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APPLICATION OF THERMOGRAVIMETRY IN THE QUALITY CONTROL OF MEBENDAZOLE

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Abstract

A study was made of the thermal behavior of the starting materials, their mixtures and the resulting mebendazole tablets. The thermal curves were obtained with a Shimadzu thermobalance, model TGA-50, using an air flow of 50 mL min^{-1} and a heating rate of 10°C min^{-1} in the temperature interval 30–900°C. The reaction constant velocities for the mebendazole salt and tablets were determined isothermally, using the Arrhenius expression. The thermal stability of mebendazole tablets is lower than that of the mebendazole salt, due to the presence of starch and lactose in the composition. Analysis of the data reveals that thermogravimetry is a powerful tool in pharmaceutical technology and quality control.

Keywords: kinetics, mebendazole, quality control, technology

Introduction

Quality control is used in the pharmaceutical industry to analyse starting materials, intermediates and finished products. The thermal decomposition of the active ingredients, due to the reactions between the constituents of pharmaceuticals, obliges producers to check for chemical incompatibilities, toxicity and validity time for each product. Thermal analytical techniques have proved useful in fundamental chemical research [1–5].

In industrial production, any errors of quality must be discovered before packaging for commercial distribution, to keep the costs to a minimum. Although quality control is essential in manufacturing processes, it includes the initial cost of the apparatus, qualified personnel costs, running costs and maintenance, and replacement of the apparatus [6]. The cost is factored in the time required for product analysis. Time-consuming procedure must be eliminated or shortened for the cost reduction.

This paper presents a study on the application of thermogravimetry in the quality control of mebendazole tablets, their components and their mixtures, with the aim of decreasing the time necessary for determination of the pharmaceutical manufacturing conditions.

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Experimental

Mebendazole salt, starch, lactose, PVP and magnesium stearate of commercial grade were acquired from the Pharmaceutical Technology Laboratory at UFPB. The mebendazole formulation utilized for each tablet in this study was: mebendazole –100 mg; starch – 147 mg; lactose – 43 mg; PVP – 5 mg; magnesium stearate – 5 mg. The mebendazole, starch and lactose were fine-sieved and homogenized. The granulate was obtained with a 75% hydroalcoholic solution containing PVP. The magnesium stearate was added before tablet compression. The drug formulations were made with the mixtures mebendazole:starch; mebendazole:lactose, mebendazole:PVP, mebendazole:magnesium stearate, mebendazole:starch:lactose, mebendazole:starch:PVP, mebendazole:starch:magnesium stearate, mebendazole:lactose:PVP and mebendazole:lactose:magnesium stearate.

The thermal curves were obtained with a Shimadzu thermobalance, model TGA-50, with an air flow of 50 mL min^{-1} and a heating rate of 10°C min^{-1}.

The reaction rate constants were determined isothermally at 200, 205, 210, 215 and 220°C and at 190, 195, 200, 205 and 210°C, during 60 min, for the mebendazole salt and mebendazole tablets, respectively, using the Arrhenius equation.

Results and discussion

Figure 1 shows the thermoanalytical profile of each starting product; curves 1 and 3 reveal the lower stability of starch and lactose. The mebendazole salt has a stability higher than that of mebendazole tablets (curves 5 and 6, respectively). The mebendazole salt undergoes thermal decomposition in three steps, in the temperature intervals 244–257°C, 340–360°C and 578–685°C. Mebendazole tablets present

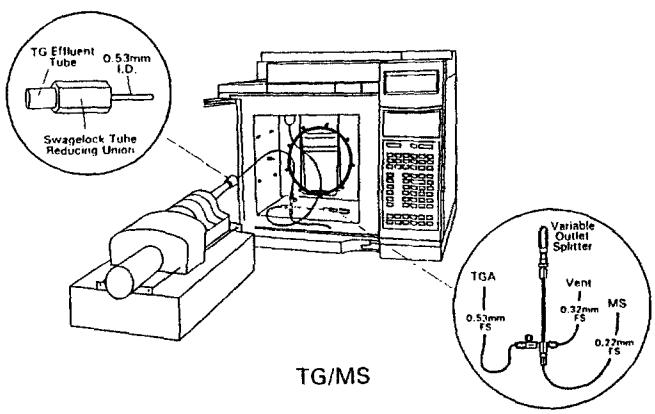

Fig. 1 TG curves of thermal decomposition of the starting materials and mebendazole tablets. Measurements were performed with a Shimadzu thermobalance, Model TGA-50. Samples (9–11 mg) were heated at a rate of 10°C min^{-1} in a dynamic air atmosphere

five stages of decomposition, in the temperature intervals 40–107°C; 226–246°C, 296–340°C, 340–516°C and 516–612°C.

Results on the mixtures containing starch are presented in Fig. 2. The TG curves confirm the lower stability of starch, which contributes to a decrease of the

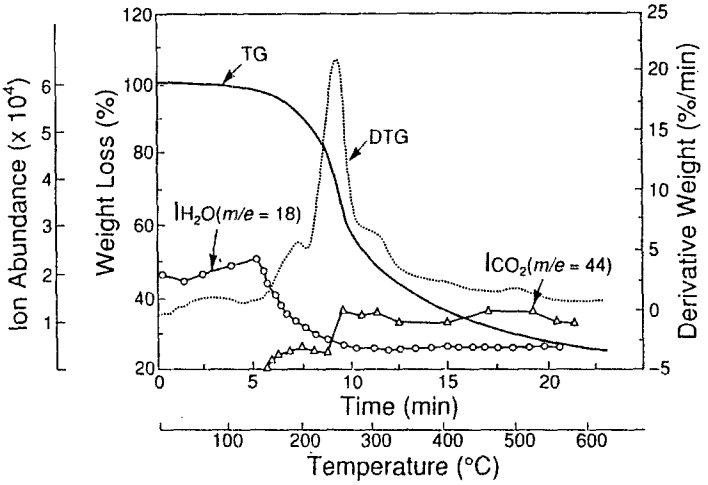

Fig. 2 TG curves of thermal decomposition of binary mixtures of the constituents of mebendazole tablets. Measurements were performed with a Shimadzu thermobalance, Model TGA-50. Samples (9–11 mg) were heated at a rate of 10°C min^{-1} in a dynamic air atmosphere

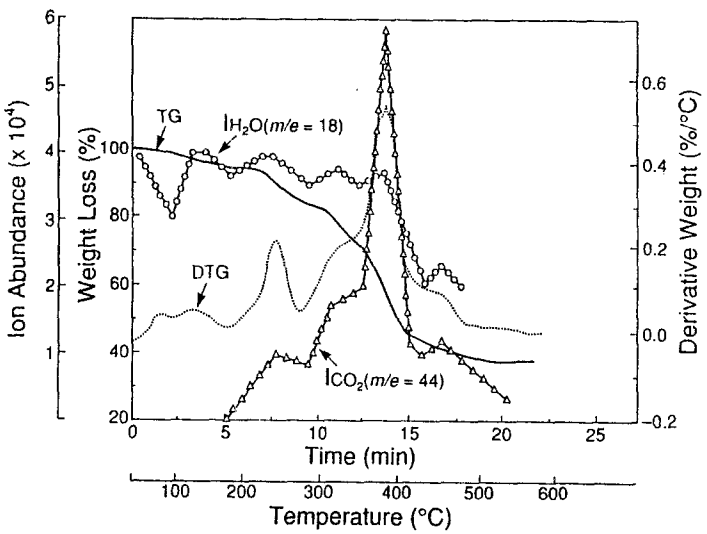

Fig. 3 TG curves of thermal decomposition of ternary mixtures of the constituents of mebendazole tablets. Measurements were performed with a Shimadzu thermobalance, Model TGA-50. Samples (9–11 mg) were heated at a rate of 10°C min^{-1} in a dynamic air atmosphere

stability of the mebendazole salt in the second and third steps. The temperature intervals of decomposition were 35–102°C, 244–260°C, 305–345°C and 518–609°C.

The mebendazole salt has a lower stability when associated with lactose (Fig. 2). Curve 3 reveals that the first stage results from partial fusion of the first two steps in the thermal decomposition of the mebendazole salt. The temperature intervals involving decomposition of the mebendazole and lactose mixture were 235–250°C, 250–359°C and 549–634°C.

The thermal curves for a mixture containing magnesium stearate and mebendazole (Fig. 2) show lower stability in the first step as compared with starch and lactose. The temperature intervals for the decomposition were 223–258°C, 309–341°C and 540–602°C.

The formulation prepared with the mebendazole salt and PVP was more stable. Figure 2 demonstrates the similarity between curves 1 and 5 for the mebendazole salt and the mebendazole salt+PVP. The thermal decomposition of this mixture was verified in the temperature intervals 239–264°C, 342–363°C and 575–670°C.

Figure 3 indicates that the tertiary mixtures of the mebendazole salt+starch+lactose and mebendazole salt+lactose+PVP (curves 1 and 4) display lower stability in the first step as compared with other mixtures.

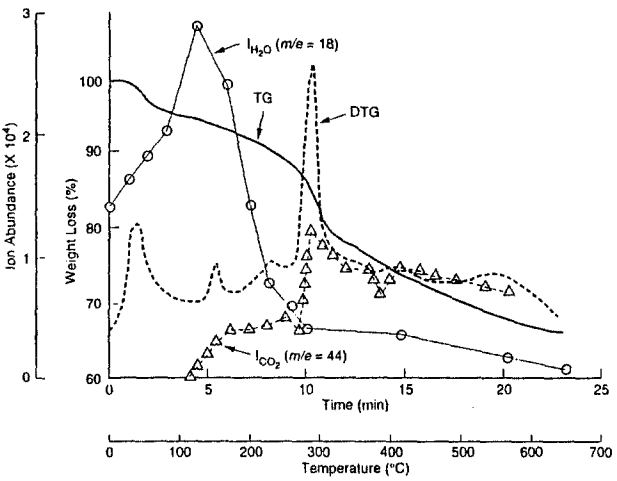

Fig. 4 Isothermal TG curves of mebendazole salt and tablets. Measurements were performed using Shimadzu thermobalace, Model TGA-50. Samples (9.2–9.5 mg) in a dynamic air atmosphere

The isothermal TG curves, Fig. 4, shows that the mebendazole salt (curves 1 and 2) was more stable when compared to mebendazole tablet (curves 3 and 4).

Kinetic studies of the thermal decomposition of the mebendazole salt and tablets under isothermal conditions demonstrate that the log*m vs. t* dependence is linear, as a sign that the reaction is of the first order.

The rate constants of thermal decomposition of the mebendazole salt and tablets were calculated from the following equation for a first-order reaction:

$$\Delta[P]/\Delta(t) = K_1[P] \quad (1)$$

Table 1 shows the reaction rate constants. It can be seen that the values for the mebendazole salt are lower than those for mebendazole tablets, indicating the higher stability of the salt.

Table 1 Thermal decomposition reaction rate constants of the mebendazole salt and tablets

Temperature/ °C	Rate constants $(K)/s^{-1}$	
	salt	tablets
190	-	1.49 E-05
195	-	3.06 E-05
200	1.29 E-05	6.04 E-05
205	2.20 E-05	10.4 E-05
210	3.00 E-05	20.1 E-05
215	4.80 E-05	-
220	6.77 E-05	-

Analysis of the data reveals the interactions of the constituents starch and lactose with the mebendazole salt, confirmed by a reduction in the temperature of thermal decomposition and an increased reaction rate constant for mebendazole tablets.

In most of the methods used in quality control, time is a limiting factor in the studies of interactions between constituents. The advantages of the thermogravimetric method in pharmaceutical quality control is its capacity to give results rapidly. Being a quantitative method, it is appropriate for quality control in different processing steps.

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