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Quality control of thiabendazole pre-formulation and tablets by TG and DSC coupled to the photovisual system

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Abstract

A stability study and thermal behavior of thiabendazole pre-formulation and tablets were investigated by TG and DSC coupled to a photovisual system. The results showed that the excipients, namely starch, PVP and magnesium stearate did not cause significant chemical interactions with the drug thiabendazole. The rate constants for the thermal decomposition reaction were determined by both an isothermal thermogravimetry and oven accelerated decomposition methods using the classical Arrhenius' equations. Thermal stability studies showed that thiabendazole tablets presented lower stability than the drug thiabendazole. The data analysis revealed that the drug thiabendazole undergoes a thermal decomposition reaction at a temperature lower that its melting point. This fact was confirmed by DSC coupled to the photovisual system and FT-IR.

Keywords: Thiabendazole; Thermal analyses; DSC photovisual; Quality control

1. Introduction

Thermal analysis is used in the pharmaceutical industry as a quich and reliable technique for quality control and for the development of new pharmaceuticals [1]. The technique is viable for stability studies of a drug and its formulations [2], purity determination [4], and the evaluation for polymorphism [4].

This work proposes to study the thermal behavior of thiabendazole drug, mixtures of drug-excipients and tablets by TG and DSC coupled to the photovisual system.

2. Experimental

2.1. Samples preparation

Samples of thiabendazole tablets were acquired in the local market, and were used as the reference product for that drug. The thiabendazole drug, starch, PVP and magnesium stearate were acquired from the Pharmaceutical Technology Laboratory at Federal Univesity from Paraíba (LTF/UFPB).

The thiabendazole formulation used for each tablet in this experiment: thiabendazole 500 mg, starch 150 mg, PVP 25 mg and magnesium stearate 10 mg. The drug, thiabendazole tablet, starch, PVP , magnesium stearate and binary and ternary mixtures were sieved and homogenized using a fine sieve of 100 mesh.

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2.2. Thermogravimetric studies

The binary and ternary mixtures were prepared under the same conditions as the formulation, respectively, as follows: thiabendazole, starch; thiabendazole, PVP; thiabendazole, magnesium stearate; thiabendazole, starch, PVP; thiabendazole, starch, magnesium stearate; and thiabendazole, PVP, magnsium stearate.

The TG curves for the binary and ternary mixtures of the raw material and thiabendazole tablet were placed in a Shimadzu thermobalance, model TGA-50H, with air flow of 50 ml min^{-1}, a heating rate of 10 °C min^{-1}, up to a temperature of 900 °C. The samples were packed in an alumina cell with a mass between 8.1 and 8.3 mg.

2.3. Stability studies

The TG-isothermal curves for the raw material and the thiabendazole tablet were placed at pre-established temperatures of 110, 120, 135, 160, 170, 180, 190, 200 and 210 °C for 4 h.

The thiabendazole drug was placed into an oven and held at temperatures of 70, 80, 90 and 110 °C. The mass losses were determined after 1, 8, 16, 21, 30, 36, 42 and 50 days.

The mass difference versus time was used to calculate the rate constants of the thermal decomposition reaction using Arrhenius' equation [3].

2.4. Calorimetric studies

The DSC curves for the raw material and thiabendazole tablet were placed into a Shimadzu calorimeter, model DSC-50 coupled to the photovisual system consisting of an Olympus microscope connected to a Sanyo camera, model VCC-D520, using a nitrogen atmosphere at 50 ml min^{-1}, heating rate of 5 °C min^{-1}, up to a temperature of 500 °C. The samples were packed into an aluminum cell with a mass of approximately 2.10 mg. The images were captured by DSC coupled to the photovisual system at a similar temperature and time compared to the conventional DSC. The purity calculations were analyzed by a Shimadzu TASYS software using the Vant Hoff's equation:

$$T_m = T_0 - \left(\frac{RT_0^2\chi^2}{\Delta H_0}\right)\left(\frac{1}{F}\right) \quad (1)$$

where T_m, sample temperature at equilibrium (K); T_0, melting point of the pure component (K); R, gas constant; χ^2, concentration of impurity (mole

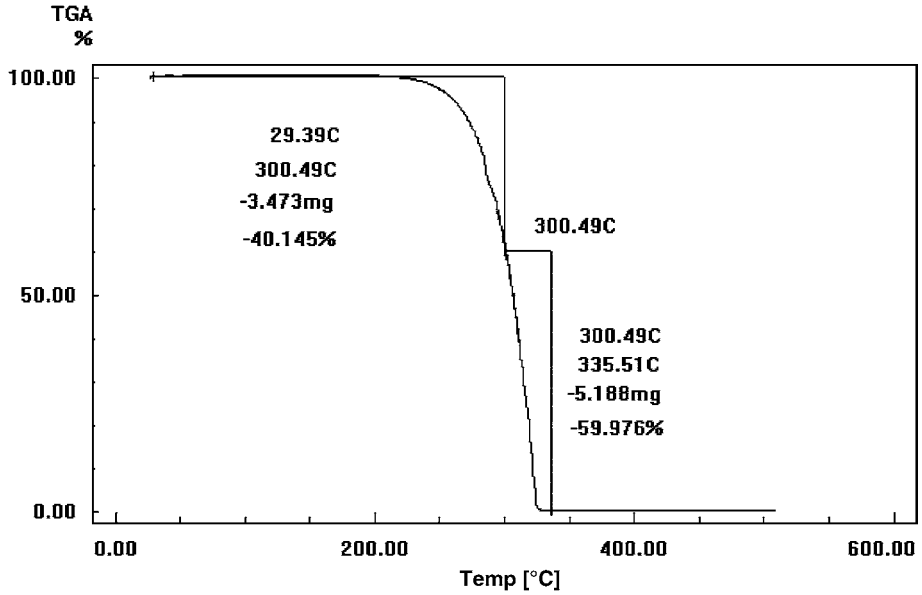

Fig. 1. TG curve for the thiabendazole drug.

fraction); ΔH_0, enthalpy of fusion of the sample; and F, fraction molten in T_m.

2.5. Spectroscopic analysis

Thiabendazole drug was placed into a muffle furnace at a temperature of 300 °C, for 10 min. The infrared spectroscopy of the drug and decomposition residues were obtained using in a BOMEM apparatus, model MB-102, in KBr pellets.

3. Results

3.1. Thermogravimetric studies

The 2-(4-thiazolyl)benzimidazole presented a one step thermal decomposition between 201 and 436 °C, representing 100% of the mass loss (Fig. 1). The binary and ternary mixtures provided a thermogravimetric profile of the thiabendazole drug (Fig. 2).

3.2. Stability studies

The TG isothermal curves for the thiabendazole drug and tablet showed a profile of only one stage of thermal decomposition. This shows that this drug decomposes in the tablet due the amount of the drug in the tablet. Figs. 3 and 4 show this decomposition profile.

The rate constant values obtained by conventional and thermogravimetric methods are presented in Table 1.

3.3. Calorimetric studies

The DSC curve showed that the thiabendazole drug presented a pseudo-melting point at 304 °C, which is in agreement with the literature [5] with 98.54% purity. The data revealed that the thiabendazole drug is in good conditions for formulation processing in the manufacturer. Fig. 5 presents the pictures A–C obtained by the DSC photovisual system, respectively, at temperatures: room temperature, 240 and 304 °C.

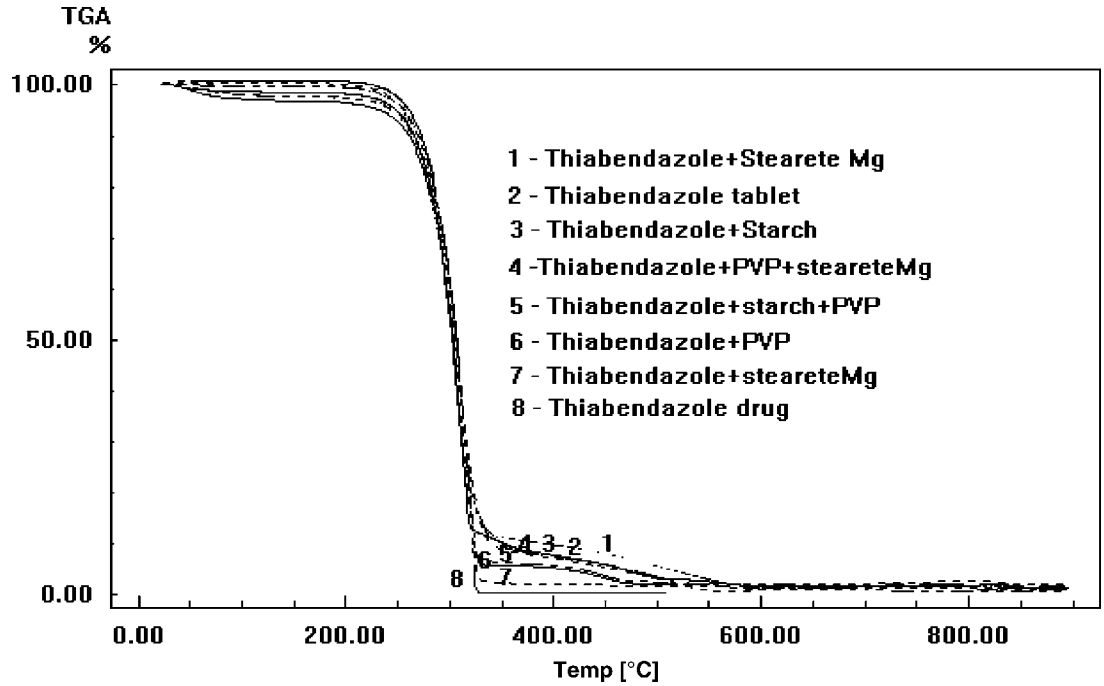

Fig. 2. TG curves of the binary and ternary mixtures for thiabendazole.

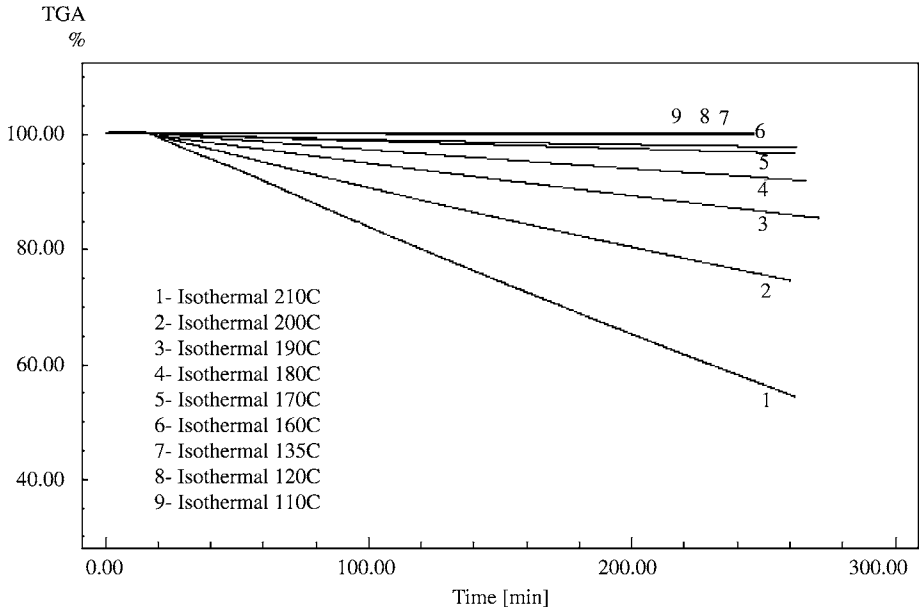

Fig. 3. TG isothermal curves for the thiabendazole drug.

The thiabendazole tablet showed a similar decomposition of the drug. At a temperature of 250 °C and at the melting point at 304 °C (Fig. 6, pictures B and C) the thermal decomposition of the tablet was observed.

3.4. Spectroscopic analysis

The comparison of the DSC and TG curves reveal that the thiabendazole begins its decomposition process

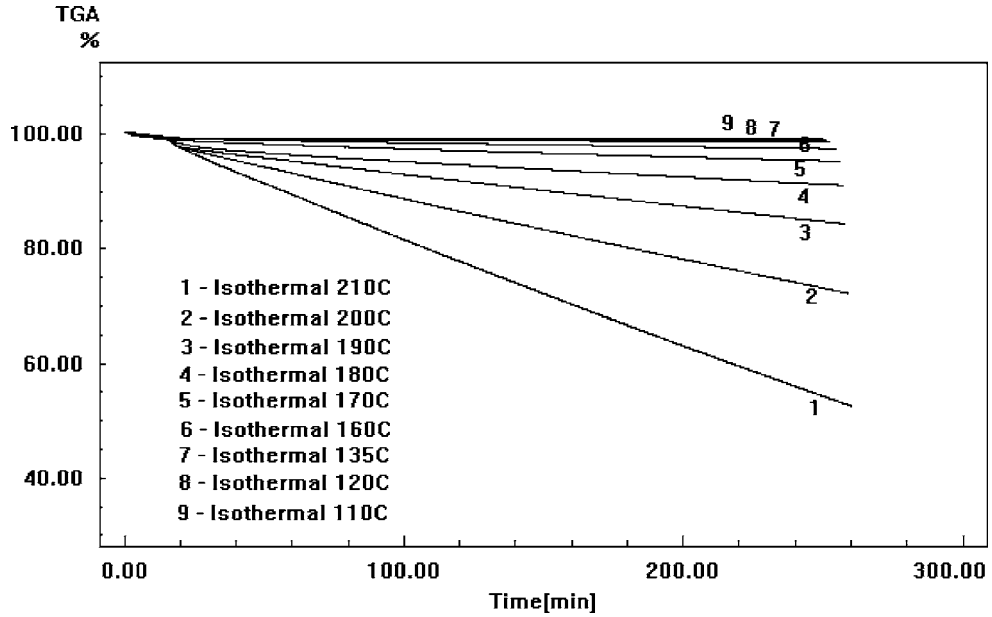

Fig. 4. TG isothermal curves for the thiabendazole tablet.

Table 1
Comparison of the conventional and thermogravimetric rate constants

Temperature (°C)	Drug: k (s^{-1})	Tablet: k (s^{-1})
Conventional method		
110	1.13×10^{-8}	
90	4.33×10^{-9}	
80	1.73×10^{-9}	
70	7.26×10^{-10}	
Thermogravimetric method		
210	4.44×10^{-6}	1.94×10^{-5}
200	2.23×10^{-6}	9.98×10^{-6}
190	1.14×10^{-6}	5.24×10^{-6}
180	6.50×10^{-7}	3.07×10^{-6}
170	2.65×10^{-7}	1.50×10^{-6}
160	1.94×10^{-7}	7.92×10^{-7}
135	1.18×10^{-7}	2.90×10^{-7}
120	7.12×10^{-8}	2.00×10^{-7}
110	3.60×10^{-8}	1.81×10^{-7}

at a lower temperature than the melting point. The thiabendazole (Spectra 1) and its residue (Spectra 2) were analyzed and compared (Fig. 7).

4. Discussions

4.1. Thermogravimetric studies

An aspect which was observed by the tangent TG analysis, between 200 and 300 °C, was that the thiabendazole decomposition, with 40.15% of mass loss, occurs before its melting point of 304–305 °C [5]. Stoichiometrically, this mass loss would correspond to the thiazolyl group in the thiabendazole molecule (42.30%) (Fig. 1).

Thermogravimetric curves for the binary and ternary mixtures showed no significant chemical interactions between the thiabendazole drug, tablet and its mixtures (Fig. 2).

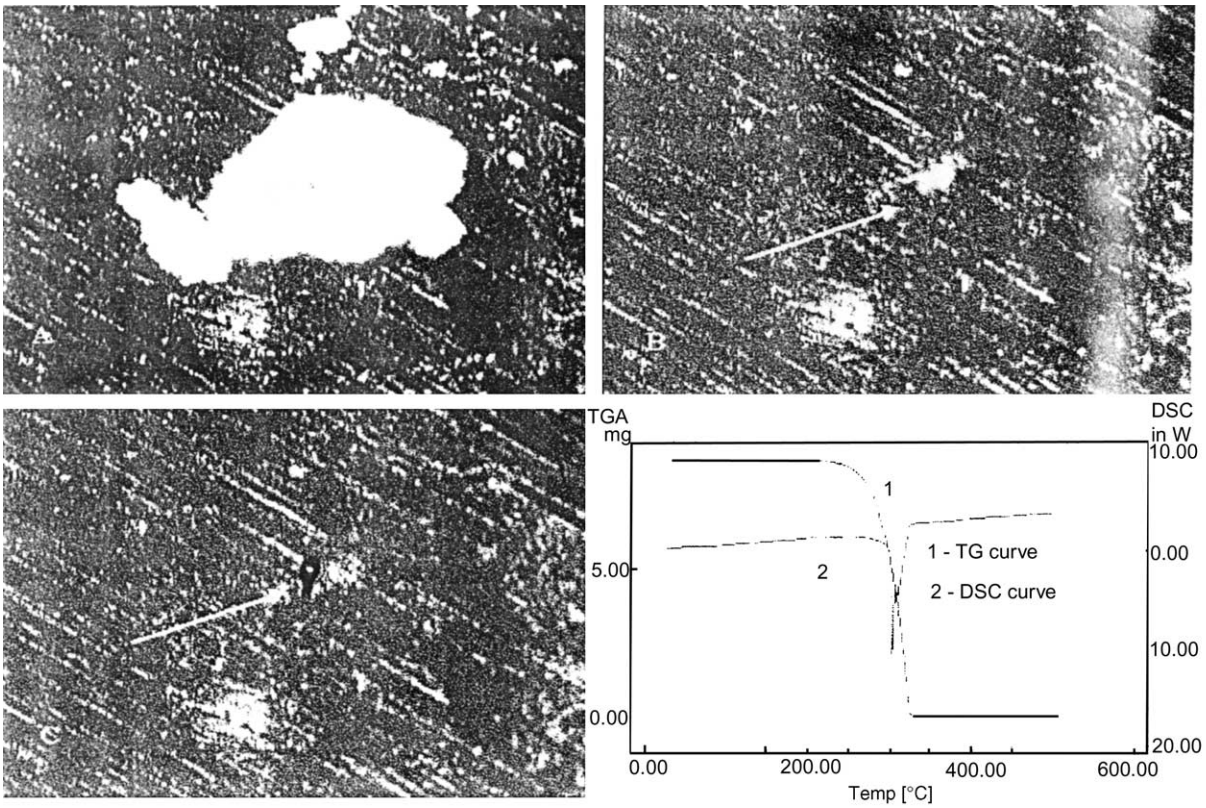

Fig. 5. Pictures and TG/DSC curves for the thiabendazole drug.

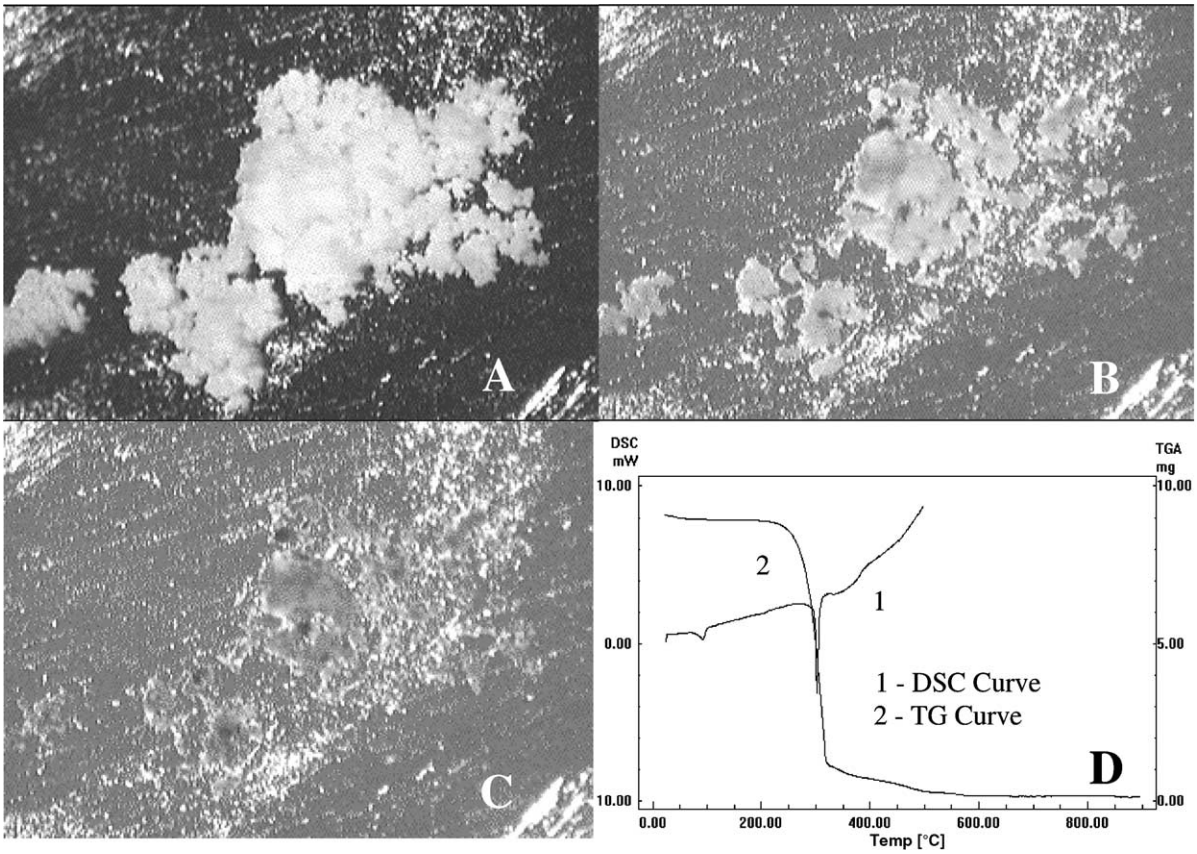

Fig. 6. Pictures and TG/DSC curves for the thiabendazole tablet.

4.2. Stability studies

The TG isothermal curves after math treatment using the Arrhenius equation showed that the drug and the thiabendazole tablet obeyed the first order kinetic model [$\log(m) \times t$]. Data analysis reveals that the rate constant values were smaller for the drug in relationship to the thiabendazole tablet. The difference can be attributed to the humidity content of the tablet, thus decreasing its thermal stability.

The comparison of the rate constants obtained by conventional and thermogravimetric methods revealed that they are similar. It was also observed that at the same temperature, for example 110 °C, the rate constant for the thermal decomposition reaction was smaller by about three times the conventional method as compared to the thermogravimetric method. Such fact can be explained by having greater efficiency in the thermogravimetric measurement.

4.3. Calorimetric studies

The images in the photovisual system confirmed the thermal decomposition of the thiabendazole drug before the melting point. Picture B showed coloration changes with mass loss in the TG curve, while picture C revealed a strong reduction in the sample volume indicating thermal decomposition was well advanced.

4.4. Spectroscopic analysis

The multiple bands (2986w–2799w–2680w cm^{-1})[1] referring to the tertiary amine (Fig. 7, Spectra 1) disappeared in the thiabendazole residue [6]. The same drug happened with the bands (1012w–986w cm^{-1})[1] indicating stretching (C–S) [7]. The medium intensity band at (903m cm^{-1})[1] corresponds to angular deformation

[1] w: weak intensity bands; m: median intensity bands.

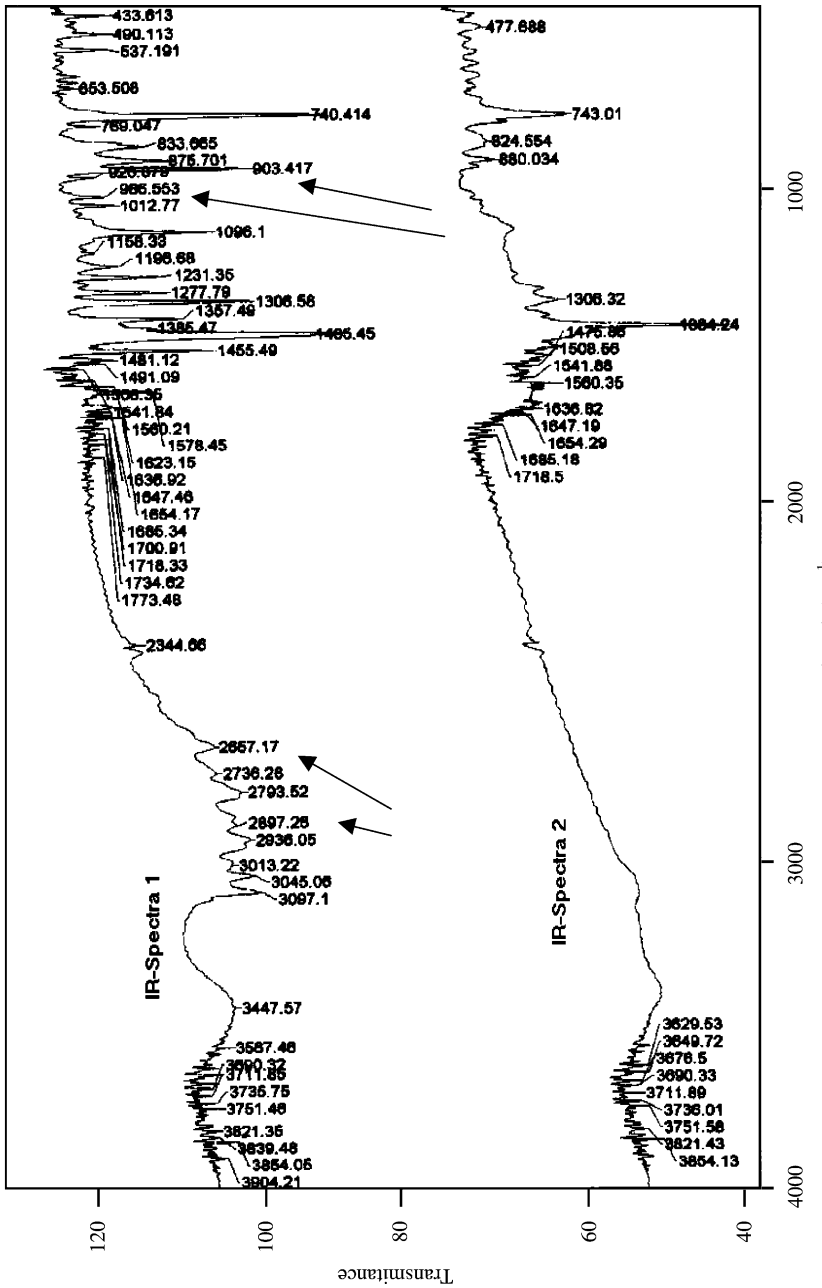

Fig. 7. Spectra 1 and 2 for thiabendazole drug and its residue.

out of the plan (=C–H) of the thiazolyl group (Fig. 7, Spectra 1). Besides the band at (953m cm^{-1}) corresponds to the aromatic isothiocianate as the thiazolyl (RSCN) [6]. The data obtained suggests that the melting point in 304 °C is not characteristic of the thiabendazole but it is one of its decomposition products.

5. Conclusion

The data analysis reveals that thiabendazole suffers a thermal decomposition reaction under natural conditions, at lower temperature than its melting point, as confirmed by the DSC photovisual system.

Acknowledgements

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