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DECOMPOSITION KINETICS OF IBUPROXAM, 2-(4-ISOBUTYLPHENYL)PROPIOHYDROXAMIC ACID

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ABSTRACT

The kinetics of the thermal decomposition of ibuproxam have been studied by isothermal thermogravimetry between 160 and 175 °C. The first part of the reaction, which corresponds to sublimation of two products, obeys the diffusion-controlled mechanism, with an activation energy of 43 kJ mol^{-1}.

INTRODUCTION

Ibuproxam is a valuable substance, having analgesic, antipyretic and anti-inflammatory properties [1]. One of the problems associated with pharmaceutical technology is that of determining the stability of active substances. This usually involves a time-consuming procedure. A stability study of ibuproxam has been carried out at temperatures of between 40 and 105 °C, for intervals of up to 8 months [2]. It was found that ibuproxam decomposes to two main products. The first of these is a white sublimate containing ibuprofen [2-(4-isobutylpropyl)propionic acid] (**II**) and 1-(4-isobutylphenyl)ethylamine (**III**). The second is an oily mass, composed of 4-isobutylacetophenone (**IV**) and 4-isobutylacetophenone oxime (**V**).

When designing new pharmaceutical formulations it is useful to have available in advance data on the stability of the active substance. In the present work we have studied the isothermal decomposition kinetics of ibuproxam.

EXPERIMENTAL

The isothermal weight changes were determined using a Mettler 2000C thermoanalyser connected to a microcomputer for data storage. Experimental conditions were as follows: platinum crucibles; sample weights, 10.0 mg;

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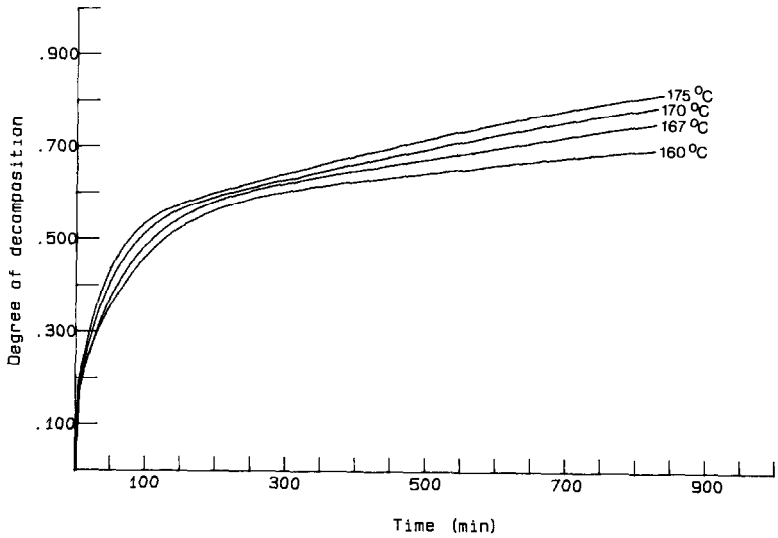

Fig. 1. Isothermal decomposition of ibuproxam.

heating rate to isothermal temperature, 15 °C min^{-1}; atmosphere, dry air with a flow rate of 35 ml min^{-1}.

RESULTS

The kinetics of thermal decomposition of ibuproxam were studied in terms of isothermal weight changes between 160 and 175 °C. The α–t curves

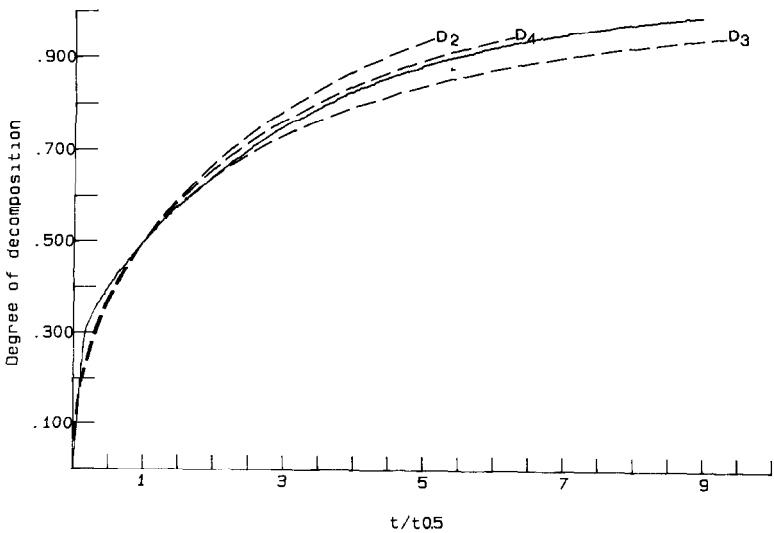

Fig. 2. $t/t_{0.5}$ test for the decomposition of ibuproxam to $\alpha = 0.60$ at 160 °C.

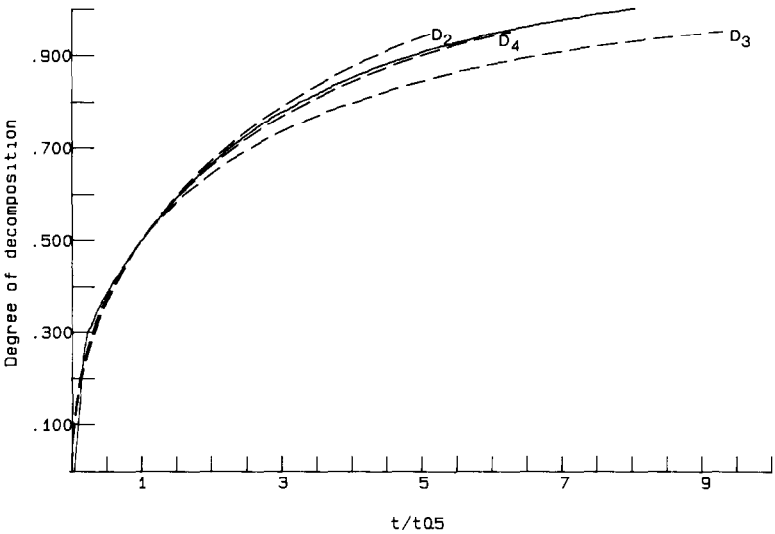

Fig. 3. $t/t_{0.5}$ test for the decomposition of ibuproxam to $\alpha = 0.60$ at 167 °C.

are shown in Fig. 1. The first part of the isothermal TG curve (up to $\alpha = 0.60$) can be ascribed to decomposition of ibuproxam with simultaneous sublimation of **II** and **III** [2]. In the second stage the remaining oily mass decomposes to **IV** and **V**, at a constant rate which is much lower than for the first stage. The mechanism of the first reaction was determined by means of

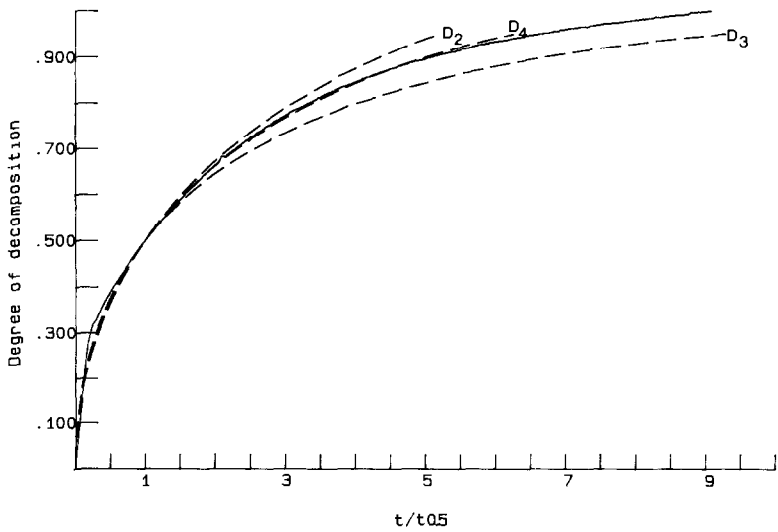

Fig. 4. $t/t_{0.5}$ test for the decomposition of ibuproxam to $\alpha = 0.60$ at 170 °C.

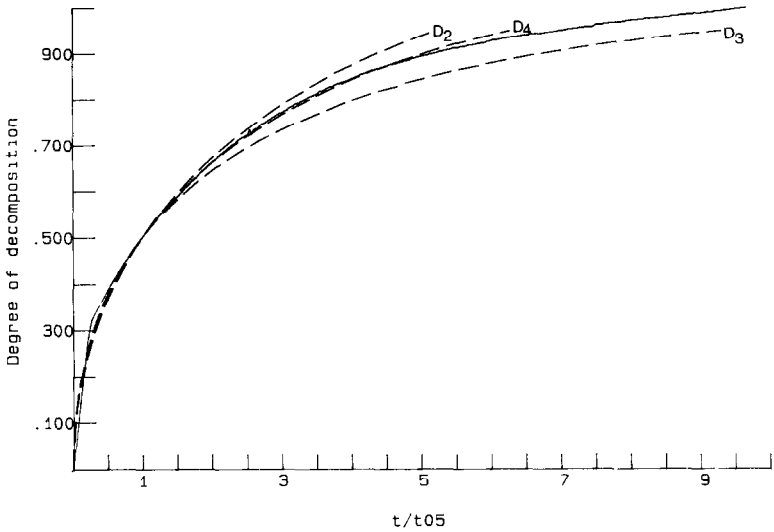

Fig. 5. $t/t_{0.5}$ test for the decomposition of ibuproxam to $\alpha = 0.60$ at 175 °C.

a $t/t_{0.5}$ test [3]. The best fit to the experimental curves was obtained for diffusion-controlled mechanisms, and among these, the D_4 mechanism (Figs. 2–5), which is given by the equation $kt = (1 - 2\alpha/3) - (1 - \alpha)^{2/3}$. This is known as the Ginstling–Brownshtein equation [4], and describes three-dimensional diffusion proceeding in spherical particles. The activation energy for this reaction, calculated from the Arrhenius plot (Fig. 6), is 43 kJ mol^{-1}.

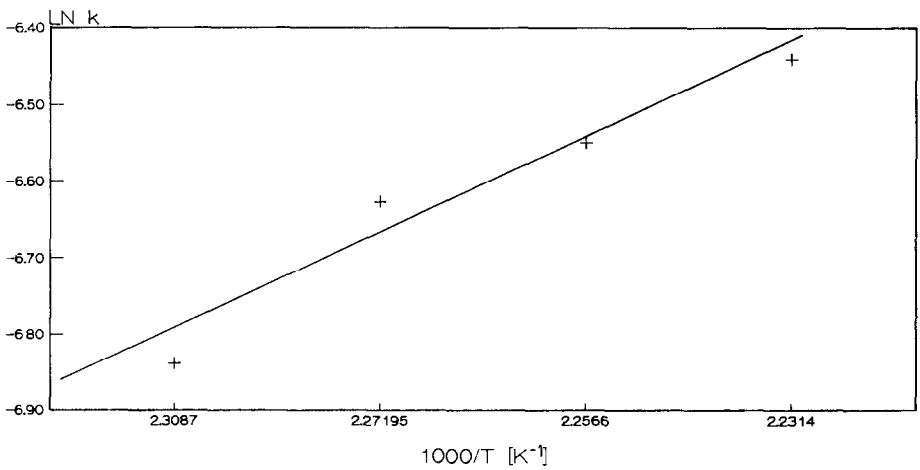

Fig. 6. Arrhenius plot for the decomposition of ibuproxam to $\alpha = 0.60$.

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