Thermal analysis of nimesulide

Análise térmica da nimesulida

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SUMMARY – The thermal stability of nimesulide was studied on the raw material and on tablets. The raw material was subjected to differential thermogravimetry and calorimetry, while the tablets were subjected to an accelerated thermal degradation. Nimesulide proved to be thermally stable. Only at 208,2°C the degradation process starts. Its melting point was determined at 149,4°C and the tablets, subjected to an accelerated thermal degradation, it didn't show any modification in your content.
KEY WORDS – Quality Control of nimesulide; thermal analysis of nimesulde; stability of nimesulide.

RESUMO *– Foi estudada a estabilidade térmica da nimesulida em estado puro e em comprimidos. Em estado puro, a substância foi submetida à termogravimetria diferencial e à calorimetria, enquanto que na forma de comprimidos, à degradação térmica acelerada, provando ter a nimesulida, estabilidade térmica até 208,2 °C quando então se inicia o processo de degradação. Seu ponto de fusão ocorre a 149,4 °C. Os comprimidos, naquele processo, não sofreram qualquer modificação.*
PALAVRAS-CHAVE *– Controle de Qualidade da nimesulida; análise térmica; estabilidade.*

INTRODUCTION

Nimesulide is a 4-nitro-2-phenoximethanesulfonanilide and finds therapeutic utilization as an anti-inflammatory, analgesic and antipiretic[1]. Nimesulide differs from most conventional anti-inflammatory drugs because it has got a noncarboxylic functional group, having as the main metabolite 4'-hydroxinimesulide[1]. The drug belongs to the sulfonanilides chemical group and is characterized by selective inhibition of the cyclo-oxigenase 2[2]. Nimesulide has been very much used at the present and the international bibliography is concerned fundamentally with the therapeutic study of the drug, as well as with its pharmacokinetic and pharmacological effects[1,2,4,5,6,7,8,9]. Fallavena, 1998[3], evaluates the photostability of this drug and observed that nimesulide suffer photodegradation under ultraviolet light, and the phenomenon only happened in solid forms. In this paper the photodegradation of nimesulide was studied using the accelerated test which involves irradiation of nimesulide in solid forms with UV light of λ=254 nm. It was accomplished analyses of ESR and the results accused the presence of a free radical phenoxy. Having in view the need of total knowledge about the stabilitiy of the nimesulide for quality control purposes, it was used the raw material and tablets in the present work to study of the thermal stability of this drug. The analytical methods used in the evaluation of the thermal stability of the drug as raw material were the thermogravimetric one (TGA) and the differential calorimetry one (DSC), while the U.V. method was used for the tablets[10,11].

EXPERIMENTS

Materials

Nimesulide raw material (Sintofarma S.A.) 99,8%. Nimesulide tablets (Sintalgin) 100 mg/tablet. Methanol p.a. (Merck).

Apparatus

The equipment used were a Fanem oven provide with a thermostat; a Perkin-Elmer Thermoscale TGS-2 Thermogravimetric Analyser (1); A Perkin-Elmer Differential Calorimeter DSC-4 with aluminium supports with a lid (2), and UV spectrophotometer Shimadzu UV 160A model (3).

Methods

Sample of 5.0834 mg was placed on (1) under the flow of 100 mL/min nitrogen at a rate of 10.00 deg/min. Sample of 4.10 mg of the drug were charged into the aluminum micropans with lids and placed in (2). Accelerated degradation tests: 10 tablets of nimesulide were placed in the oven adjusted to 95°C and analyzed after a seven day period. Thereafter the samples were pulverized and weighed analytically. Samples of 0.4296 of the tablet powder, containing a quantity equivalent to 100 mg of the drug were transferred to volumetric 100 mL flasks, dilute in about 60 mL methanol and stirred for 40 minutes in a mechanical stirrer. After this period, the volumes were completed with methanol and samples stirred and filtered. The first 10 mL being disposed of. Amounts of 1.0 mL were taken into 50 mL volumetric flasks and the volumes were adjusted with methanol, in such a way as to obtain samples around 20 mg/mL. UV readings were carried out with methanol blank at 295 nm. The concentration calculations of nimesulide were effected by the straight line equation originating from a calibration curve.

The same procedure was carried out for the control samples, not subjecting to heating.

RESULTS AND DISCUSSION

The results of the thermal stability

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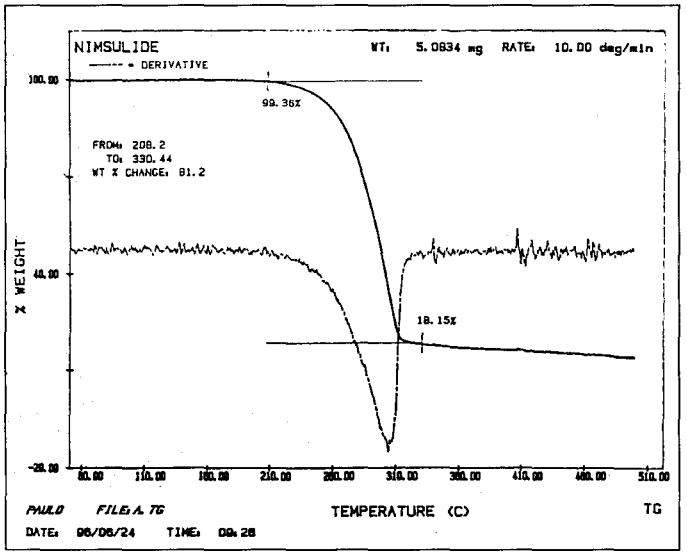

Fig. 1: Thermogravimetric analysis of nimesulide. The degradation process starts at 208,2 °C.

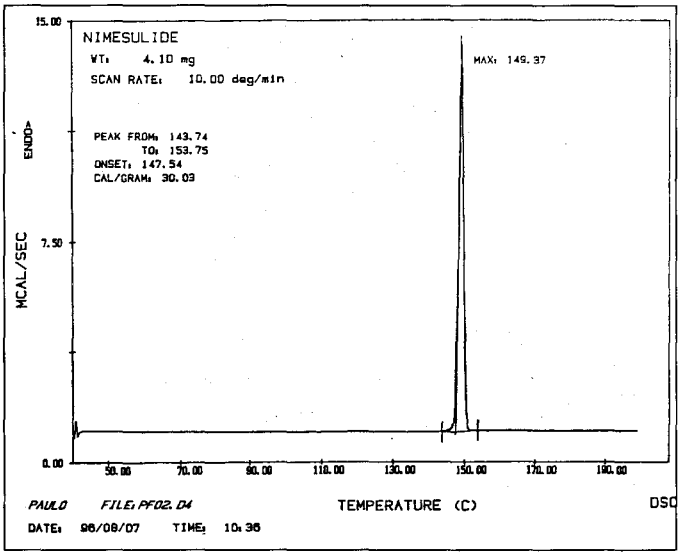

Fig. 2: Analysis of nimesulide by differential Calorimeter. The melting point is observed in 149,4 °C.

TABLE I
Results obtained in the accelerate degradation test of nimesulide tablets

Sample	Control* (absorbance)	Concentration (µg/mL)	Heated samples (absorbance)	Concentration (µg/mL)
1	0.425	19.730	0,412	19.120
2	0.428	19.840	0.416	19.300
3	0.425	19.730	0.427	19.820
4	0.421	19.540	0.427	19.820
5	0.414	19.230	0.414	19.190
6	0.424	19.680	0.431	19.990
7	0.425	19.730	0.417	19.370
8	0.428	19.730	0.412	19.120
9	0.427	19.890	0.432	20.030
10	0.424	19.840	0.412	19.110
Average	0.424	19.694	0.420	19.490
sd	0.004	0.190	0.008	0.382

TABLE II
Results of Student "t" test for samples subjected to heating

Statistic	Control	Sample heated
Average	19.694	19.490
Sd	0.190	0.382
Calculated "t"	1.530	1.530

Critical "t" (0,05) 2,100

tests can be observed in Figures 1 and 2. Figure 1 shows the spectra of the thermal analisys carried out on nimesulide raw material and informs that the drug is stable in temperatures of up to 208°C, and from that point on the decomposition process starts, which does not produce any stable intermediates. In Figure 2 it is possible to observe the melting point of the drug, which is at 149,37 °C. Table I presents the experimental data relative to the accelerated degradation test of the tablets. The average presented in the table have been subjected to Student test for comparison of the averages.

CONCLUSION

The tests accomplished on nimesulide indicate a great thermal stability, wherein the thermal decomposition process only occur as from 208°C, which decomposition does not give rise to stable products. The tablets subjected to 7 days of heating under 95°C temperature did not show variations in concentration of nimesulide, indicating thus that the drug is heat stable. These results added to the found by Fallavena (1998) supply a good idea of the stability of the drug and they can serve as parameter for new studies.

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