) followed by the evaporation process with complete loss of the ibuprofen. The loss of moisture from the starch can be seen on the TG plot, and the separate degradation of the starch can also be observed. All the processes were endothermic.

The details of the thermal analysis in nitrogen of all the mixtures are set out in Tables 1 and 2. The data shown in the tables are the mean values and the SD of such experiments. Table 1 sets out the temperature limits and characteristic for each mixture. Upon heating the ibuprofen–starch mixtures, four major events occur in the following order: (i) starch dehydration, (ii) ibuprofen melting, (iii) ibuprofen evaporation, and (iv) starch degradation.

First of all, the starch gradually dehydrates, and this process is complete at about 145°C as seen in Table 1 (see T_{TG1}) when starch alone is subjected to the heat treatment. However, in the mixtures, as starch loses its moisture, ibuprofen begins to melt and reaches the liquid state at temperature T_{TG1}. It can be seen that a large variation in T_{TG1} as indicated by SD value, resulted from the gradual mass loss of the dehydration process of starch. As seen on the DTA trace, below the temperature of 150°C, the melting endotherm of ibuprofen can be seen, and it overlaps with the endothermic peak due to loss of moisture from starch (see Fig. 3). From Table 1, the peaks labeled on the DTA data as T_{DTA1} refer to melting of the ibuprofen. This is unaffected by the overlapping loss of moisture and the presence of the starch.

The next event is the evaporation of ibuprofen. The liquid ibuprofen vaporizes upon heating and is completely gone at temperature T_{TG2} when no more ibuprofen is left in the system. The DTG peak (T_{p1}) shows that the temperature at this point increases as the percentage of ibuprofen is increased. The DTA data for this event (T_{DTA2}) also support this observation. However, the onset temperatures do not show this because the departure from the baseline for the DTA plot is initially very gradual (see Fig. 3) in this region.

Finally, the starch slowly degrades to carbon up to the temperature T_{TG3}. Beyond this point, the mass loss of the residue gradually progresses causing a large variation in reported T_{TG3} (see SD value). The DTG peak for this event (T_{p2}) and the DTA peak temperature (T_{DTA3}) increase as the original composition of starch in the mixtures decrease. This is interesting as it shows that ibuprofen, which has disappeared by the time the starch degrades, has had some effect on the

Table 1
Temperature data for TG, DTG, and DTA for binary mixtures of ibuprofen and starch heated in nitrogen[a]

Mixture (%)		TG (°C)			DTG (°C)		DTA (°C)					
Ibuprofen	Starch	T_{TG1}[b]	T_{TG2}[c]	T_{TG3}[d]	T_{p1} (ibuprofen evaporation)	T_{p2} (starch degradation)	T_{DTA1} (ibuprofen melting)		T_{DTA2} (ibuprofen evaporation)		T_{DTA3} (starch degradation)	
							Onset	Peak	Onset	Peak	Onset	Peak
0.0	100.0	145.1	–	496.5	–	306.4	–	–	–	–	287.7	309.9
25.0	75.0	120.0	207.5	481.1	197.9	310.2	74.2	77.0	177.1	200.1	295.0	312.4
50.0	50.0	109.2	225.0	439.0	216.6	312.3	73.8	77.5	187.6	217.7	292.9	315.9
75.0	25.0	106.0	231.9	364.1	224.8	316.0	74.5	77.8	190.7	225.9	292.6	318.2
80.0	20.0	101.6	234.8	353.1	226.7	316.7	74.5	77.6	194.2	228.1	291.5	320.1
85.0	15.0	105.5	234.3	402.1	227.6	318.2	74.8	78.0	195.0	228.4	297.2	321.3
90.0	10.0	120.6	236.5	347.1	228.1	317.7	74.0	77.7	193.1	229.7	–	324.4
95.0	5.0	119.8	237.6	344.4	229.6	318.7	73.5	77.3	196.9	230.9	–	335.8
100.0	0.0	119.7	237.7	–	230.6	–	74.0	77.4	195.8	231.8	–	–
Greatest SD in a set of three		13.41	2.63	12.17	1.36	1.34	0.88	2.09	3.25	1.56	3.26	2.87

[a] All the data represents the mean value of three thermal analysis runs. The greatest standard deviation among a set of three runs is recorded at the bottom of the table.
[b] Water losses and/or ibuprofen melts up to this temperature.
[c] Ibuprofen evaporates up to this temperature.
[d] Starch degrades up to this temperature.

Table 2
The DTG peak area and peak height for the ibuprofen evaporation process in the ibuprofen–starch mixtures[a]

Mixture (%)		DTG peak area (%)		DTG peak height (% min^{-1})	
Ibuprofen	Starch	Ibuprofen evaporation	Starch degradation	Ibuprofen evaporation	Starch degradation
0.0	100.0	–	78.04	–	24.76
25.0	75.0	21.96	55.69	8.76	17.34
50.0	50.0	48.36	35.69	17.95	11.07
75.0	25.0	73.09	19.27	26.08	5.94
80.0	20.0	81.28	14.70	28.59	4.41
85.0	15.0	84.10	12.24	29.41	3.43
90.0	10.0	88.81	7.13‘	31.05	2.10
95.0	5.0	90.77	3.59	31.45	1.02
100.0	0.0	98.58	–	32.55	–
Greatest SD in a set of three		1.47	1.21	0.52	0.53

[a] All the data represents the mean value of three thermal analysis runs. The greatest standard deviation among a set of three runs is recorded at the bottom of the table.

subsequent starch degradation. It can be speculated that the suspension of the starch in the liquid ibuprofen is aggregated by the evaporation process rendering it less active and that aggregation is enhanced if the original concentration of starch is kept low.

Table 2 records the DTG signals for the ibuprofen evaporation and the starch degradation process in the ibuprofen–starch mixtures. The plots of percentage ibuprofen against the DTG peak area and peak height are shown in Fig. 4. The linear regression equations which can be fitted to these data are given below:

For DTG peak area (with $R^2 = 0.995$)

$$Y_1 = 1.01\,X_{ibu} - 2.50 \quad (1)$$

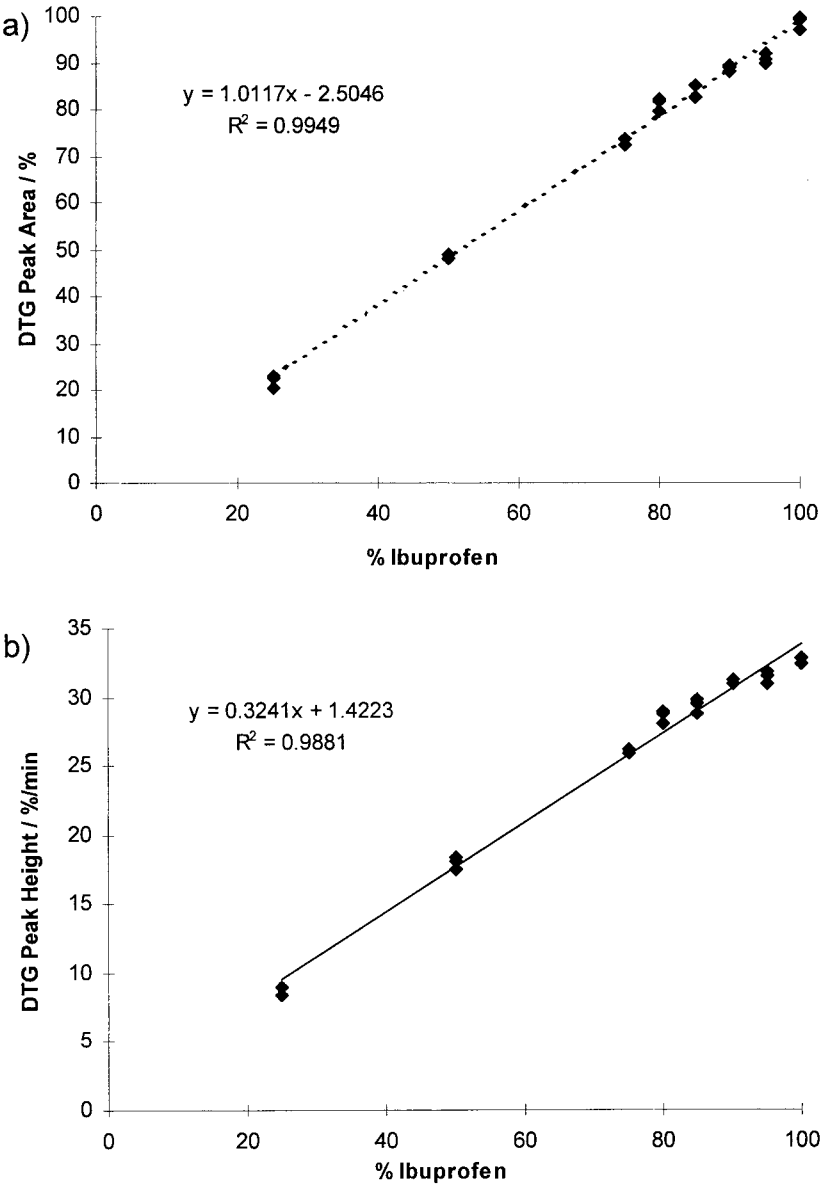


Fig. 4. The DTG plots for the evaporation process of ibuprofen in the ibuprofen–starch mixtures (a) peak area, (b) peak height.

For DTG peak height (with $R^2 = 0.988$)

$$Y_2 = 0.32\,X_{ibu} + 1.42 \quad (2)$$

where X_{ibu} is the percentage of ibuprofen in the mixtures, Y_1 the DTG peak area of ibuprofen with units of %, and Y_2 the DTG peak height of ibuprofen with units of %/min.

The plots of percentage starch against the DTG peak area and peak height are shown in Fig. 5. The linear regression equations which can be fitted to these data are given below.

For DTG peak area (with $R^2 = 0.997$)

$$Y_3 = 0.77\,X_{st} - 0.46 \quad (3)$$

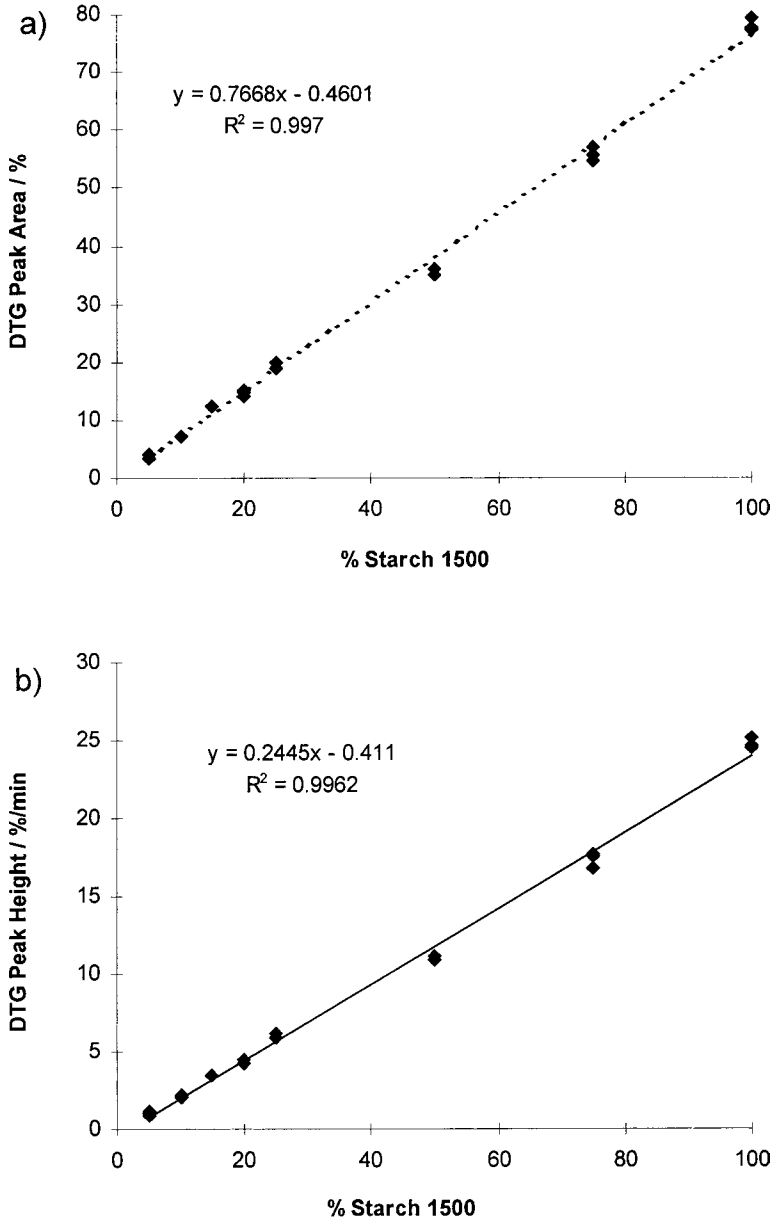


Fig. 5. The DTG plots for the degradation process of starch in the ibuprofen–starch mixtures (a) peak area, (b) peak height.

For DTG peak height (with $R^2 = 0.996$)

$$Y_4 = 0.24\,X_{st} - 0.41 \quad (4)$$

where X_{st} is the percentage of starch in the mixtures, Y_3 the DTG peak area of starch with units of %, and Y_4 the DTG peak height of starch with units of %/min.

It can be seen that the DTG plots provide data in terms of peak area or peak height for the ibuprofen evaporation and starch degradation that can be used for analytical purposes. The R^2 value for ibuprofen evaporation indicates that the relationship to the peak area is the best to use. The R^2 value for starch

degradation indicates that either the peak area or the peak height on the DTG plot can be employed for analysis. However, the peak height is the easier of the two to measure.

4. Conclusions

The simultaneous thermal analysis of ibuprofen–starch mixtures in nitrogen reveals that the thermal features of ibuprofen, namely melting followed by evaporation, are retained in the mixtures. Likewise, the thermal features of starch, namely loss of moisture followed by thermal degradation to carbon are also retained in the mixtures. Analysis of the thermal data indicates that the temperature range for the ibuprofen evaporation increases as the percentage of ibuprofen increases in the mixtures. The starch degradation temperature also increases as the original ibuprofen content in the mixtures increases in spite of the fact that all the ibuprofen has disappeared before the starch degrades. The mass loss in both the ibuprofen evaporation process and the starch degradation process allows such data to be used to estimate percentage composition in ibuprofen–starch mixtures. It is recommended that the DTG peak area of the evaporation process be used for estimation of the ibuprofen content while the peak height for the starch degradation be used for estimation of the starch content in the mixtures.

Acknowledgements

The author wishes to thank Prof. Dollimore for advice in writing this paper. His thoughtful and kindly guidance has always been appreciated. Wising you a very happy 70th birthday.

References

[1] S. Lerdkanchanaporn, D. Dollimore, J. Therm. Anal. 49 (1997) 879.
[2] N. Udupa, Drug Devel. Industr. Pharmacy 16 (1990) 1591.
[3] V. Labhasetwar, S.V. Deshmukh, A.K. Dorle, Drug Devel. Industr. Pharmacy 19 (1993) 631.
[4] A.J. Romero, L. Savastano, C.T. Rhodes, Int. J. Pharm. 99 (1993) 125.
[5] A.J. Romero, C.T. Rhodes, J. Pharm. Pharmacol 45 (1993) 258.
[6] S. Budavari, The Merck Index, 11th ed., Merck and Co., Rahway, NJ, 1989, p. 1386.
[7] K.H. Meyer, M. Wertheim, P. Bernfeld, Helv Chim. Acta 23 (1940) 865.
[8] C.M. Earnest (Ed.), Compositional Analysis by Thermogravimetries, ASTM Publication, Philadelphia, PA, 1988, 293 pp.
[9] C.O. Moore, J.V. Tuschoff, C.W. Hastings, R.V. Schanefelt, in: R.L. Whistler, J.N. Bemiller, E.F. Paschall (Eds.), Starch: Chemistry and Technology, ch. 19, 2nd ed., Academic Press, Orlando, FL, 1984, p. 578.
[10] D. Costa, G. Costa, Chim. Ind. Milan 33 (1951) 71.
[11] A.T. Perkins, H.L. Mitchell, Trans. Kansas Acad. Sci. 60 (1957) 437.
[12] H. Morita, Anal. Chem. 28 (1956) 64.
[13] H. Morita, Anal. Chem. 29 (1957) 1095.
[14] M.C.P. Varma, J. Appl. Chem. (London) (1958), pp. 8, 12 and 117.
[15] P. Aggarwal, D. Dollimore, Talanta 43 (1996) 1527.