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Quantitative Differential Thermal Analysis of Cycloserine

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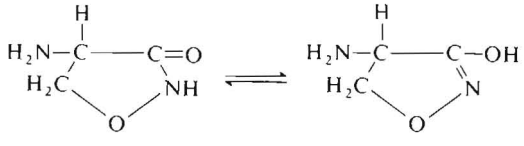
A rapid and accurate quantitative differential thermal analytical procedure for the assay of cycloserine and its tablets was developed. The reproducibility of the method was verified by spiking the cycloserine tablets with accurately weighed amounts of authentic cycloserine. The results revealed that the proposed method for the determination of cycloserine gives accuracy of 99.1% ± 3.2.



Cycloserine is of a simple chemical structure, which possesses antibiotic activity and is used as an antitubercular drug. Its structure has been determined (Kuchl 1955) and (Hidy 1955) to be D.4-amino-3-isoxazolidone.

Harned (1957) reported that the melting point of the compound is 154–156 °C and elaborated for it a qualitative differential thermal identification where a melting endotherm followed by a rapid exotherm were observed. The heating rate was 20 °C/min where the endotherm peaked at 152 °C and the exotherm at 160 °C. The same author reported on thermogravimetric analysis of the compound which showed a 1.0% weight loss at 147 °C. Weight loss occurred rapidly as the temperature approached the melting point. The measurement was performed under nitrogen sweep at a heating rate of 5 °C/min. Spectrophotometric measurements

at 219 nm have been used as a criterion of purity and as a quantitative test of cycloserine in pharmaceutical formulations. The routine chemical assay in the British Pharmacopaeia (1973), depends on its reaction with nitropentacyanoferrate in slightly acid medium giving a complex measurable at 625 nm. This method can be applied also to determine cycloserine in different biological fluids.

Experimental

Apparatus

The instrument used was the differential thermal analysis system TA 2000 manufactured by Mettler, Greifensee, Zurich, Switzerland. The instrument was equipped with GA 11 Mettler recorder.

Materials

Cycloserine authentic powder and tablets were kindly supplied by Roche, Basle, Switzerland.

Application of the proposed method

A. *For the authentic powder.* Triturate cycloserine authentic compound using a small pestle and mortar. Weigh accurately in aluminium crucibles five samples ranging between 1 and 5 mg of the triturated sample. Record the differential thermograms. Photocopy the traces of the peaks, cut, weigh on an analytical balance and plot the weights of peak areas versus the mass of cycloserine. The experimental data are indicated in Fig. 1.

B. *For the tablets.* For cycloserine tablets weigh accurately twenty tablets and compute the average weight of tablet. Pulverize the tablets as done for cycloserine authentic powder. Weigh aliquots of the powder such that the quantity of the active ingredient in the samples weighed ranges between 1 to 5 mg. Record the differential thermograms and proceed as explained in the previous paragraph. Find out the amounts of cycloserine from the calibration curve (Fig. 1).

For spiking experiments add a known weight of authentic cycloserine powder to a known weight of the powdered tablets and transfer quantitatively to the aluminium crucible. Record the differential thermograms and proceed as explained in the previous paragraphs. The results obtained are given in Table 1.

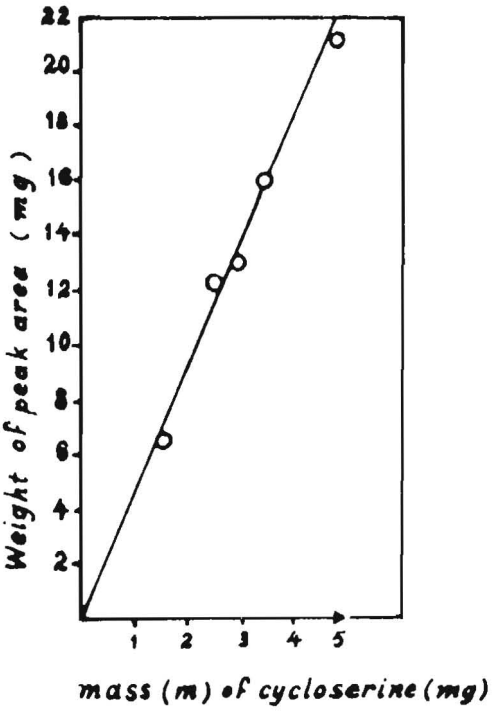


Fig. 1. Calibration curve of authentic cycloserine.

Table 1. The proposed quantitative differential thermal analysis of cycloserine.

Pharmaceutical compound	Cycloserine				
	Stated (mg)	Authentic powder added (mg)	Found (mg)	% Recovery	
Cycloserine tablets	1.5	—	1.45	96.6	Mean: 99.1%
	2.6	—	2.7	103.9	Standard Deviation: ±3.2
	2.9	—	2.8	96.5	
	3.4	—	3.3	97.0	
	4.8	—	4.9	102.0	
Cycloserine tablets	1.3	1.6	2.0	103.4	
	2.8	2.0	4.65	94.8	

Results and Discussion

In this communication a simple, rapid, and accurate method for the analysis of cycloserine powder and cycloserine tablets is reported. This proposed method is based on the electric voltage generated by a thermocouple due to difference in temperature (ΔT) between sample and a reference material for an interval of time (t) during which the phase change (fusion process) occurs as the system is linearly heated. Wendlant (1974) reported a monograph describing the differential thermogram obtained by a differential thermal analysis system according to

$$A = \frac{Gm}{k}\Delta H,$$

where A is the peak area ($\Delta T \times$ time), G is a calibration factor that depends on the particle size and packing of the sample, k is a constant related to the thermal conductivity, ΔH is the enthalpy change accompanying the fusion process, and m is the mass of the sample. ΔH may be assumed constant under the established experimental conditions. To maintain G and k constant with the exception of m, cycloserine samples were finely powdered, weighed, and carefully packed in aluminium crucibles. The reference material (empty aluminium crucible) and cycloserine sample were placed in the furnace prior to the heating process. The heating rate was maintained at 5 °C/min. Typical differential thermograms obtained are shown in Fig. 2.

Areas under the ΔT time curves were obtained by cutting and weighing xerox copies of the traces. Under the established experimental conditions, the relationship between the peak area (A) and the mass (m) of the authentic cycloserine powder was demonstrated to be linear (Fig. 1) as the mass of cycloserine sample varied

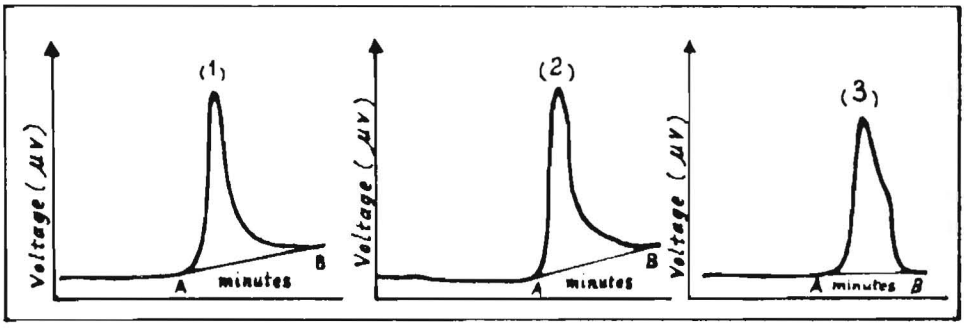


Fig. 2. Differential thermograms (1), (2), and (3) represent, respectively, authentic cycloserine powder, cycloserine tablets, and cycloserine tablets spiked with authentic cycloserine powder. AB is the base line.

between 1 and 5 mg. Cycloserine tablets were treated under the established experimental condition and the amount of the active ingredient was determined graphically from Fig. 1.

To verify the reproducibility of the method, samples of cycloserine tablets were spiked with the authentic cycloserine and the results obtained are summarized in Table 1. The data in Table 1 reveal that the proposed method for the determination of cycloserine gives accuracy of 99.1% ± 3.2 and percentage of recovery 99.1.

In conclusion, the method described in this report is simple, rapid, and accurate.

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التحليل الحرارى التفاضلى لمركب السيكلوسيرين

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يشتمل هذا البحث على تقديم طريقة سريعة ودقيقة للتحليل الحرارى التفاضلى لمركب السيكلوسيرين وفى صوره الصيدلية • ولقد أثبتت الطريقة فعاليتها فى تحليل المركب وأمكن التأكد من ذلك باضافة كميات معلومة من المركب النقى واعادة التحليل للتثبت من دقة الطريقة المقترحة ولقد تبين ذلك من النتائج حيث وصلت الدقة فى النتائج الى ١ر٩٩ ± ٢ر٣ فى المائة •