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THERMAL DECOMPOSITION OF 5-NITRO-2-FURALDEHYDE SEMICARBAZONE

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Nitrofurazone, 5-nitro-2-furaldehydesemicarbazone, pharmaceutical compound, has been synthesized and its thermal behaviour studied by DTA, DSC and TG. The resulting thermoanalytical curves, showing that the maximum change in mass occurred at 516.5 K, with a 67% weight loss, are in good correlation with the enthalpy of the decomposition reaction, 326.93 kJ mol^{-1}. On the basis of the results, it is possible to establish the mechanism of the thermal decomposition and to acquire information on the stability of the analyzed organic compound, 5-nitro-2-furaldehydesemicarbazone.

Nitrofurans are fairly broad-spectrum antimicrobial agents effective against both Gram-positive and Gram-negative bacteria, aerobic and anaerobic [1–10]. Of the nitrofurans synthesized earlier [6–8], many have clinical applications. Of these, the most widely used as a topical agent is nitrofurazone, 5-nitro-2-furaldehyde-semicarbazone [2, 5, 6].

Studies of the thermal behaviour of pharmaceutical compounds and the change in their application properties with temperature started with the thermal analyses of antibiotics [11], sulphonamides [12, 13], arylazohydroxynaphthoic acids [14] and pyrazolinoimides [15], but the use of the thermal analysis of nitrofuran derivatives was very limited. Balepin et al. [16] investigated the thermochemical properties of some 5-nitro derivatives by means of a semimicrocalorimetric method and found that the nitro group had a destabilizing effect on the furan ring.

The aim of this paper was to obtain information concerning the thermal behaviour, the decomposition pathway and the thermal stability of the practically important 5-nitro-2-furaldehydesemicarbazone, using DTA, DSC and TG.

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Experimental

The IR spectrum was recorded with a Pye Unicam SP 1100 spectrophotometer by the KBr disc technique. The UV spectrum was obtained on a Pye Unicam SP 800 spectrophotometer. The ^1H NMR spectrum was taken in $CdCl_3$ on a Varian 60A instrument, using tetramethylsilane (TMS) as internal standard. The melting point of the synthesized organic compound was determined on a Hereaus Fus–O–Mat, and elemental analysis was done using a Carlo Erba CHNO analyser, model 1102.

Synthesis. A solution of 2.4 g (0.01 *mol*) of 5-nitro-2-furaldehyde diacetate in 10 ml of ethanol, 10 ml of water and 1 ml of H_2SO_4 was mixed with a solution of 1.1 g (0.01 *mol*) of semicarbazide hydrochloride in 10 ml of water and 10 ml of ethanol. The resulting mixture was refluxed at 358 K for a reaction period of 1.8×10^3 s. The yellow solid precipitate of crude 5-nitro-2-furaldehyde semicarbazone, after washing and drying (1.8 g, 90% yield), with melting point at 512 K, was recrystallized from a mixture of ethanol and dimethylformamide (1 : 1) to give pure 5-nitro-2-furaldehydesemicarbazone with melting point at 516.5 K and it was subsequently analysed for CHNO, and its UV, IR and ^1H NMR spectra were recorded.

Thermal analysis

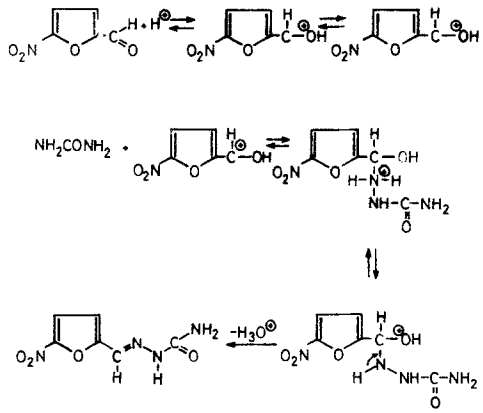
The thermal analysis of the synthesized 5-nitro-2-furaldehydesemicarbazone was performed on a DuPont 951 thermogravimetric Analyzer, a DuPont 910 differential scanning calorimeter and a Netzch 407 derivatograph in an atmosphere of air.

Thermogravimetric and differential thermal analyses were carried out under the following conditions: samples of 5-nitro-2-furaldehydesemicarbazone in weights of 8.67 and 150 mg were heated in the temperature range from 293 to 1273 K, at a heating rate of 10 deg min^{-1}. The sensitivity of the balance was 1 μm and the sensitivity of the DTA galvanometer was 1/1. The reference standard substance was in all cases Al_2O_3. DSC analysis was carried out with 2.2 mg of examined compound at 293–625 K, at a heating rate of 10 deg min^{-1}. The sensitivity of the DSC calorimeter was 10 μJ s^{-1}.

Results and discussion

The synthesis of 5-nitro-2-furaldehydesemicarbazone is a typical acid-catalyzed carbonyl-amine condensation reaction occurring in two steps. In the initial step, in

the presence of an electrophilic catalyst, an unstable addition product was formed, which in the second step stabilized through proton rearrangement, and 1,2-cleavage resulted in a Schiff base and subsequently the final reaction product *(Scheme 1)*.



Mechanism of 5-nitro-2-furaldehydesemicarbazone synthesis from 5-nitro-2-furaldehyde and semicarbazide

The melting point of the synthesized 5-nitro-2-furaldehydesemicarbazone was found to be 516.5 K. Elemental analysis gave the empirical formula of $C_6H_6N_4O_4$: Anal. Calcd. for $C_6H_6N_4O_4$: C, 36.37; H, 3.05; N, 28.28 and O, 32.30; Found: C, 36.30; H, 3.06; N, 28.30 and O, 32.34.

Infrared spectrum: 3480 (N—H); 3280 (N—H); 3160 (C=C); 2920 (C=C); 1740 (C=C); 1580 (C=N); 1520 (NO_2); 1350 (NO_2); 1260, 1205, 1030 and 975 (C—H).

Ultraviolet spectrum, in tetrahydrofuran: 265 and 380 nm.

^{1}H NMR spectrum, ppm: 2.50 (TMS); 3.35 (H_2O); 6.50 (s, 2H, azomethine NH); 7.20 (d, 1H, furan CH); 7.70 (d, 1H, furan CH); 7.80 (d, 1H furan CH); 10.75 (s, 1H, azomethine NH).

The changes in the DTA, DSC and TG curves of the synthesized 5-nitro-2-furaldehydesemicarbazone during thermal analyses are presented in Figs 1, 2 and 3.

Analysis of the DTA curve (Fig. 1) indicated the occurrence of two exothermic and two endothermic processes during heating of the examined sample of 5-nitro-2-furaldehydesemicarbazone. The first clear and sharp peak in the curve was that of the exothermic effect reaching its maximum at 515 K. This exothermic effect during heating of the sample was confirmed by the DSC analysis (Fig. 2), with the

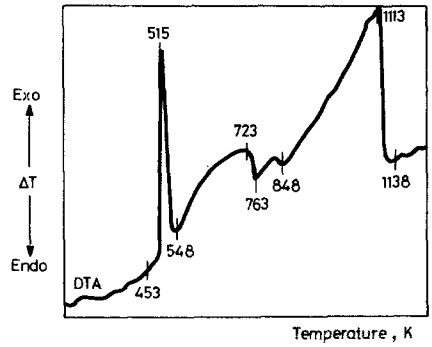


Fig. 1 DTA curve of 5-nitro-2-furaldehydesemicarbazone

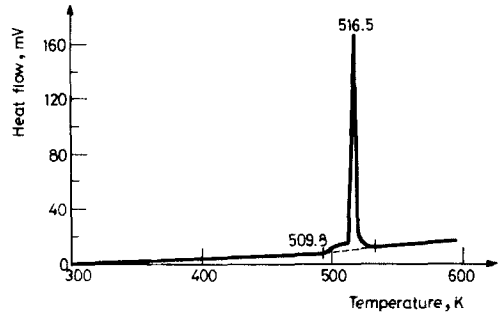


Fig. 2 DSC curve of 5-nitro-2-furaldehydesemicarbazone

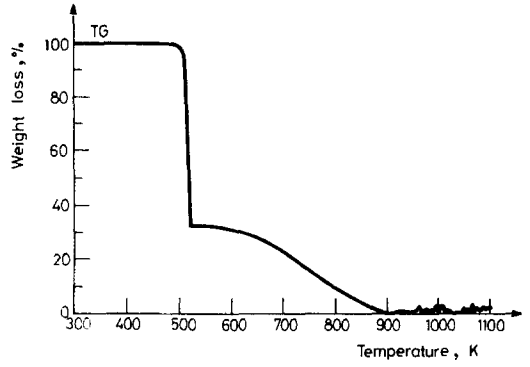


Fig. 3 TG curve of 5-nitro-2-furaldehydesemicarbazone

maximum found at 516.5 K. The exothermic behaviour of the synthesized compound during heating in the temperature range from 515 to 516.5 K related to the mass change maximum in the TG analysis curve (Fig. 3) in the temperature range from 510 to 517 K. Analysis of the TG curve (Fig. 3) showed that immediately after melting of the sample tested (m.p. 516.5 K) a sudden loss of

about 67% occurred due to the rapid thermal decomposition of the compound. After this process, in the temperature range from 763 to 1138 K, two additional weakly expressed endothermic effects occurred, with maxima at 763 and 848 K, respectively, and one expressed exothermic process, with maximum at 1113 K. These changes accompanied further destruction of the molecule of the examined compound, i.e. further mass loss and the formation of a new structural phase.

On the basis of the results of DTA, DSC and TG analyses, it can be concluded that 5-nitro-2-furaldehydesemicarbazone underwent cleavage of the side C_2—C and C_5—NO_2 bonds, in addition to separation of the azomethine sequence linked to atom C_2, and the NO_2 group linked to atom C_5 of the furan ring, at 516.5 K.

The energy required for decomposition of 5-nitro-2-furaldehydesemicarbazone was 326.93 kJ mol^{-1}, which value was determined from the result of DSC analysis. The temperature at which the exothermic process of decomposition of the compound tested occurred, 516.5 K, is a measure of the thermal stability of 5-nitro-2-furaldehydesemicarbazone, and it may serve to establish the technological characteristics and criteria in the production of this compound as a pharmaceutical preparation or drug, i.e. in drying and tabletting.

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Zusammenfassung — Das Arzneimittel Nitrofurazon (5-Nitro-2-furaldehyd-Semicarbazon) wurde synthetisiert und dessen thermisches Verhalten mittels DTA, DSC und TG untersucht. Die erhaltenen thermoanalytischen Kurven, die einen Gewichtsverlust von 67 Gew.-% mit maximaler Geschwindigkeit der Gewichtsabnahme bei 516,5 K zeigen, sind in guter Übereinstimmung mit der Enthalpie der Zersetzungsreaktion von 326,93 $kJ \cdot mol^{-1}$. Aus den Versuchsergebnissen können der Mechanismus der thermischen Zersetzung abgeleitet und Informationen über die Stabilität von 5-Nitro-2-furaldehyd-Semicarbazon erhalten werden.

Резюме — Методом ДТА, ДСК и ТГ изучено термическое поведение фармацевтического препарата нитрофуразона — семикарбазона 5-нитрофурфурола. Термоаналитические кривые, показывающие максимальную потерю веса (67%) при температуре 516,5 К, хорошо коррелируются с энтальпией реакции разложения, равной 326,93 $кдж \cdot мол^{-1}$. На основании полученных результатов представилось возможным установить механизм термического разложения и получить информацию об устойчивости исследуемого препарата.