*Journal of Thermal Analysis, Vol. 46 (1996) 1645-1655*

# THERMAL DECOMPOSITION OF SOME ANALGESIC AGENTS

*Y. A. Ribeiro*[a], *J. D. S. de Oliveira*[b], *M. I. G. Leles*[b], *S. A. Juiz*[b] *and M. Ionashiro*[b*]

[a]Faculdade de Ciéncias Farmacéuticas, Universidade Estadual Paulista, Araraquara, São Paulo, C. P. 502, CEP. 14801-902
[b]Instituto de Química, Universidade Estadual Paulista, Araraquara, São Paulo, C. P. 355, CEP. 14800-900, Brazil

(Received January 25, 1995; in revised form May 23, 1995)

## Abstract

Thermogravimetry, derivative thermogravimetry (TG, DTG) and differential scanning calorimetry (DSC), were used to study the thermal behaviour of mefenamic acid, ibuprofen, acetaminophen, sodium diclofenac, phenylbutazone, dipyrone and salicylamide. The results led to thermal stability data and also to the interpretation concerning the thermal decomposition.

**Keywords:** acetaminophen, dipyrone, ibuprofen, mefenamic acid, phenylbutazone, salicylamide, sodium diclofenac, thermal decomposition

## Introduction

Several studies have been carried out on the applicability of thermal analysis to investigate analgesic agents. Identification of nonprescription internal analgesics has been investigated by means of TG and DTA [1]. Dipyrone and its mixture with scopolamine-N-butylbromide [2], phenylbutazone [3], acetylsalicylic acid [4], acetylsalicylic acid and *p*-chloroaniline [5] aspirin [6, 7] and ibuprofen [8], have also been investigated. The use of thermal analysis to study solid pharmaceutical tablet mixtures has already been described [9–12].

The present work investigates some analgesics already studied, as acetaminophen, phenylbutazone, dipyrone, salicylamide, and others not yet studied as mefenamic acid and sodium diclofenac by means of TG, DTG and DSC methods.

* Author to whom all correspondence should be addressed.

*0368–4466/96/ $ 5.00*

*John Wiley & Sons, Limited*
*Chichester*

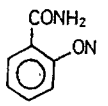
## Experimental

DIPYRONE, monohydrated sodium salt of [(2,3-dihydro-1,5-dimethyl-3-oxo-2-phenyl-1H-pyrazol-4-yl) methylamino] methanesulfonic acid;

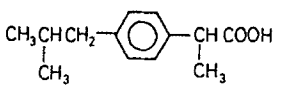
PHENYLBUTAZONE, 4-butyl-1,2-diphenyl-3,5-pyrazolidinedione and SODIUM DICLOPHENAC, sodium salt of 2-[(2,6-dichlorophenyl)amino] benzeneacetic acid were obtained from Biogalenica Quimica e Farmaceutica Ltda.

ACETAMINOPHEN, N-acetyl-p-aminophenol, SALICYLAMIDE, 2-hydroxybenzamide, IBUPROFEN, α-methyl-4-[2-methylpropyl]-benzeneacetic acid and MEFENAMIC ACID, 2-[(2-3-dimethylphenyl amino] benzoic acid were obtained from Merrel Lepetit Farmaceutica Ltda, Roche Quimicos e Farmaceuticos S.A., Rhodia S.A. and Aché Laboratorios Farmaceuticos S.A., respectively.

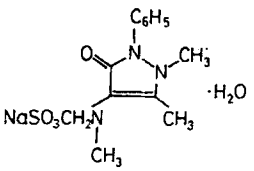
TG, DTG and DSC curves were obtained by using a Mettler TA-4000 thermoanalyser system with an air flux of ≈150 ml $min^{-1}$, heating rate of 10°C $min^{-1}$ and with a sample weighing about 8 mg. An alumina crucible was used for the TG and DTG, and an aluminium crucible with a perforated cover for the DSC studies.



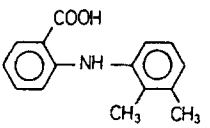

Salicylamide



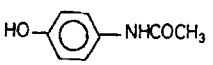

Ibuprofen



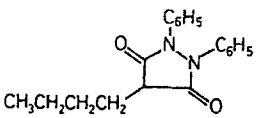

Dipyrone



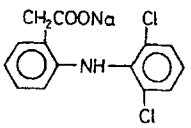

Mefenamic acid




Acetaminophen




Phenylbutazone




Sodium diclofenac

## Results and discussion

### *Salicylamide, ibuprofen and phenylbutazone*

The analgesics studied in this work, salicylamide, ibuprofen and phenylbutazone, show similar TG and DTG curves with mass losses in a single step, except for phenylbutazone (Figs 1–3). Similar thermal stabilities were observed for salicylamide and ibuprofen, the total mass losses occurring between 120 and 280°C. For the thermally more stable phenylbutazone, 98.9% of the mass loss occurs between 200 and 320°C, with formation of a carbonaceous residue and the slow pyrolysis of this residue occurs between 320 and 650°C.

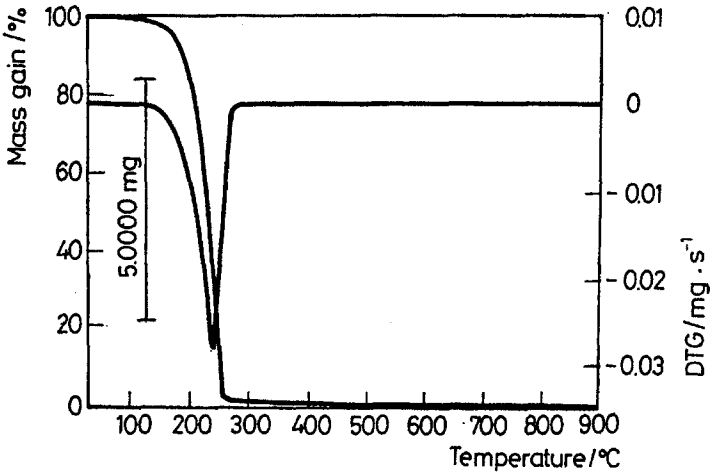



**Fig. 1** TG and DTG curves of salicylamide

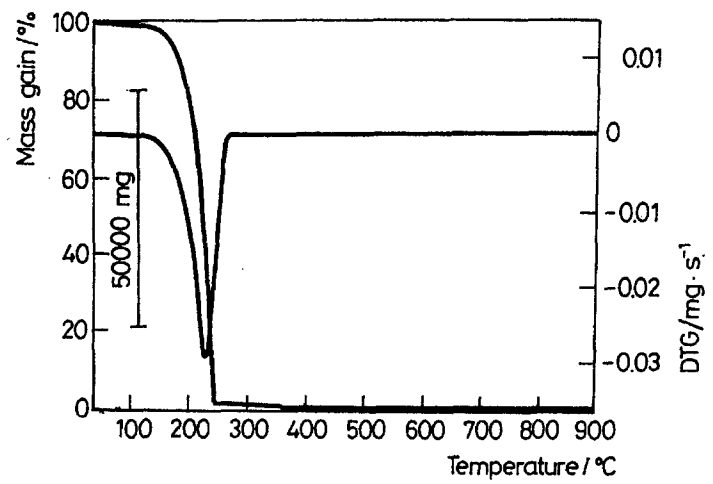



**Fig. 2** TG and DTG curves of ibuprofen

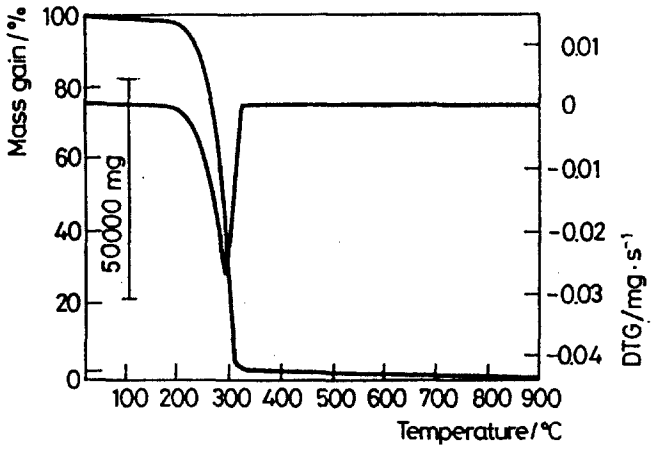



**Fig. 3** TG and DTG curves of phenylbutazone

The DSC curves (Figs 4–6) show endothermic and exothermic peaks. For salicylamide the sharp endothermic peak at 144°C followed by a broad endothermic peak at 244°C are due to fusion and vaporization of the compound. The small deviation of the fusion temperature from the value reported in [1] is probably due to the different manufactures of the analgesic. For ibuprofen (Rac-IB) the sharp endothermic peak at 76°C is due to fusion and it is in agreement with

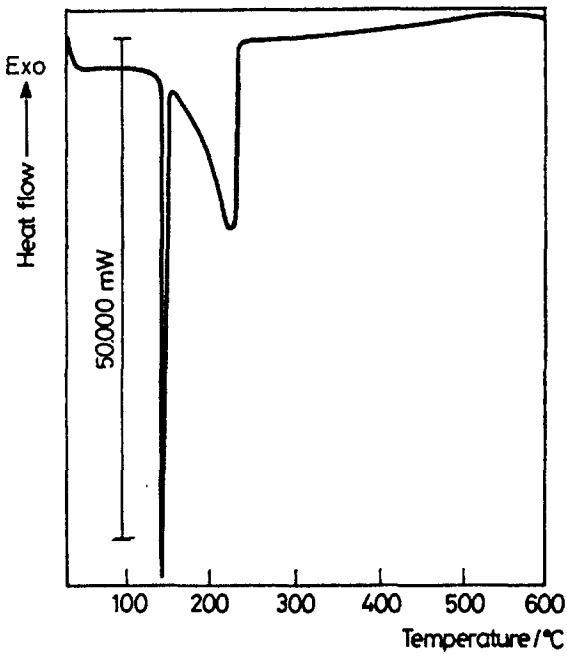



**Fig. 4** DSC curve of salicylamide

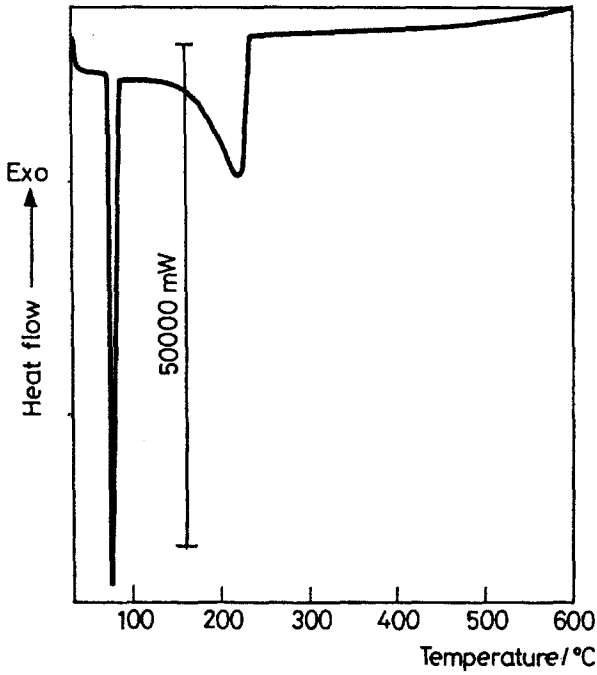



**Fig. 5** DSC curve of ibuprofen

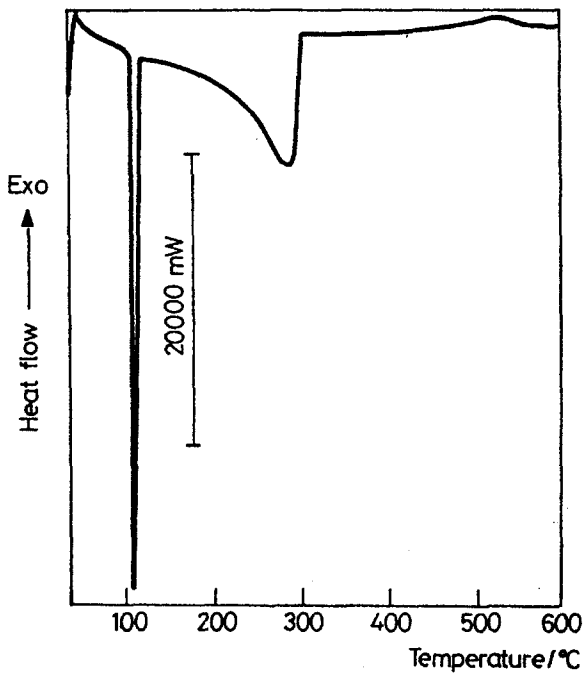



**Fig. 6** DSC curve of phenylbutazone

[8] and the broad endothermic peak at 220°C is ascribed to vaporization. For phenylbutazone the sharp endothermic peak at 107°C is due to fusion and it is in agreement with [3]. The broad endothermic peak at 280°C is due to vaporization with a slight decomposition and the small exothermic peak at 510°C is ascribed to the thermal decomposition of the compound and pyrolysis of the carbonaceous residue.

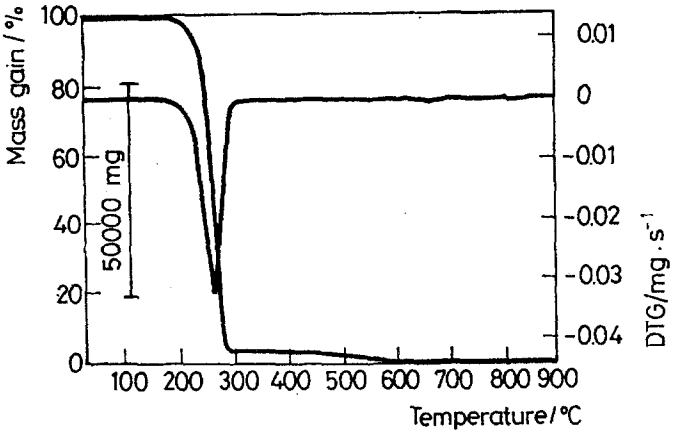



**Fig. 7** TG and DTG curves of mefenamic acid

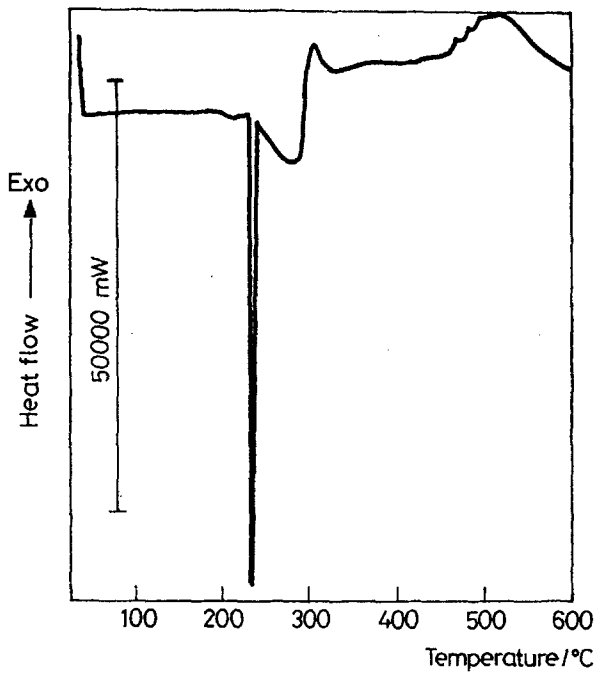



**Fig. 8** DSC curve of mefenamic acid

## *Mefenamic acid*

The TG and DTG curves of mefenamic acid (Fig. 7) show that the compound is thermally stable up to 190°C; between 190 and 650°C, the TG curve shows mass losses in two steps, while the DTG curve only shows one peak due to the small mass loss that occurs very slowly in the second step. The first step between 190 and 300°C, a fast process with a mass loss of 97.7%, is ascribed to the thermal decomposition of the compound with formation of a carbonaceous residue. The second step between 300 and 650°C where the mass-loss process is completed, is due to pyrolysis of the carbonaceous residue.

The DSC curve (Fig. 8) shows endothermic and exothermic peaks. The first sharp endothermic peak at 234°C is due to fusion of the compound. The endothermic peak at 280°C followed by an exothermic peak at 300°C are ascribed to vaporization and decomposition and the exothermic peak at 500°C is ascribed to pyrolysis of the carbonaceous residue.

## *Acetaminophen*

The TG and DTG curves of acetaminophen are shown in Fig. 9. While the TG curve shows mass losses in two consecutive steps, the DTG curve hardly shows evidence of the second mass loss because it occurs very slowly. The first step, a fast process with a mass loss of 95.7%, is ascribed to thermal decomposition with formation of a small quantity of carbonaceous residue. The second mass loss between 325 and 630°C is due to pyrolysis of the carbonaceous residue.

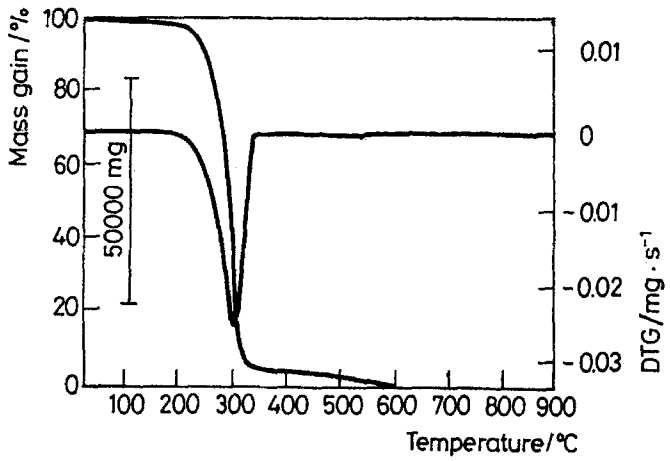



**Fig. 9** TG and DTG curves of acetaminophen

In the DSC curve (Fig. 10) the first sharp endothermic peak at 172°C, followed by a broad endothermic peak at 300°C are ascribed to fusion and to vaporization with slight decomposition, respectively. the exothermic peak be-

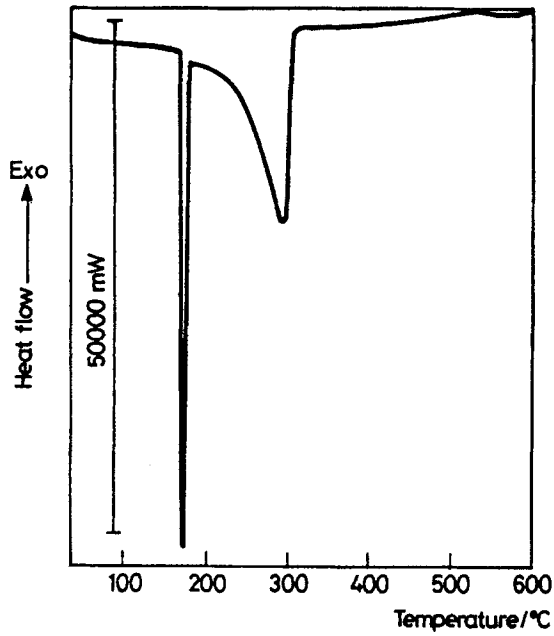



**Fig. 10** DSC curve of acetaminophen

tween 440 and 560°C is due to pyrolysis of the carbonaceous residue. The slight deviation of the fusion and vaporization temperature from those reported in [1] fusion at 180°C and broad vaporization at 240°C) is probably due to the different manufacturers of the samples.

## *Dipyrone*

The TG and DTG curves of dipyrone are shown in Fig. 11. The TG curve indicates mass losses in three steps, between 60 and 740°C. The first mass loss up to 140°C is ascribed to the loss of $H_2O$ (TG=5.0%; calcd=5.13%). The second mass loss between 220 and 580 °C that occurs in a fast process followed by a slow process is due to the thermal decomposition of the anhydrous compound with loss of the organic part (TG=65.0%; calcd=65.55%), with formation of $0.5Na_2S_2O_6$. the last step between 580 and 740°C is due to the thermal decomposition of this compound, with loss of $0.5SO_2$ (TG=9.2%; calcd=9.12%), with formation of sodium sulphate. A qualitative test with the final residue confirmed the presence of sodium sulphate.

In the DSC curve (Fig. 12) the first endothermic peak at 105°C is due to dehydration of the compound. The sharp endothermic peak at 218°C is due to fusion, and it is followed by a sharp exothermic peak at 220°C and an exotherm between 280 and 420°C that are ascribed to the thermal decomposition corresponding to the second step of the TG curve.

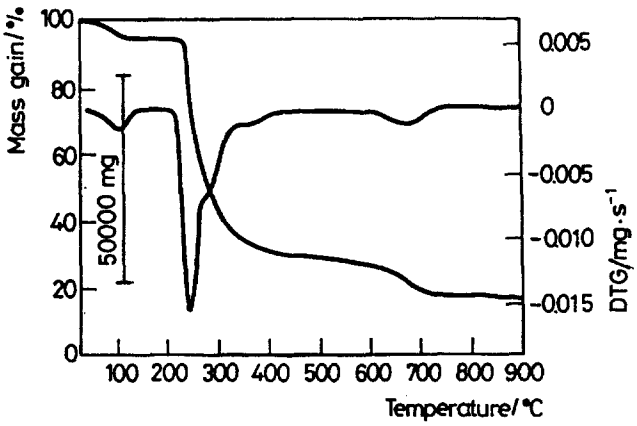



**Fig. 11** TG and DSC curves of dipyrone

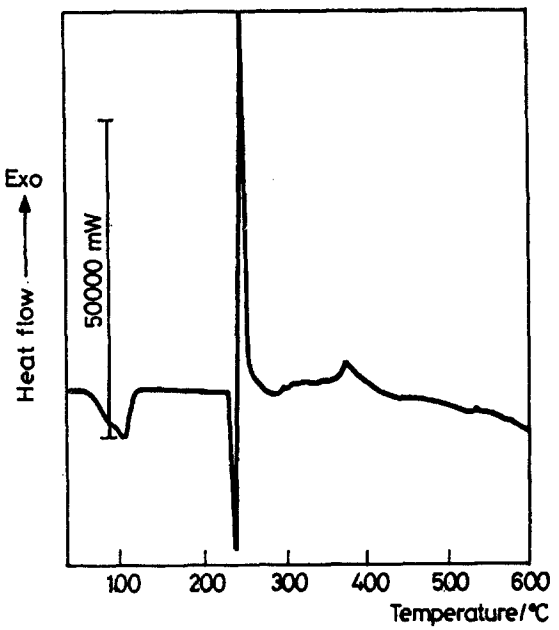



**Fig. 12** DSC curve of dipyrone

## *Sodium diclofenac*

The TG and DTG curves of sodium diclofenac (Fig. 13) reveal mass losses in five steps up to 900°C. The first step up to 70°C is due to dehydration with loss of $H_2O$ (TG=6.07%, calcd=5.36%). The second mass loss (260–400°C) is ascribed to elimination of HCl, NH and CH, 0.5CO with formation of $0.5Na_2CO_3$ and a carbonaceous product (TG=23.5%; calcd=23.65%). In the

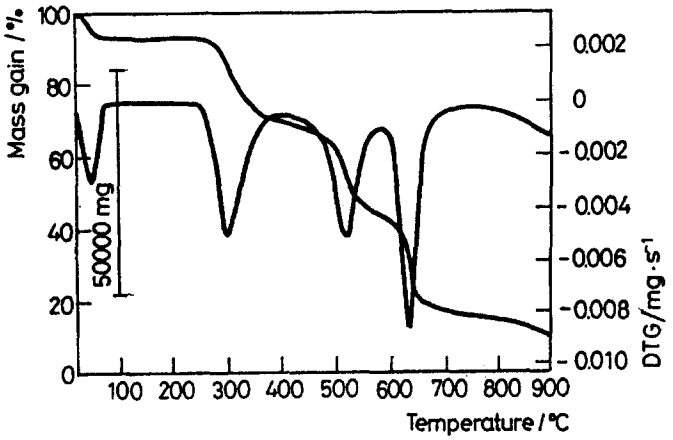



**Fig. 13** TG and DTG curves of sodium diclofenac

third step (400–545°C), the mass loss corresponds to the thermal decomposition of ⟨⬡⟩ (TG=22.49%); calcd=22.64%), and in the fourth step the mass loss correspond to the thermal decomposition of ⟨⬡⟩-H and elimination of 0.5 ($CO_2$, $H_2O$) from the sodium carbonate (TG=30.76%; calcd=30.96%) with formation of sodium chloride and a small quantity of carbonaceous residue. The partial mass loss up to 900°C in the last step is ascribed to pyrolysis of the carbonaceous residue and partial loss of sodium chloride.

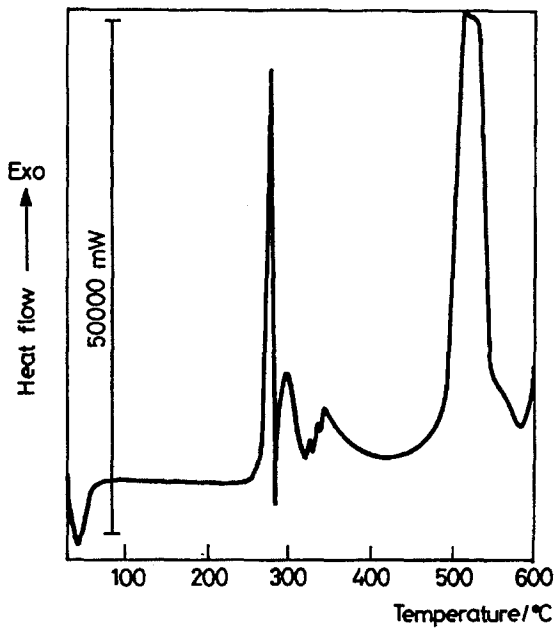



**Fig. 14** DSC curve of sodium diclofenac

A qualitative test confirmed the presence of chloride ions in the eliminated product when the sample was heated up to 400°C, and confirmed the formation of sodium chloride when the sample was heated up to 800°C. During this experiment, fusion followed by thermal decomposition with formation of carbonaceous product was also observed.

In the DSC curve (Fig. 14), the first endothermic peak at 45°C is due to dehydration and it is in agreement with the first mass loss in the TG and DTG curve. The sharp exothermic peak at 280°C is probably due to a polymorphic transition and it is followed by an endothermic peak at 285°C ascribed to fusion and exothermic peaks at 300 and 350°C ascribed to the thermal decomposition corresponding to the second mass loss in the TG and DTG curves. The exothermic peak at 510°C is ascribed to the thermal decomposition corresponding to the third mass loss in the TG and DTG curves.

## Concluding remarks

The TG, DTG and DSC curves permitted studies on the thermal stability and the thermal decomposition of some analgesic agents.

* * *

The authors thank the FAPESP (Proc. 90/2933-4) and Biogalenica Quimica e Farmaceutica Ltda, Merrel Lepetit Farmaceutica Ltda, Roche Quimicos e Farmaceuticos S.A., Rhodia S.A. and Aché Laboratorios Farmaceuticos S.A., for supplying the analgesic agents.

## References

1 W. W. Wendlandt and L. W. Collins, Anal. Chim. Acta, 71 (1974) 411.
2 G. Margomenou-Leonipoulou, K. Theodoratos and G. G. Macris, Arch. Pharm. (Athens), 30 (1974) 100.
3 A. Chauvet and J. Masse, Trav. Soc. Pharm. Montpellier, 38 (1978) 31.
4 E. Domagalina and T. Slawik, Acta Pol. Pharm., 33 (1976) 623.
5 C. Martinez Recari, J. M. Sanches Monge, J. A. Perez de Ciriza and F. Marcótegni, Rev. Asoc. Esp. Farm. Hosp., 6 (1982) 57.
6 D. J. Ager, K. S. Alexander, A. S. Bhatti, J. S. Blackburn, D. Dollimore, T. S. Koogan, K. A. Mooseman, G. M. Muhvic, B. Sims and V. J. Webb, J. Pharm. Sci, 75 (1986) 77.
7 G. Gupchup, K. Alexander and D. Dollimore, Thermochim. Acta, 196 (1992) 279.
8 S. K. Dwivedi, S. Sattari, F. Jamali and A. G. Mitchell, Int. J. Pharmaceutics, 87 (1992) 95.
9 A. Radecki and M. Wesolowski, J. Thermal Anal., 17 (1979) 73.
10 M. Wesolowski, Mikrochim. Acta, 1 (1980) 199.
11 M. Wesolowski, Acta Pharm. Jugosl., 32 (1982) 303.
12 D. Giron, J. Pharm. Biomed. Anal., 4 (1986) 755.