Determination of Iodine by ISE after Drug Digestion by Microwave-Induced Combustion for Indirect Quantification of Levothyroxine

Alessandra Cortes Teotonio (IC)*, Filipe S. Rondan (IC), Diogo L. Novo (PG), Carla A. Hartwig (PG), Vanize C. Costa (PG), Marcia F. Mesko (PQ)* (marcia.mesko@pq.cnpq.com.br)

Centro de Ciências Químicas, Farmacêuticas e de Alimentos, Universidade Federal de Pelotas, Pelotas, RS, Brasil.

Keywords: *Levothyroxine, iodine, MIC, ISE*

Introduction

Levothyroxine (L-T_4) is a synthetic hormone used in the physiological maintenance of patients with deficiency of thyroxine (T_4), and it is usually administrated in very low dosage (µg per tablet).[1] Therefore, the control of hormone concentration in tablets is very important to assure the quality of the drug. Methods to assay L-T_4 are found in official compendiums. However, in general, they are complex and expensive, involving the use of determination techniques with low sensibility or sample preparation procedures with low throughput.[2,3] In this sense, an alternative for sample preparation is the microwave-induced combustion (MIC) method, which has a high throughput and allows obtaining high temperatures and pressures, promoting a complete decomposition of organic compounds. In this study, the MIC was evaluated for decomposition of drugs for subsequent indirect quantification of L-T_4 through determination of I by potentiometry with ion-selective electrode (ISE).

Results and Discussion

Drug samples were purchased in a local market (Pelotas – RS) and were grounded using mortar and pestle. The drugs were dried in an oven at 60 ºC for 3 h. For decomposition by MIC, samples (400 mg) wrappers in polyethylene film were disposed on the base of a quartz holder, with a small filter paper disc, and 50 µL of 6 mol L^{-1} NH_4NO_3 was added. The holder was placed into the quartz vessel containing 6 ml of absorbing solution (ultrapure water or 50 and 100 mmol L^{-1} $(NH_4)_2CO_3$). The vessels were closed, pressurized (20 bar of O_2), fixed to the rotor, and placed inside the microwave oven (Multiwave 3000™, Anton Paar). The microwave-heating program was as follows: 1400 W/5 min, 0 W/20 min. The accuracy of the proposed method was evaluated by recovery tests using L-T_4 standard solution. Iodine concentrations determined by ISE, after MIC digestion using water or $(NH_4)_2CO_3$ as absorbing solution, as well as results obtained by indirect quantification of L-T_4, are shown in Table 1. As can be observed in Table 1, when water was used as absorbing solution, the results obtained for I presented significant differences (ANOVA, $p<0.05$) with those obtained using $(NH_4)_2CO_3$ solutions. Probably, the lower concentration observed (around 5 times lower) is related to pH of final solutions (pH 3.5), which can affect the stability of I in the solution.[4] However, the results obtained for L-T_4, after MIC using $(NH_4)_2CO_3$ solutions, were in agreement (better than 90%) with the value reported by the manufacturer (100 µg/tablet).

Table 1. Results for I and L-T_4 in drug after MIC digestion and I determination by ISE (n=3).

Absorbing solution	I (µg/tablet*)	L-T_4 (µg/tablet*)
H_2O	12.2 ± 0.4	19.1 ± 0.6
$(NH_4)_2CO_3$ (50 mmol L^{-1})	58.5 ± 1.6	91.3 ± 2.6
$(NH_4)_2CO_3$ (100 mmol L^{-1})	57.3 ± 3.1	89.6 ± 4.8

*equivalent to a tablet with 100 mg.

Thus, in order to evaluate the accuracy of the proposed method, recovery tests were carried out by the addition of L-T_4 standard (0.1875 mg) in the samples (400 mg) and MIC digestion was performed. In these conditions, the maximum I recovery obtained using water as absorbing solution was 49%. However, when $(NH_4)_2CO_3$ solutions were used, I recoveries were around 97%, showing a similar behavior observed in the initial studies using the drug sample. Thus, 50 mmol L^{-1} $(NH_4)_2CO_3$ solutions or higher were considered suitable for absorption of I after drug decomposition by MIC and subsequent indirect L-T_4 quantification. Moreover, RSDs were lower than 3% when 50 mmol L^{-1} $(NH_4)_2CO_3$ was used.

Conclusion

The use of MIC and ISE was suitable for indirect quantification of L-T_4 in drug samples. The proposed method allowed the sample digestion with a high throughput using diluted alkaline solutions, and it is possible to use in routine analyses. Moreover, it is important to mention that this study is in process and that this method will be applied for other concentration of L-T_4 from different manufactures.

Acknowledgments

FAPERGS, CAPES, CNPq and UFPel.

[1] Gilman, A. G., et al.; As Bases Farmacológicas da Terapêutica. **2005**. 10 . 1175-1200.

[2] International pharmacopeia. Levothyroxinum sodium. Available: <http://apps.who.int/phint/en/p/docf>. Access at 03.Dez.2014.

[3] The United States Pharmacopeia. Levothyroxinum sodium. 2000. 24. 965-967.

[4] Nóbrega, J. A., et al.; *Spectrochim. Acta Part B*, **2006**, 61, 465.