Journal of Thermal Analysis, Vol. 33 (1988) 1231–1234

USE OF DIFFERENTIAL SCANNING CALORIMETRY TO ANALYSE THE QUALITY OF CERTAIN VITAMIN DRUGS

M. Sh. Lvova, N. I. Garber and *E. I. Kozlov*

"VITAMINY" SCIENTIFIC-INDUSTRIAL UNION, MOSCOW 117246, U.S.S.R.

The use of DSC to evaluate the quality of drugs is demonstrated via some typical problems: purity determination of nicotinamide, granulation of calcium D-(+)-pantothenate, drying of menadione sodium bisulfite, stability of α-hydroxyvitamin D on storage, and purification of calcium homo-pantothenate, pyridoxal-5'-phosphate and pyridoxal-hydrochloride.

Thermal analysis by differential scanning calorimetry (DSC) has found wide use in recent years for study of the physicochemical properties of various compounds, including drugs.

In the present study, DSC was used together with other conventional analytical procedures to estimate the quality of certain drugs, such as the calcium salts of D-(+)-pantothenic (vitamin B_3) and homopantothenic acids, nicotinamide, menadione sodium bisulfite (Vikasol), α-hydroxyvitamin D, pyridoxal-5'-phosphate (the coenzyme form of vitamin B_6) and pyridoxal hydrochloride.

Experimental

The analysis was performed on a Perkin-Elmer DCS–2C instrument with a nitrogen flow rate of 20 ml min^{-1}, heating rates of 1.25–10 deg min^{-1}, and a heat flux sensitivity of 5 mcal s^{-1}. The samples (1–3 mg) were weighed to an accuracy of 0.001 mg. Indium of 99.9999% purity was used as standard.

Results

Nicotinamide. DSC was used to study the effect of recrystallization from enthanol on the quality of a preparation whose purity was shown by chemical analysis [1] to remain unchanged (>99%) upon purification. The DSC technique gave a highly accurate estimate for the content of impurities in the starting and recrystallized materials (Table 1) and demonstrated the

John Wiley & Sons, Limited, Chichester
Akadémiai Kiadó, Budapest

Table 1 Data on purity of different nicotinamide preparations

Preparation	Melting point of 100% pure substance, °C	Melting point depression, °C	Melting heat ΔH, J/mol	Molar content of impurities, %
Commercial product without additional purification	129.49	0.16	26.000	0.32 ± 0.04
Upon recrystallization	129.31	0.11	26.080	0.22 ± 0.02

value of the purification procedure employed. Details of the procedure and design formulae are to be found elsewhere [2–4].

Calcium D-(+)-pantothenate. DSC was used to study the possibility of obtaining microgranules from a vitamin substance powder from which tablet formation is difficult. Analyses were carried out on samples of the starting preparation, microgranules obtained from this, and a product known to be microgranulated (Fig. 1). Melting curves b and c are identical. They both have two broad and flat peaks at 60–70° and 171–173°, and differ drastically from the curve for the starting preparation, which has one distinct endothermic peak at the melting point of 196–197°.

Vikasol. DSC can help to distinguish the preparation containing crystal water from the anhydrous compound (Fig. 2), and thus it permits elucidation of the drying regime and study of the processes occurring during storage.

α-Hydroxyvitamin D. Changes in the melting point and DSC curve haviour (the peak becomes more gentle) allow one to follow the stability of a preparation during storage (Fig. 3). The melting point correlates with the content of the main component in the preparation.

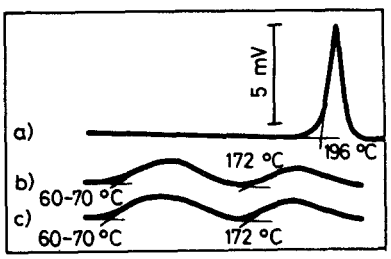

Fig. 1 DSC melting curves for different preparations of calcium D-(+)-pantothenate (a) substance, (b) microgranules obtained, (c) product known to be microgranulated.

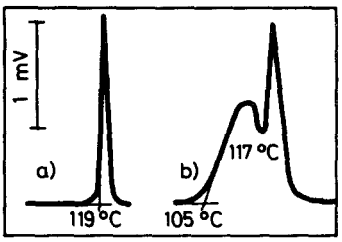

Fig. 2 DSC melting curves for Vikasol (a) anhydrous substance, (b) preparation containing crystal water.

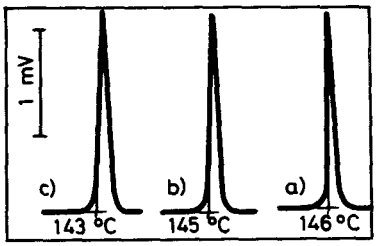

Fig. 3 DSC melting curves for different specimens of α-hydroxyvitamin D (a) newly obtained preparation, (b) and (c) specimen stored at 20° for 1 and 2 months, respectively.

Table 2 Melting points for certain preparations of various degrees of purity

Preparation	Melting point, °C		
	starting compound	upon single recrystallization	upon double recrystallization
Calcium homopantothenate	144.0 145.1	150.1 151.2	152.5 154.8
Pyridoxal-5'-phosphate	136.0 134.5	137.2 137.2	138.0 138.7
Pyridoxal hydrochloride	169.5 172.5	176.0 177.0	– –

Pyridoxal-5'-phosphate, pyridoxal hydrochloride and calcium homopantothenate. DSC, together with other analytical procedures, was used to assess the quality of samples of these preparations, which then served as primary standards in the quantitative spectro-photometric assay of the given compounds. The index of quality here is the melting point. Samples with

various degrees of purity were analysed. Additional purification by recrystallization was shown to elevate melting points markedly, i.e. to improve the quality (Table 2). DSC parameters were found to correlate with other indices of quality for these substances.

References

1 USSR State Pharmacopoesia, 10th Edition, Moscow, 1968, p. 733 (Russ.).
2 N. J. De Angelis and G. J. Papariello. J. Pharm. Sci., 57 (1968) 1868.
3 A. P. Arzamastsev and P. L. Senov, Primary Standards of Drugs (in Russian), Moscow, 1978. p. 61–83.
4 M. Sh. Lvova, A. M. Drabkina and E. I. Kozlov, Khim. Farm. Zh., (1984) (II) p. 1393–1395 (Russ.).

Zusammenfassung – Der Einsatz der DSC zur Untersuchung der Qualität pharmazeutischer Produkte wird an einigen typischen Beispielen demonstriert:
– Reinheitsbestimmung von Nicotinamid
– Granulierung von Calcium-D(+)-pantothenat
– Trocknen von Menadion-Natriumbisulfit
– Stabilität von α-Hydroxyvitamin D beim Lagern
– Reinigung von Calcium-homopantothenat, Pyridoxal-5'-phosphat und -hydrochlorid.

РЕЗЮМЕ — Использовании метода ДСК для оценки качества лекарственных препаратов показано на таких примерах, как определение чистоты никотинамида, гранулирование Д-(+)-пантотената кальция, высушивание натрий бисульфитной соли менадиона, определение устойчивости α-оксивитамина Д при хранении, очистка гомо-пантотената кальция, пиридоксаль-5-фосфата и его гидрохлорида.