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THERMAL ANALYSIS OF PHARMACEUTICAL COMPOUNDS

IV. EVALUATION OF SULPHONAMIDES BY THERMAL ANALYSIS

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Some sulphonamides are evaluated by means of thermal analysis. Use is made of their characteristic endothermic DTA peaks (melting peaks), where the area changes linearly with variations in the amount of sulphonamides. The method is suitable for the determination of 30–100 mg of sulphathiazole, sulphisomidine, sulphaguanidine, sulphacetamide sodium and sulphamethoxypyridazine with reasonable accuracy. As for sulphisoxazole, two peaks are used for its determination: an endothermic one to determine 30–100 mg, and an exothermic one to determine 6–30 mg.

Some compounds used in the food industry and in pharmacy can be identified through the study of their thermal analytical behaviour [1–9].

Thermal analysis is not used for determination, except in a few cases [10].

The characterization of sulphonamides by thermal analysis, with study of the different thermal reactions, prediction of the thermal decomposition pathway and analysis of sulphonamide mixtures was carried out by the authors in a previous publication [6].

In the present work, an attempt is made to determine sulphonamides by means of thermal analysis.

Experimental

Materials and apparatus:

Sulphonamide samples:

1 – Sulphathiazole[+]
2 – Sulphisoxazole[+]
3 – Sulphisomidine (SWISSPHARMA)
4 – Sulphacetamide sodium[+]
5 – Sulphaguanidine (Merck)
6 – Sulphamethoxypyridazine[+]

Aluminium oxide (May & Baker) previously heated to 1200° for two hours.
Derivatograph and planimeter MOM, Hungary.

[+] Sulphonamides from ELNASR Pharmaceutical Chemicals Co., Abu Zaabal, Egypt, A.R.E.

0.1 g sample was examined with the derivatograph at a heating rate of 5°/min.

For each sulphonamide, the clearest characteristic DTA peak (occurring at the lowest temperatures) was chosen for determination purposes.

For each compound, different amounts in the range 30 – 100 mg were thermally analyzed at higher DTA galvanometer sensitivity. The area under the DTA peak of interest for each weight was measured planimetrically; tangents were drawn at the beginning and ending of the peak, and the points of intersection were connected. Figure 1 illustrates the determination of the peak area for 50 mg sulphisomidine.

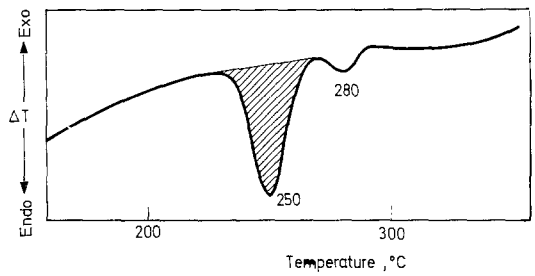

Fig. 1. DTA peak for 50 mg of sulphisomidine

Results and discussion

The purities of the sulphonamides were determined by a pharmacopoeial method [11, 12] and found to be 99.85, 99.49, 99.90, 99.97, 100.08 and 99.51% for sulphathiazole, sulphisomidine, sulphisoxazole, sulphacetamide sodium, sulphaguanidine and sulphamethoxypyridazine, respectively. All the results obtained have been appropriately corrected accordingly.

Table 1

Determination of sulphathiazole by thermal analysis

	Amount taken, mg	Amount found, mg	Recovery, %
1	39.9	39.9	100.0
2	49.9	51.0	102.2
3	54.9	54.9	100.0
4	59.1	61.0	101.8
5	64.9	64.9	100.0
6.	69.9	68.0	97.3
7	74.9	74.9	100.0
8	79.9	79.9	100.0

Mean recovery = 100.16 ± 1.23% (P = 0.05)

Figure 2 shows collective DTA curves of the examined sulphonamides. Figures 3–8 illustrate the relations between the concentration of sulphathiazole, sulphisomidine, sulphisoxazole, sulphaguanidine, sulphacetamide sodium and sulphamethoxypyridazine and the area under the peak as measured from the curves for each compound. Tables 1–7 present the determination of the above-mentioned sulphonamides by the proposed DTA method.

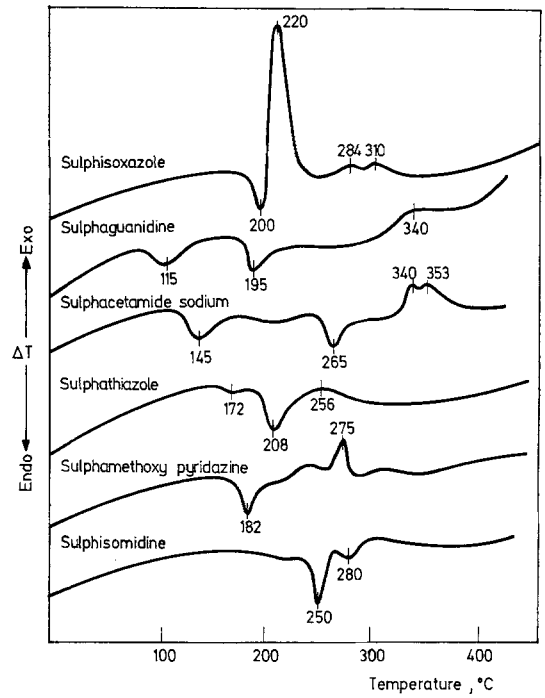

Fig. 2. Collective DTA curves of sulphonamides

Table 2

Determination of sulphisomidine by thermal analysis

	Amount taken, mg	Amount found, mg	Recovery, %
1	39.8	41.0	103.0
2	49.8	49.8	100.0
3	54.7	56.5	103.3
4	59.7	61.5	103.0
5	69.6	69.6	100.0
6	74.6	74.6	100.0
7	79.6	78.0	97.9
8	89.5	89.5	100.0

Mean recovery = 100.90 ± 1.63 % (P = 0.05)

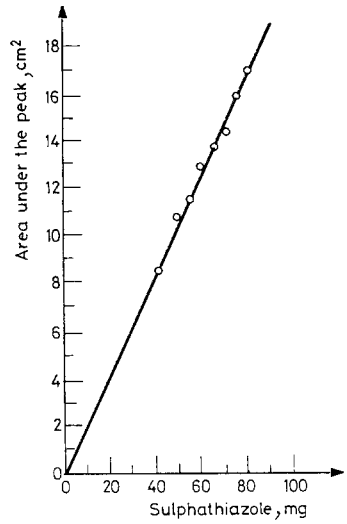

Fig. 3. The relation between the amount of sulphathiazole and the area under the DTA peak

The DTA peaks chosen for the determination of the sulphonamides are the clearest characteristic endothermic peak occurring at the lowest temperature (in most cases the melting peak): for sulphathiazole, sulphisomidine, sulphaguanidine, sulphamethoxypyridazine, sulphisoxazole and sulphacetamide sodium, at 208, 250, 195, 182, 200 and 145°, respectively. As for sulphisoxazole, the exothermic peak at 220° is also used. Generally, no displacement of the base line was noticed for the chosen peaks at such melting temperatures. From Figs 3–8, linear relations are obtained between the area and the concentration, allowing the determination of these compounds by thermal analysis, as illustrated in Tables 1–7.

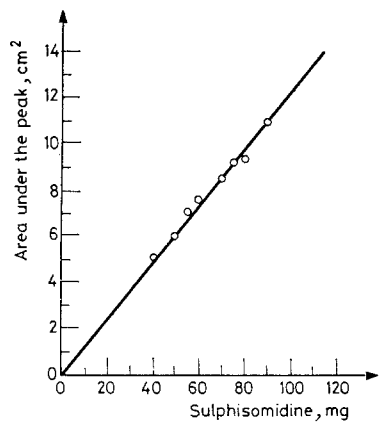

Fig. 4. The relation between the amount of sulphisomidine and the area under the DTA peak

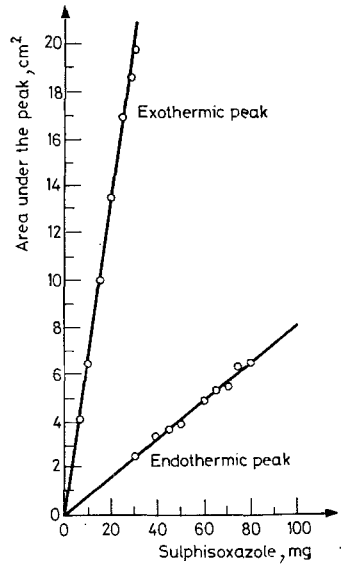

Fig. 5. The relation between the amount of sulphisoxazole and the area under the DTA peak

The method is suitable for the determination of 30 – 100 mg of each of sulphathiazole, sulphisomidine, sulphaguanidine, sulphacetamide sodium and sulphamethoxypyridazine with accuracies ($p = 0.05$) of 100.16 ± 1.23%, 100.90 ± ± 1.63%, 98.55 ± 1.73%, 100.93 ± 2.03% and 99.56 ± 2.16%, respectively.

As for sulphisoxazole, a linear relation was also found between its amount and the area under the exothermic peak at 220°. The change in the area of this peak was very sensitive towards small variations in the sulphisoxazole concentration. The exothermic peak is of advantage in the determination of small amounts of sulphisoxazole, as is evident from Table 3. In this case, it is possible to determine 6 – 30

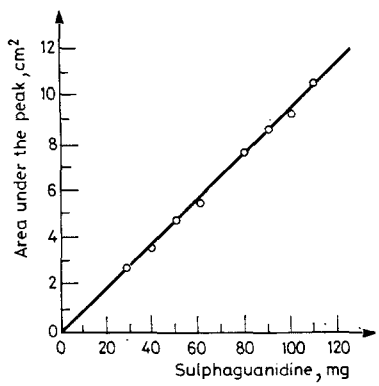

Fig. 6. The relation between the amount of sulphaguanidine and the area under the DTA peak

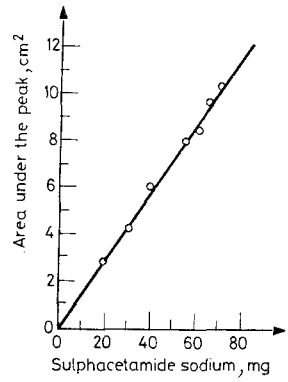

Fig. 7. The relation between the amount of sulphacetamide sodium and the area under the DTA peak

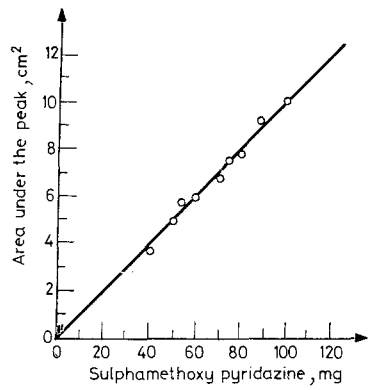

Fig. 8. The relation between the amount of sulphamethoxy pyridazine and the area under the DTA peak

Table 3

Determination of sulphisoxazole by thermal analysis. (Exothermic peak)

	Amount taken, mg	Amount found, mg	Recovery, %
1	6	6	100.0
2	10	10	100.0
3	15	15	100.0
4	20	20	100.0
5	25	25	100.0
6	28	27.5	98.2
7	30	29	96.7

Mean recovery = 99.27 $\pm$ 1.22% (P = 0.05)

Table 4

Determination of sulphisoxazole by thermal analysis. (Endothermic peak)

	Amount taken, mg	Amount found, mg	Recovery, %
1	30	30	100.0
2	40	41	102.5
3	45	45	100.0
4	50	48.5	97.0
5	59.9	59.9	100.0
6	64.9	64.9	100.0
7	69.9	68.0	97.3
8	74.9	76.0	101.5
9	79.9	79.9	100.0

Mean recovery = 99.81 $\pm$ 1.33% (P = 0.05)

Table 5

Determination of sulphaguanidine by thermal analysis

	Amount taken, mg	Amount found, mg	Recovery, %
1	30	30	100.0
2	40	38	95.0
3	50	50	100.0
4	60.1	58.0	96.5
5	80.1	80.1	100.0
6	90.1	90.1	100.0
7	100.1	97.0	96.9
8	110.1	110.1	100.0

Mean recovery = 98.55 $\pm$ 1.73% (P = 0.05)

Table 6

Determination of sulphacetamide sodium by thermal analysis

	Amount taken, mg	Amount found, mg	Recovery, %
1	20	20	100.0
2	30	30	100.0
3	40	41.5	103.8
4	55	55	100.0
5	60	58.5	97.5
6	65	67	103.1
7	70	71.5	102.1

Mean recovery = 100.93 $\pm$ 2.03% (P = 0.05)

Table 7

Determination of sulphamethoxy pyridazine by thermal analysis

	Amount taken, mg	Amount found, mg	Recovery, %
1	39.8	37.5	94.2
2	49.8	49.8	100.0
3	54.7	57.0	104.2
4	59.7	59.7	100.0
5	69.7	68.0	97.6
6	74.6	74.6	100.0
7	79.6	78.0	97.9
8	89.6	91.5	102.1
9	99.5	99.5	100.0

Mean recovery = 99.56 ± 2.16% (P = 0.05)

mg sulphisoxazole with an accuracy ($p = 0.05$) of 99.27 ± 1.22%. As for higher concentrations of the compound, the exothermic peak is found to be highly sensitive to small variations in the concentration, which shoot the peak out of the chart. It is suggested that the sensitivity of the DTA galvanometer be decreased, but this would deprive the method of its sensitivity for small amounts. A better compromise is to use the endothermic peak for the determination of larger amounts of sulphisoxazole, its area being smaller. In this case the method is suitable for the determination of 30–100 mg sulphisoxazole with an accuracy of 99.81 ± 1.33%.

In conclusion, thermal analysis can be used for the determination of sulphathiazole, sulphisomidine, sulphaguanidine, sulphacetamide sodium and sulphamethoxypyridazine with accuracies ($p = 0.05$) of 100.16 ± 1.23%, 100.90 ± 1.63%, 98.55 ± 1.73%, 100.93 ± 2.03% and 99.56 ± 2.16%, respectively. Sulphisoxazole can be determined through two peaks, an endothermic and an exothermic one with accuracies ($p = 0.05$) of 99.81 ± 1.33% and 99.27 ± 1.22%.

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ZUSAMMENFASSUNG — Einige Sulphonamide wurden durch thermische Analyse bestimmt, wobei von der linearen Abhängigkeit der Fläche der charakteristischen endothermen DTA-Peaks (Schmelzpeaks) von der Menge der Sulphonamide Gebrauch gemacht wurde. Mit der Methode können 30—100 mg Sulphathiazol, Sulphisoimidin, Sulphaguanidin, Natrium-Sulphacetamid und Sulphamethoxypyridazin mit ausreichender Genauigkeit bestimmt werden. Bei der Bestimmung von Sulphisooxazol wurde ein endothermer Peak für Mengen von 30—100 mg und ein exothermer für geringere Mengen von 6—30 mg herangezogen.

Резюме — С помощью термического анализа проведена оценка некоторых сульфонамидов. Оценка проведена на основе их характеристических эндотермических ДТА-пиков (пики плавления), площадь которых изменяется линейно с изменением количества сульфонамидов. Метод является приемлемым для определения 30—100 мг сульфатиазола, сульфизомедина, сульфагуанидина, сульфацетамида натрия и сульфаметоксипиридазина с достаточной точностью. Для определения сульфизооксазола были использованы два пика, из которых эндотермический пик — для определения количеств от 30 до 100 мг, а экзотермический — для определения количеств от 6 до 30 мг вещества.