In vitro Evaluation of Dissolution Profiles and Thermal Properties of Some Commercial Formulations of Nevirapine Tablets

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SUMMARY. This report describes results of an in vitro study in which tablets containing nevirapine (200 mg) from different Brazilian manufacturers were evaluated. The original product was the reference in comparison to five similar products (A, B, C, D and E). Initially, the stability and thermal behavior of nevirapine (NVP) and various excipients using thermoanalytical techniques were investigated. These studies have been carried out to find potential incompatibility between the active component and the other ingredients of the formulation. The commercial tablets were analyzed following a common protocol based on the pharmacopeial methodologies. Pharmacotechnic tests (uniformity of weight, disintegration, friability, hardness) and dissolution of active ingredient were performed. Differential scanning calorimetry (DSC) curve of pure NVP showed a sharp endothermic transition at 244 °C corresponding to the melting point of the drug. A second event corresponds to the decomposition of the material in endothermic reaction in peak temperature at 303 °C. Thermogravimetry (TG) curve of drug showed the thermal decomposition in one step Δm = 99.8% in the temperature of derivative thermogravi

RESUMEN. “Evaluación in vitro” de los perfiles de disolución y de las propiedades térmicas de algunas formulaciones comerciales de comprimidos de nevirapina”. Este informe describe los resultados de un estudio in vitro en el que fueron evaluados comprimidos de nevirapina (200 mg) de diferentes laboratorios brasileros. El producto original fue la referencia, en comparación con cinco productos similares (A, B, C, D y E). Inicialmente se investigó la estabilidad y el comportamiento térmico de la nevirapina (NVP) y varios excipientes utilizando técnicas termoanalíticas. Estos estudios han sido llevados a cabo para determinar la incompatibilidad potencial entre el compuesto activo y los otros ingredientes de la formulación. Los comprimidos comerciales fueron analizados siguiendo un protocolo común basado en metodologías farmacopeicas. Se realizaron los ensayos farmacotécnicos usuales (uniformidad de peso, desintegración, friabilidad, dureza), así como la disolución del ingrediente activo. La calorimetría diferencial de barrido (DSC) de NVP mostró una aguda transición endotérmica a 244 °C, correspondiente al punto de fusión de la droga. Un segundo evento corresponde a la descomposición del material en la reacción endotérmica en el pico de temperatura a 303 °C. La termogravimetria (TG) de la droga mostró que la descomposición térmica se produce en un solo paso (Δm = 99.8%) en la temperatura a 298 °C de la termogravimetría diferencial (DTG). La comparación del perfil termoanalítico de mezclas 1:1 (p/p) de NVP con almidón, glicolato de sodio, celulosa microcrystalina, lactosa y disódico de silicona coloidal con los perfiles de los compuestos individuales no mostró ninguna evidencia de interacciones. En el caso de PVP, la mezcla droga-polímero demostró un ensanchamiento del pico endotérmico NVP junto con un corrimiento hacia una temperatura más baja. La mayoría de los productos ensayados cumplieron con los requerimientos farmacopeicos en relación a uniformidad de peso, desintegración, friabilidad, dureza y contenido. En relación al ensayo de disolución y a los perfiles termoanalíticos, los datos no mostraron variaciones significativas entre los distintos productos.

KEY WORDS: HIV/AIDS, Nevirapine (NVP), Solid-state interactions, Thermal analysis.

PALABRAS CLAVE: Análisis térmico, HIV/SIDA, Interacciones en estado sólido, Nevirapina

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INTRODUCTION

The antiviral drug nevirapine (NVP, BI-RG-587, Fig. 1) is a potent inhibitor of HIV-1 replication and the first non-nucleoside reverse transcriptase inhibitor (NNRTI) approved in 1997 by Food and Drug Administration (FDA) for use in combat of human immunodeficiency virus (HIV) \(^{1,2}\). They target a non-substrate binding site of transcriptase reverse enzyme and do not require activation through cellular metabolism. Treatment with NVP monotherapy is notorious for rapidly eliciting resistance due to mutations of the amino acids surrounding the NNRTI binding site \(^3\). However, in association with two other antiretroviral products, nucleoside reverse transcriptase inhibitors (NRTIs) and/or protease inhibitors (PIs), NVP significantly reduces the viral load and increases CD4 cell count, particularly in treatment-naive patients \(^4,5\).

The bioavailability of a drug is dependent on many physical parameters. In vitro dissolution testing is an important tool in the development and quality control of solid dosage forms \(^6\). Basically, the test consists of measuring the rate of release of drug from a solid dosage form into an aqueous environment under defined conditions. Others tests are commonly used for the evaluation of the attributes of a good tablet are as follows: hardness, friability, disintegration, weight variation, content uniformity and stability \(^7,8\).

The development of analytical methods for determination of drugs has received considerable attention in recent years because of their importance in quality control in pharmaceutical analysis. The kinetic studies of dissolution appear as a tool to detected the influence of critical variables of the technological process as binder effect, of mixture, excipient type, and in the correlation studies in vitro/in vivo in solid dosage forms \(^7,8\). The implementation of the thermal analysis and kinetic studies of dissolution appears as comparative analytical method, producing fast and reproducible results that can be used in selection of formulations with pharmaceutical equivalence candidates to the bioequivalence studies. These are techniques widely used in the pharmaceutical sciences for the characterization of solid drugs and excipients \(^9,10\). The main applications of thermal analysis in the pharmaceutical area include the characterization of materials, solvates, hydrates, polymorph forms, determination of purity, drug/excipient compatibility study, thermal stability and kinetic analysis \(^11,12\).

Thermal analysis provides efficient tools for measuring fundamental thermodynamic properties such as enthalpies, heat capacities, and temperatures of phase transitions. Wendlant describe the term thermal analysis as a group of techniques in which a physical property of a substance and/or its reaction products is measured as a function of temperature whilst the substance is subject to a controlled temperature program \(^13\). The most widely used techniques are differential thermal analysis (DTA), differential scanning calorimetry (DSC) and thermogravimetry/derivative thermogravimetry (TG/DTG).

DTA is a technique in which the difference in temperature between the sample and a thermally stable reference material is monitored against time or temperature while the temperature is programmed in a specified atmosphere. DSC technique involves the application of a heating or cooling signal to a sample and a reference. When the sample undergoes a thermal event, the difference in heat flow to a sample (pan) and to a reference (pan) is monitored against time or temperature while the temperature is programmed in a specified atmosphere. Consequently, the temperature and energy associated with events such as melting, oxidation and reduction reactions, glass transition, boiling, sublimation, decomposition, crystallization or gel to liquid crystal transition can be evaluated. When such events are evaluated for mixtures of drugs and excipients, possible interactions may be discerned \(^9-12\). TG is a thermal analysis technique in which the change in sample mass is determined as a function of temperature and/or time whilst sample is subjected to a controlled temperature program. In derivative thermogravimetry, the derivative of the mass-change with respect to time, \(dm/dt\), is recorded as a function of time (\(t\)) or temperature (\(T\)). In other cases, the derivative of the mass-change with respect to temperature, \(dm/dT\), is recorded as a function of time or temperature. In either case, the resulting curve is the first derivative of TG curve, giving a series of peaks, instead of a stepwise curve. A horizontal plateau in the TG curves gives a corresponding horizontal plateau in the DTG curve because \(dm/dt = 0\). A maximum in the DTG curve is obtained when the TG curve has
an inflection point where mass is being lost the most rapidly.\textsuperscript{13}

The DSC and TG/DTG were applied to analysis on NVP. The potential incompatibilities of several commonly used pharmaceutical excipients (lactose, sodium starch glycolate, microcrystalline cellulose, colloidal silicon dioxide, and polyvinylpyrrolidone) with NVP were evaluated using thermal analyses. These techniques have increased its use for quick evaluation of the interactions between the formulation components through the comparison of thermal curves of pure substances with the curve obtained from 1:1 physical mixtures.

Viramune\textsuperscript{®}, produced by Boehringer Ingelheim Pharmaceuticals is the innovator and reference product in Brazil. Others five NVP tablets are considered as similar products that have the same active ingredient and dosage.

From a public health point of view, these products should be interchangeable and have assured quality and clinical response. Thus, the aim of this article was to evaluate the pharmaceutical equivalence between five different commercial samples of NVP tablets (200 mg) available in the Brazilian market and compare with the reference product. The products were analyzed following a common protocol based on the methodologies described in the European (Ph.Eur.), British (BP), and/or United States Pharmacopeia (USP). Pharmacotechnical tests (uniformity of weight, hardness, disintegration, content, friability, and humidity), identification and dissolution of active ingredient were performed by six products available in the local markets. These samples were also analyzed by thermal analysis, where the thermal decomposition mechanism and kinetic parameters were studied under non-isothermal conditions, the Ozawa equation was used to analyze the non-isothermal decomposition process.

**MATERIALS AND METHODS**

**Chemicals**

Nevirapine (C\textsubscript{15}H\textsubscript{14}N\textsubscript{4}O), (11-cyclopentyl-5,11-dihydro-4-methyl-6H-dipyrido-[3,2-b:2′,3′-e][1,4]diazepin-6-one), was obtained from Hetero Labs Limited (lot. NV 0321001). In the compatibility study were tested the following excipients: starch glycolate sodium (Gerbrás, lot. 11966), lactose spray dried (Gerbrás, lot. 15898), microcrystalline cellulose (Blanver, lot. 1219/00), colloidal silicon dioxide (Comercial Granulab, lot. 11562), polyvinylpyrrolidone (Gerbrás, lot. 11743). All the materials were used as supplied by the manufacturers. All other solvents and reagents were have analytical or HPLC grade. Five NVP tablets (200 mg) of different Brazilian pharmaceutical companies (A, B, C, D and E) and the reference product (R) were analyzed.

**Preformulation study**

The mixed samples consisted of equal weights of NVP and each excipient was individually weighed into amber glass vials to give composite weights of 20 mg. The physical mixtures was gently prepared at a 1:1 (NVP/excipient) weight ratio by simple mixing with a spatula.

DSC curves were obtained in a DSC-50 cell (Shimadzu) using aluminum crucibles with about 2 mg of samples, under dynamic N\textsubscript{2} atmosphere (50 mL.\textperminute\textsuperscript{-1}) and heating rate of 10 °C min\textsuperscript{-1} in the temperature range from 25 to 600 °C. The DSC cell was calibrated with indium (m.p. 156.6 °C; \(\Delta H_{\text{ fus.}} = 28.54\) J g\textsuperscript{-1}) and zinc (m.p. 419.6 °C). TG/DTG curves were obtained with a thermobalance model TGA 50 (Shimadzu) in the temperature range 25-900 °C, using platinum crucibles with ~3 mg of samples, under dynamic nitrogen atmosphere (50 mL.min\textsuperscript{-1}) and heating rate of 10 °C.min\textsuperscript{-1}.

**Pharmacotechnical test and in-vitro dissolution**

The friability of the tablets was determined in a Vankel friabilator using 10 tablets, 100 rotations for 5 min. Tablet disintegrations were conducted using the BP test using one tablet per tube. Each value reported is the mean of six determinations. The disintegration time in minutes was determined at 37 °C in 600 ml of water. The dissolution studies were performed using the USP dissolution apparatus II with 50 rpm paddle rotational speed. The dissolution test was carried out at 37 ± 0.5 °C in 900 mL of HCl 0.1 N using a Vankel dissolution test station, model VK 7010, containing 8 vessels. Samples were taken automatically employing an auto-sampler (Vankel VK 8000). The analysis was accomplished in quadruplicate and collected at times: 2, 4, 6, 8, 10, 15, 20 and 30 min. The values reported are the mean of twelve determinations.

The content of NVP was determined by high-performance liquid chromatography (HPLC). These experiments were operated in Shimadzu spectrophotometer at a wavelength of 237 nm (detector UV/VIS SPD 10 Avp). The mobile phase consisted of methanol:water (70:30, v/v), which was degassed by filtering through a 0.45 (m (pore size) membrane filter (Millipore, USA) before use. The pump was run at a flow-
rate of 1.0 mL min⁻¹. A sample volume of 20 µl was injected into the C₁₈ column (Supelco® 250 x 4.6 mm, 5 µm).

**Thermal stability of the formulations and Kinetics parameters**

In this study was used a TGA-50 system (Shimadzu) in a temperature range of 25-900 °C using a platinum crucibles with ~4 mg of the sample. The determinations of the kinetic parameters of the tablets content degradation were obtained from thermogravimetric data. The results were obtained for a weight loss range at 5% data by application of the Ozawa’s method in which the slope of the plot of log (heating rate) vs 1/T gives the activation energy (Eₐ) of the process. In this work the heating rates used were: 2.5-5.0-7.5-10 and 15 °C min⁻¹. The values kinetic parameters for Ozawa method have obtained by the Tasys Shimadzu programa.

**RESULTS AND DISCUSSION**

DSC curve of pure NVP showed a sharp endothermic transition at 244 °C corresponding to the melting point of the drug. Second events correspond to the decomposition of the material in endothermic reaction in peak temperature at 303 °C (Fig. 2). TG curve of drug showed the thermal decomposition in one step ∆m=99.8% in the temperature of DTG peak at 298 °C (Fig. 3). The thermal behavior of lactose is illustrated in the Figs. 2 and 3. The DSC curve shows a peak (endothermic event) corresponding the dehydration at 148 °C, an exothermic event due to crystalline transition (peak temperature at 176 °C), melting point at 217 °C followed of thermal decomposition (Fig. 2). From TG/DTG curves it four steps of weight losses can be observed: dehydration (∆m₁ = 5.4% and DTGpeak = 144 °C), thermal decomposition (∆m₂ = 19.3% and DTGpeak = 248 °C and ∆m₃ = 47.9% and DTGpeak = 306 °C), and carbonization initializing about 320 °C (∆m₄ = 32.7%) of the excipient (Fig. 3). The DSC and TG curves (NVP/lactose) presented in the illustrations 4 and 5, respectively, showed that the events relative to NVP not changed. Thus, there is no incompatibility between the two compounds.

Figure 2 and 3 show the thermal behavior of aerosil. From TG/DTG curves, a weight loss is observed, occurring in the temperature range of 25 to 100 °C and associated with desorption of physically adsorbed water vapor and possibly other gases on material surface. DSC data agree with TG/DTG results, indicating that this material is thermostable up to 600 °C. The thermal behaviors of the binary mixture of NVP and aerosil (Figs. 4 and 5) show the endothermic and exothermic characteristics of drug, indicating the presumable absence of incompatibility.

The DSC curve of magnesium stearate (Fig. 2) by itself had two endothermic transitions occurring at 81 and 110 °C that was assigned to dehydration. Magnesium stearate showed a thermal stability in the range of 130 to 300 °C and a broad peak relative to the endothermic event between 300 and 465 °C due to thermal decomposition. TG curve of magnesium stearate (Fig. 3) showed the dehydration of excipient in a temperature about 35 °C (∆m=4.3%), and confirmed that the endothermic event indicated above is relative to thermal decomposition of material in one step at about 305 °C (∆m = 86.4%). By observing the representative curves of magne-
sium stearate and NVP (Figs. 4 and 5) and comparing to the curve profile obtained from the physical mixture of these components we can verify that there was an add up of events. This indicates that, between components, there is not interaction.

DSC curve of PVP showed an endothermic event in the temperature range at 25 and 135 °C due to polymer dehydration. After this event, the DSC curve presented a plateau between 135 and 300 °C indicating the thermal stability of the material in this temperature range. The thermal decomposition of PVP was registered in two stages; one endothermic and another exothermic (Fig. 2). This data were corroborated with TG/DTG curves where was verified a first event of weight loss in temperature range at 25 and 130 °C (Δm = 7.4%), following to thermal decomposition event after 300 °C (Δm = 85.3%) (Fig. 3). The thermoanalytical profile of the 1:1 w/w mixed system with NVP showed a different thermal behavior. In case of PVP, the drug-polymer physical mixture demonstrated a broadening of the NVP endothermic peak together with a shift to a lower temperature (Fig. 4). This behavior, which resembles that already described for other drugs such as naproxen 14, piroxicam 15, and ketoprofen 16 itself, indicates that a strong solid-solid interaction has occurred. However it does necessarily indicate pharmaceutical incompatibility, but could be explained by the formation of crystalline microaggregates of the drug and their considerable dispersions within the amorphous polymeric matrix 11.

The comparison of the thermoanalytical profiles of the mixtures and individual compounds not evidenced interactions (Table 1).

All formulations were relatively robust in terms of friability and hardness. According to the obtained results all the samples followed the specifications for the friability and hardness. The results presented in Table 2 show that the NVP content was computed from a standard curve prepared for this purpose using pure NVP. The uniformity of content was determined by individually assaying 10 randomly selected tablets. The results show that the acceptance criteria of the United States Pharmacopeia test for content uniformity (no tablet outside of 85% to 115% of label claim, and the RSD not greater than 6.0%). In the assay of tablets all results between 97 and 101% of amount labeled. The method followed

<table>
<thead>
<tr>
<th></th>
<th>( T_{\text{ onset}} \text{ melting (°C)} )</th>
<th>( \Delta H ) (J/g)</th>
<th>( T_{\text{ onset}} \text{ decomp. (°C)} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>nevirapine (NVP)</td>
<td>244</td>
<td>146</td>
<td>255</td>
</tr>
<tr>
<td>binary mixtures microcrystalline cellulose</td>
<td>244</td>
<td>68</td>
<td>252</td>
</tr>
<tr>
<td>polyvinylpyrrolidone</td>
<td>-</td>
<td>-</td>
<td>251</td>
</tr>
<tr>
<td>lactose</td>
<td>239</td>
<td>63</td>
<td>248</td>
</tr>
<tr>
<td>colloidal silicon dioxide</td>
<td>239</td>
<td>65</td>
<td>253</td>
</tr>
<tr>
<td>sodium starch glycolate</td>
<td>244</td>
<td>65</td>
<td>252</td>
</tr>
</tbody>
</table>

Table 1. DSC and TG/DTG results for NVP and binary mixtures with excipients used in pharmaceutical formulations.
for the determination of NVP content was the same as that of the assay. For disintegration time ranged from 1 to 3 min for the different tablets.

Dissolution profiles of the NVP tablets (200 mg) commercialized in the Brazilian market is shown in Figure 6. Each data point represents the mean of twelve dosage forms. This graphic shows that all tablets presented a similar profile, and 85% release in 8 min. The percentage of NVP released from the tablets was 95.4%, 96.4%, 96.3, 97.1%, 97.8% and 97.7%.

Figs. 7 and 8 show the DSC and TG-DTG curves, respectively, for the different NVP tablets. The commercial drugs tested show two-stages of weight loss relative to dehydration process. In the temperature range of 30 and 107 °C was verified the weight losses corresponding to release of superficial water, and the second stage (temperature range of 107 and 189 °C) is representative to dehydration of the lactose present in all formulations. The TG/DTG curves indicate that the thermal decomposition process of the formulations occurs in four stages in the following temperature range: 187-275 °C, 275-334 °C, 234-420 °C and 420-600 °C. The shape of all thermoanalytical curves was similar. Short differences between the TG and DTG profiles are occasioned in function of the excipients concentrations in each product.

The basic data for kinetic analysis was obtained from TG curves for different NVP tablets samples for heating rates 2.5, 5.0, 7.5, 10.0 and 15.0 °C min^{-1}. The method established by Ozawa is an integral method for determining the ac-

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Specifications</th>
<th>R</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medium weight (mg)</td>
<td>&gt; 800 mg ±5%</td>
<td>808.8 ±0.8</td>
<td>811.2±1.8</td>
<td>805.4±3.1</td>
<td>732.9±2.1</td>
<td>798.5 ± 1.6</td>
<td>666.9±1.3</td>
</tr>
<tr>
<td>Hardness (Kgf/cm²)</td>
<td>&gt; 3</td>
<td>12.17±0.96</td>
<td>11.2±1.18</td>
<td>10.6±2.22</td>
<td>11.8±1.15</td>
<td>12.02 ± 1.45</td>
<td>13.4±1.27</td>
</tr>
<tr>
<td>Friability (%)</td>
<td>&lt; 1.5</td>
<td>0.08</td>
<td>0.10</td>
<td>0.17</td>
<td>0.04</td>
<td>0.07</td>
<td>0.11</td>
</tr>
<tr>
<td>Disintegration (min)</td>
<td>&lt; 30</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>1:20</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Dissolution (%)</td>
<td>&gt;80% *</td>
<td>95.4 ±1.6</td>
<td>96.4 ±1.9</td>
<td>98.9 ±1.4</td>
<td>96.3 ±1.4</td>
<td>97.5 ±3.2</td>
<td>97.7 ±1.3</td>
</tr>
<tr>
<td>Content (%)</td>
<td>95 ±105</td>
<td>101.6±0.42</td>
<td>100.5±0.9</td>
<td>99.6±0.6</td>
<td>99.5±0.7</td>
<td>97.4±0.52</td>
<td>101.4±0.5</td>
</tr>
<tr>
<td>Uniformity of content (%)</td>
<td>85 ±115</td>
<td>101.21 ±1.8</td>
<td>99.2±1.8</td>
<td>99.6±1.5</td>
<td>99.36 ±1.2</td>
<td>97.33 ±1.6</td>
<td>101.2±2.1</td>
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<tr>
<td>Humidity (%)</td>
<td>&lt;5</td>
<td>5.1</td>
<td>4.9</td>
<td>4.5</td>
<td>5.01</td>
<td>4.94</td>
<td>5.2</td>
</tr>
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Table 2. Pharmacotechnic tests for evaluation of different NVP tablets commercialized in Brazilian market. * 30min/HCl 0.1 M.

Figure 6. The percent of NVP released from the commercial tablets (200 mg) in HCl 0.1 N.

Figure 7. DSC curves of NVP commercial tablets, obtained in dynamic nitrogen atmosphere (50 mL min^{-1}) and rate heating 10 °C min^{-1}.

Figure 8. TG and DTG curves of NVP commercial tablets, obtained in dynamic nitrogen atmosphere (50 mL min^{-1}) and rate heating 10 °C min^{-1}. The insert figure shows the DTG curves.
activation energies in the dynamic heating rates, q, as a function of the inverse of temperature, 1/T, for a constant g(α). The data from five TG curves were applied in Ozawa’s method in order to determine the activation energy for the beginning of the main decomposition step at around 187 - 275 °C for a weight loss of 5%. The activation energy was calculated from the average value for the different conversions resulting a value between 130 and 171 kJ mol⁻¹ (Table 3).

CONCLUSION

From the results obtained in this work, it can be concluded that not significant variation exist in the in vitro release pattern of NVP from solid dosage forms commercially available formulations in Brazil. Thermal analytical methods have become important tools for the development of medicinal compounds. There are several advantages in using these techniques; small quantities of samples, quick scanning technique for solid-state stability studies, and information about physical and chemical properties. This study shows the application of thermal analysis as a quick and efficient technique in the characterization of NVP and evaluation of the compatibility with excipients used in solid dosage forms. In case of the physical mixture NVP-polyethylene glycol no peak characteristic of NVP was detected. This shows that NVP has a high degree of solubility in molten PVP. An important implication of this study is present the comparison between different in vitro experimental techniques in the control quality of medicines. The results showed correlation between thermal analysis and dissolution test can be used as a parameter in the studies of pharmaceutical equivalence.

Acknowledgements. The authors acknowledge to Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) for the financial support.

<table>
<thead>
<tr>
<th>Products</th>
<th>Melting point (°C)</th>
<th>Dehydration Stages (%)</th>
<th>Decomposition step Tc (°C)</th>
<th>Ea (kJ mol⁻¹)</th>
<th>Fator Frequency</th>
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<tbody>
<tr>
<td>R</td>
<td>239</td>
<td>2.2, 2.3</td>
<td>233</td>
<td>171</td>
<td>1.071x10¹⁶</td>
</tr>
<tr>
<td>A</td>
<td>238</td>
<td>1.9, 2.6</td>
<td>227</td>
<td>150</td>
<td>1.047x10¹⁴</td>
</tr>
<tr>
<td>B</td>
<td>237</td>
<td>1.1, 2.5</td>
<td>227</td>
<td>129</td>
<td>7.711x10¹¹</td>
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<tr>
<td>C</td>
<td>238</td>
<td>1.8, 2.5</td>
<td>226</td>
<td>147</td>
<td>5.440x10¹³</td>
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<tr>
<td>D</td>
<td>238</td>
<td>2.4, 2.6</td>
<td>226</td>
<td>130</td>
<td>1.249x10¹²</td>
</tr>
<tr>
<td>E</td>
<td>237</td>
<td>1.4, 2.5</td>
<td>235</td>
<td>159</td>
<td>6.604x10¹⁴</td>
</tr>
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Table 3. Onset temperatures (Tc), mass loss percentage and kinetic parameters obtained from dynamic TG measurements for the decomposition of the NVP tablets commercialized in Brazilian market.

REFERENCES