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Original Article

Randomized Clinical Trial on Effect of taking *Ilex paraguariensis* as an infusion (mate or terere) on intestinal absorption of levothyroxine sodium

Ensayo Clínico Aleatorizado sobre el Efecto de administración de *Ilex paraguariensis* como infusión (mate o tereré) en la absorción intestinal de levotiroxina sódica

Bueno Colman, Elvio[1]; Ruiz Díaz Benítez, Daisy[1]; Benítez García, Aldo[1]; Palacios, Mafalda[1]; Jiménez, Jorge[1]; Argüello Ayala, Rocío[1]; Fernandez Miranda, Liliana[1]; Ruiz Diaz Benítez, Dalila[2]; Pérez Gayoso, Adriana[3]; Pintos Belotto, Misael[3]; Ruiz Diaz Politeo, Oscar[4]; Cuevas de Villalba, María[5]; Segovia Cuquejo, Clotilde[5]

[1]Universidad Nacional de Asunción, Facultad de Ciencias Médicas, Hospital de Clínicas, Departamento de Endocrinología y Metabolismo. San Lorenzo | Paraguay.
[2]Universidad Nacional de Asunción, Facultad de Ciencias Médicas, Hospital de Clínicas, Departamento de Neonatología. San Lorenzo | Paraguay.
[3]Universidad Nacional de Asunción, Facultad de Ciencias Médicas, Hospital de Clínicas, Departamento de Cadiología. San Lorenzo | Paraguay.
[4]Universidad Nacional de Asunción, Facultad de Ciencias Médicas, Hospital de Clínicas, Departamento de Imagenología. San Lorenzo | Paraguay.
[5]Universidad Nacional de Asunción, Facultad de Ciencias Médicas, Hospital de Clínicas, Departamento de Laboratorio Central. San Lorenzo | Paraguay.

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ABSTRACT

Introduction: Absorption of levothyroxine (LT4), is affected by medications and food. The intake of *Ilex Paraguariensis* (IP) as an infusion with hot water (Mate) or with cold water (Terere) is popular in the southern Cone of Latin America. **Objective:** To compare LT4 absorption with IP versus plain water. **Methods and Materials:** A pharmacokinetic study was conducted in healthy euthyroid volunteers. 1000 ug LT4 was administered with mate, plain water and terere respectively. Serial dosages of serum total thyroxine (TT4) were performed, mean maximum plasma concentrations of TT4 (Cmax), mean time to reach Cmax (Tmax), thyroid-stimulating hormone (TSH) variation in 24 hours (Δ TSH) and estimated percentage of LT4 absorption (%Abs) were compared. The protocol was approved by the Ethics Committee. **Results:** Twenty volunteers completed the study. Differences in Cmax, Tmax and %Abs when comparing LT4 and

Corresponding author: Dr. Elvio Dario Bueno Colman. Universidad Nacional de Asunción, Facultad de Ciencias Médicas, Hospital de Clínicas, Departamento de Endocrinología y Metabolismo. San Lorenzo | Paraguay. **Email:** buenoelvio@hotmail.com.
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*Universidad Nacional de Asunción, Facultad de Ciencias Médicas. San Lorenzo, Paraguay.
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plain water versus LT4 and mate, were statistically significant (Cmax: 17.38ug/dl vs 14.95ug/dl, p=0.02; Tmax: 3hs vs 4.2hs, p=0.03; and %Abs 104.83% vs 76.42%, p=0.05). There were no statistical differences when comparing LT4 and plain water versus LT4 and tereré (Cmax: 16.36ug/dl, p=0.29; Tmax: 4hs, p=0.09; and %Abs 90.76%, p=0.15). Regarding ΔTSH, LT4 and plain water resulted in 1.1uIU/ml versus LT4 and matte 1.09uIU/ml (p= 0.96) or LT4 and terere 1.35uIU/ml (p= 0.31), without statistically significant differences. **Conclusions:** The absorption of LT4 was lower when the administration was with mate and not with terere, compared with plain water.

Keywords: levothyroxine, *ilex paraguariensis*, yerba mate, terere, absorption.

RESUMEN

Introducción: La absorción de levotiroxina (LT4) se ve afectada por medicamentos y alimentos. El consumo de *Ilex paraguariensis* (IP) como infusión con agua caliente (mate) o con agua fría (tereré) es popular en el Cono Sur. **Objetivo:** Comparar la absorción de LT4 con IP frente a agua simple. **Materiales y Métodos:** Se realizó un estudio farmacocinético en voluntarios eutiroideos sanos. Se administraron 1000 µg de LT4 con mate, agua y tereré respectivamente. Se realizaron dosificaciones seriadas de tiroxina total en sangre (TT4), se compararon las concentraciones plasmáticas máximas medias de TT4 (Cmax), tiempo medio para alcanzar la Cmax (Tmax), variación de la hormona estimulante de la tiroides (TSH) en 24 horas (Δ TSH) y porcentaje estimado de absorción de LT4 (%Abs). El protocolo fue aprobado por Comité de Ética. **Resultados:** Veinte voluntarios completaron el estudio. Las diferencias en Cmax, Tmax y %Abs de LT4 y agua frente a LT4 y mate fueron estadísticamente significativas (Cmax: 17,38µg/dl vs 14,95µg/dl, p=0,02; Tmax: 3hs vs 4,2hs, p=0,03; y %Abs 104,83% vs 76,42%, p=0,05). No hubo diferencias estadísticamente significativas al comparar LT4 y agua frente a LT4 y tereré (Cmax: 16,36µg/dl, p=0,29; Tmax: 4hs, p=0,09; y %Abs 90,76%, p=0,15). En cuanto a ΔTSH, LT4 y agua resultaron en 1,1uUI/ml versus LT4 y mate 1,09uUI/ml (p= 0,96) o LT4 y tereré 1,35uUI/ml (p= 0,31), sin diferencias estadísticamente significativas. **Conclusiones:** La absorción de LT4 fue menor cuando la administración fue con mate y no con tereré, en comparación con agua.

Palabras clave: levotiroxina, *Ilex paraguariensis*, yerba mate, terere, absorción.

Introduction

Intestinal absorption of levothyroxine (LT4), a synthetic hormone indicated for hypothyroidism, is affected by medications and foods [1–9]. Mate and tereré are traditional ways of consuming *Ilex paraguariensis* (IP) as hot and cold infusions, respectively, widely consumed in Paraguay and other Southern Cone regions [10–13]. No studies evaluating LT4 absorption with IP were identified in the reviewed literature.

The objective of this study was to assess whether IP infusions reduce LT4 bioavailability using a pharmacokinetic model comparing LT4 absorption with mate/tereré versus plain water in healthy euthyroid adult volunteers.

Materials and Methods

Study Design and Participants

This was a randomized, pharmacokinetic, controlled, crossover, open-label clinical trial in which twenty (20) healthy volunteers were randomly selected by order of enrollment to participate from January to June 2022. The main inclusion criteria were being over 18 years of age and having signed informed

consent. All volunteers underwent an initial evaluation (clinical, laboratory, and imaging assessments) and were determined to be healthy euthyroid individuals not taking any medication and without thyroid disease history. The main exclusion criteria were pregnancy or breastfeeding; allergy to levothyroxine; and lactose intolerance. Subjects were excluded if a urine pregnancy test was positive or indeterminate, or if a serum thyrotropin (TSH) test was abnormal.

Interventions

A single 1000 µg dose of LT4 (Synthroid®, Abbott Laboratories) was administered with plain water, mate (500 mL, 80–85 °C), and tereré (500 mL, 2–5 °C), with a three-week washout period between administrations (Figure 1). All participants followed a standardized diet supervised by a certified nutritionist throughout each study day. Organic yerba mate (*Ilex paraguariensis*), 100% organic (Itabo®, Agroindustrial Chololó), from the same production batch and without any added compounds, was used.

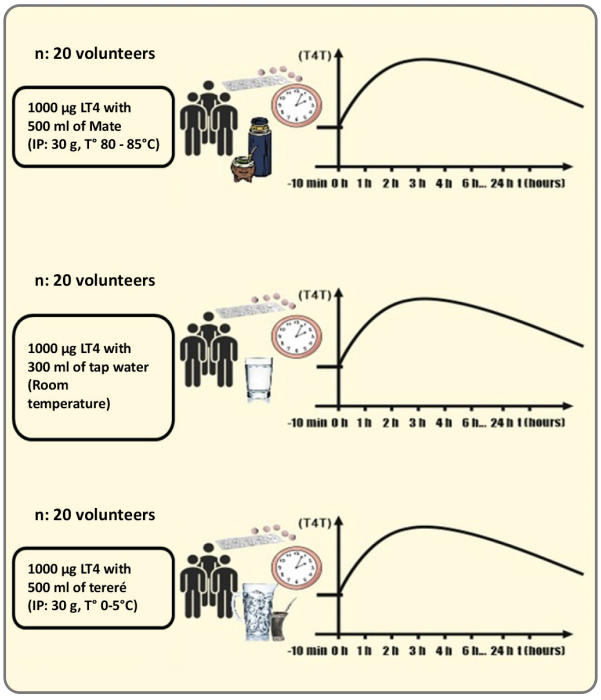

Figure 1. Evaluation of levothyroxine absorption with the consumption of mate and tereré in euthyroid volunteers. *n* = sample; LT4 = levothyroxine; TT4 = total thyroxine; *t* = time; IP = infusion preparation; T° = temperature in Celsius; µg = microgram; g = gram; mL = milliliter.

Assessments

After venous catheterization, serial blood samples for total thyroxine (TT4) were collected at -10 minutes, 0 hours (hs), 1, 2, 3, 4, 6, and 24 hours, comparing mean hourly TT4 concentrations, mean peak plasma TT4 concentrations (Cmax), time to Cmax (Tmax), thyroid-stimulating hormone (TSH) variation (ΔTSH), and estimated percentage of TT4 absorption (%Abs) which was calculated by multiplying the maximum increase in TT4 (ΔTT4max) by the volume of distribution (Vd). The volume of distribution is correlated with body mass index (BMI) using the following equation: Vd = 0.442 x BMI.

Statistics

Sample size was determined to ensure sufficient power to detect a clinically relevant difference in the estimated percentage of LT4 absorption (%Abs) between the groups consuming LT4 with plain water and those consuming it with mate or tereré. Based on preliminary pilot studies and a review of the existing literature, we anticipated a minimum detectable difference in %Abs of 15% between treatments, with an expected standard deviation of 20%. Assuming a significance level (α) of 0.05 and aiming for a power (1-β) of 80%, the required sample size was calculated using the formula for comparing means in two independent samples. Blood TSH and TT4 measurements were performed using electrochemiluminescence immunoassay. All Synthroid® tablets used for the study were from the same manufacturing lot. Area under the curve (AUC) values were constructed for serum TT4 concentrations versus time.

Before comparing the treatment effects on serum TT4 concentrations, we assessed the homogeneity of variances between groups using Levene's test. The results indicated that variances were homogeneous between groups ($p > 0.05$), allowing the use of paired t-tests for statistical comparisons. For each participant, differences in pharmacokinetic parameters were compared between mate and tereré versus tap water. We used paired t-tests to assess the mean differences in Cmax, Tmax, %Abs, and ΔTSH associated with mate or tereré intake versus tap water, and p-values <0.05 were considered statistically significant.

Results

Forty two volunteers enrolled and were screened according to the inclusion and exclusion criteria. Twenty volunteers were ultimately included, randomly selected according to the order of enrollment. All selected participants completed the trial (Figure 2). The mean age of these participants was 27.8 ± 0.71 years, with 15 women and 5 men, and an average BMI of 24.12 ± 1.99 kg/m². The Cmax with LT4 and tap water compared to LT4 and mate was 17.38 ± 2.75 µg/dl and 14.95 ± 2.64 µg/dl, respectively (p=0.02), while with LT4 and plain water compared to LT4 and tereré it was 16.36 ± 2.46 µg/dl (p=0.29) (Figure 3).

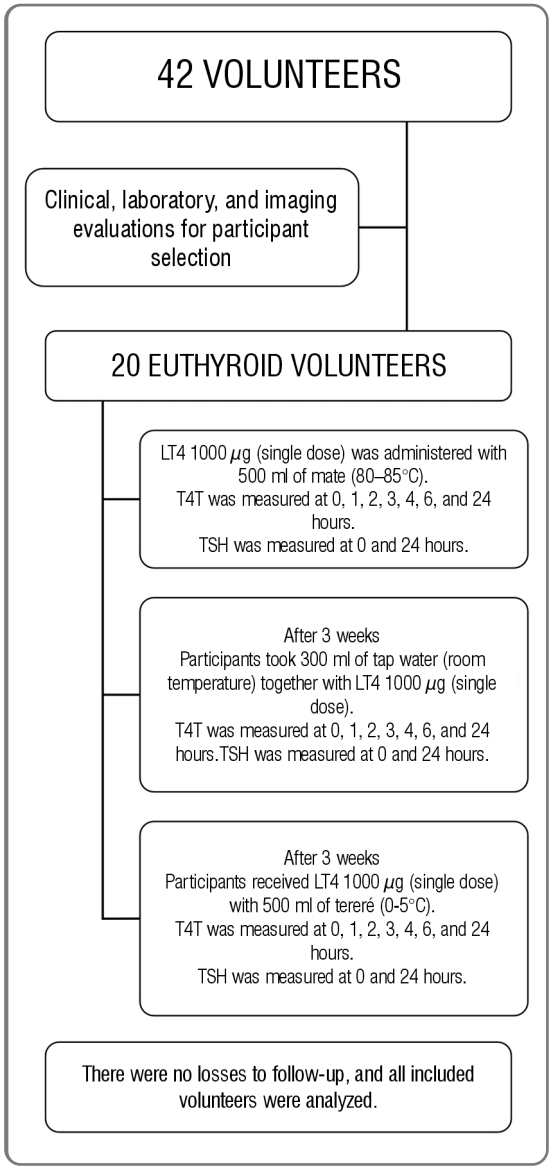

Figure 2. Flow diagram of participants according to CONSORT.

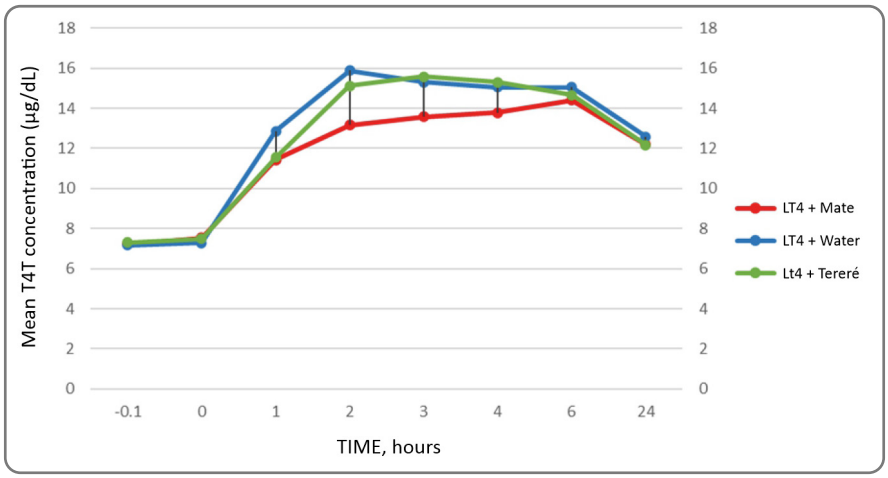

Figure 3. Maximum concentrations (Cmax) and time to reach Cmax (Tmax) of total thyroxine in blood (TT4), and percentage of levothyroxine absorption (LT4) (%Abs) in volunteer subjects, FCM UNA-2022.

A—Mean maximum plasma concentrations of TT4 (Cmax); the difference was statistically significant for mate compared with tap water, but not for tereré compared with tap water.

B—Mean time to reach TT4 Cmax (Tmax); the difference was statistically significant for mate compared with tap water, but not for tereré compared with tap water.

C—Mean estimated percentage of LT4 absorption (%Abs); the difference was statistically significant for mate compared with tap water, but not for tereré compared with tap water.

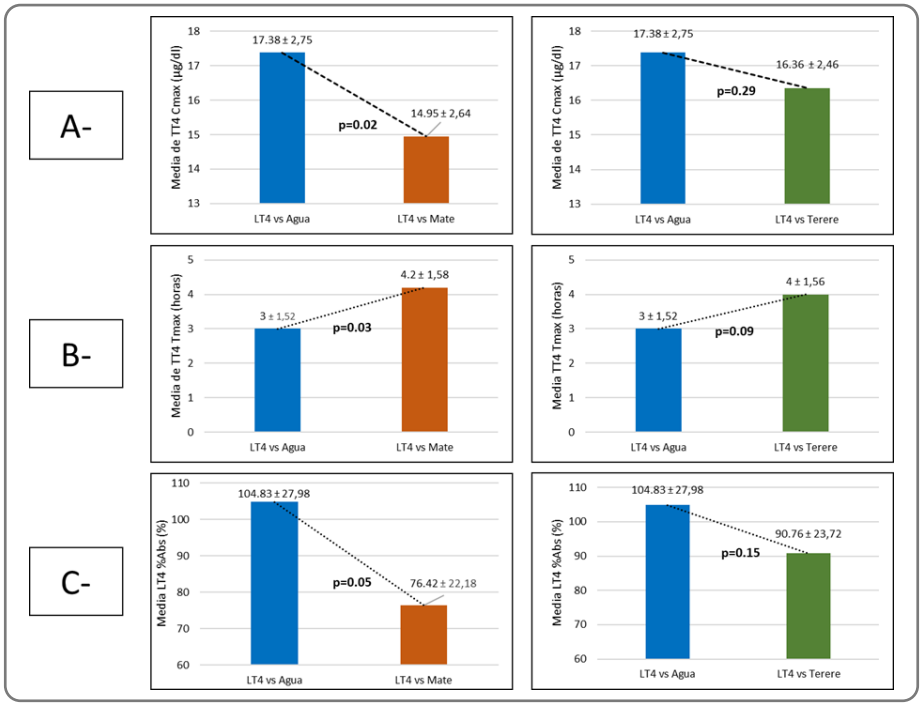

Figure 4. Serum TSH concentration before and after 24 hours of LT4 administration in volunteer subjects, HCSL-2022. No statistically significant differences were observed with any of the *Ilex paraguariensis* infusions compared with tap water. TSH = thyroid-stimulating hormone; LT4 = levothyroxine

The Tmax with LT4 and tap water versus LT4 and mate was 3 ± 1.52 h and 4.2 ± 1.58 h respectively (p=0.03) and compared with LT4 and tereré it was 4 ± 1.56 h (p=0.09). The %Abs with LT4 and tap water was 104.83% ± 27.98% compared with LT4 and mate 76.42% ± 22.18% (p=0.05) and LT4 and tereré 90.76% ± 23.72% (p=0.15). The differences were statistically significant for Cmax, Tmax and %Abs when comparing LT4 and running water versus LT4 and mate, however, there were no statistically significant differences in these 3 variables when comparing LT4 and water versus LT4 and tereré (Figure 4).

Regarding ΔTSH, when comparing the value achieved with running water it was 1.1 ± 0.45 uIU/ml, mate 1.09 ± 0.40 uIU/ml (p=0.96), tereré 1.35 ± 0.92 uIU/ml (p=0.31), there were no statistically significant differences when comparing LT4 and water versus LT4 and mate and LT4 and running water versus LT4 and tereré (Figure 5).

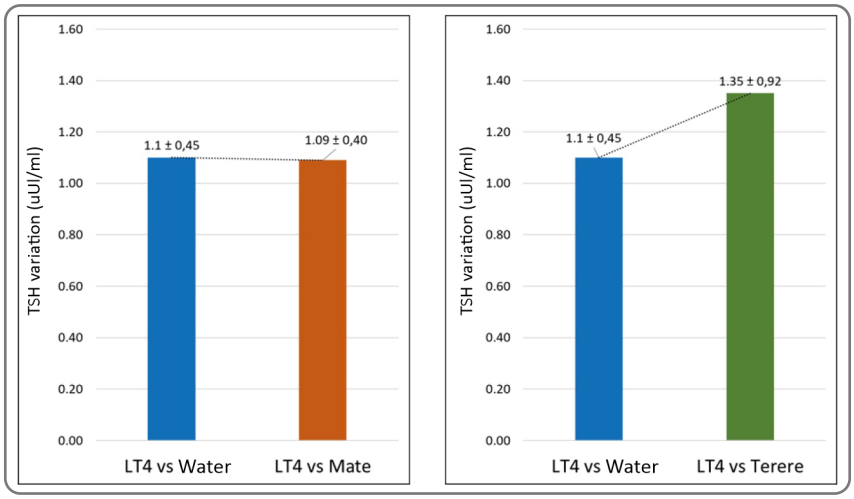

Figure 5. Total blood thyroxine (TT4) absorption after ingestion of 1000 µg of oral levothyroxine (LT4) with mate, tereré, and tap water.

Discussion

This paired experimental clinical trial observed significant differences in sodium LT4 absorption depending on the IP infusion used to administer the drug, with lower absorption occurring with mate but not with tereré compared to plain water. Several factors, including age, weight, patient adherence to treatment, medications such as calcium [14-15], proton pump inhibitors [3,16], ferrous sulfate [17], foods such as coffee [5,18], milk [4], grapefruit juice [19], as well as chronic pathologies and malabsorptive diseases, gut microbiota, and pregnancy, have been associated with decreased LT4 absorption [20-23].

Benegas et al., in 1995, observed the lack of decrease in TSH in patients who consumed LT4 close to breakfast and by separating breakfast one hour from the drug they corroborated the improvement in the therapeutic objectives, coinciding with the observations of Wenzel, in 1977 [24].

In 1993, a trial determined that the consumption of various fiber supplements (oat bran, soy fiber, and psyllium husk) reduced the bioavailability of LT4 in 13 patients with hypothyroidism, explaining the decrease in drug absorption through an adsorption mechanism. However, Chiu and Sherman evaluated the influence of administering 3.4 grams of psyllium husk on the absorption of 600 µg of levothyroxine and, after verifying that the amount of drug absorbed, determined during the 6 hours

following ingestion, decreased by only 9%, concluded that this fiber does not cause malabsorption of levothyroxine [25]. It can be deduced that drug absorption depends not only on fasting but also on other factors in the intestinal lumen. LT4 is poorly soluble in water and its uptake depends on transmembrane transporters, of which OATP-A and OATP-E have been reported to be expressed in the intestinal wall, which could be involved in the absorption of LT4 [26-27].

In the present study, a statistically significant decrease in the absorption of LT4 administered with mate was observed compared to administration with tap water. However, this phenomenon was not replicated when LT4 was administered with tereré. Whether this is due to the activation of absorption-inhibiting compounds by the increased temperature of the infusion or is an effect of temperature "per se" is a question that warrants further investigation.

The xanthines found in IP include theophylline (1,3-dimethylxanthine), theobromine (3,7-dimethylxanthine), and caffeine (1,3,7-trimethylxanthine). The latter is present in higher concentrations, from 1% to 2% of the dry weight, followed by theobromine, at 0.3% to 0.9% of the dry weight. The caffeine concentration in a hot infusion of IP is approximately 78 mg of caffeine in one cup of tea (approximately 150 ml). Compared to coffee, this is a very similar amount of caffeine consumption, approximately 85 mg per cup. However, the typical volume of mate consumed prepared using the traditional method can be around 1000 ml, resulting in 520 mg or more of total caffeine [28]. A study published in 2021 at the 6th meeting of researchers of the Scientific Society of Paraguay analyzed several domestically produced infusions of ibuprofen (IP) at different temperatures and found a higher concentration of certain trace elements when the infusion was consumed as mate compared to tereré (iron 1.98 ± 0.14 mg/100g of IP vs 0.12 ± 0.03 mg/100g of IP; manganese 2.31 ± 0.6 mg/100g of IP vs 1.77 ± 0.8 mg/100g of IP; potassium 93.5 ± 10.8 mg/100g of IP vs 64.6 ± 24.4 mg/100g of IP; sodium 1.52 ± 1.12 mg/100g of IP vs 0.87 ± 0.37 mg/100g of IP) [29]. These differences in composition in the infusion forms would initially answer the questions raised in the previous paragraph.

Another factor observed in the present study is the variation in the rate of infusion ingestion. When mate was administered, the average consumption of 500 ml took approximately 30 to 40 minutes, whereas for tereré, this time decreased to between 15 and 20 minutes. This variability could account for the change in absorption, coinciding with the other measured variables.

Among the strengths of the study, one could cite the standardization of the diet for all participants under the direction of a certified nutritionist, to avoid variations related to differences in intake during the measurement period, and the use of organic yerba mate without additives that could alter the interpretation of the data, considering that there is a variety of commercially available yerba mate with different added contents such as flavorings.

Limitations of the study include the small sample size and the inclusion of healthy subjects; therefore, the findings cannot be strictly extrapolated to patients with hypothyroidism and other comorbidities. However, it is presumable that these results could be reproduced, potentially to an even greater extent, in the population with the pathology.

Based on these findings, it is suggested that research continue and be extrapolated to prospective studies in patients with hypothyroidism, in order to provide recommendations on IP infusions for the population consuming LT4. However, careful monitoring of subjects taking mate and concomitant levothyroxine could be considered to detect changes in thyroid function tests. If such a change occurs, it would be advisable to separate the infusion and the levothyroxine [30-32].

Based on our findings, a reasonable approach would be to carefully monitor subjects consuming mate concomitantly with LT4 to detect fluctuations in thyrotropin levels, and even to advise separating the ingestion of these infusions from levothyroxine administration, in the same manner as recommended for other previously studied products.

The habit of consuming Ilex paraguariensis (IP) in the form of infusions specifically tereré and mate in Paraguay, and mate particularly in Argentina, Uruguay, and Brazil is part of the ancestral culture of the countries in the region and is a widespread practice across populations of all socioeconomic levels. Given that hypothyroidism is a very common endocrinological disorder, our data are of public health interest with a view toward optimizing treatment for patients affected by this condition.

In conclusion, in this clinical trial of healthy volunteers, it was found that LT4 absorption was lower when administered with mate, whereas this was not the case when administered with tereré, compared to administration with plain water. Therefore, these data are of interest for optimizing hypothyroidism treatment in regions of the world where this custom prevails.

Ethical Considerations

The principles of autonomy and justice were respected; during the selection of the study population, no discrimination of any kind was exercised. During the trial, participants were free to withdraw from the study at any time upon request. The principle of non-maleficence was adhered to; all selected participants entered the protocol following an exhaustive clinical assessment. The LT4 doses used in the trial were well below the toxic doses described in the literature. Toxicity has not been observed with doses lower than 5 mg; reaching the toxicity threshold would require ingesting between 30 and 40 times the daily dose (30,31,32).

Study and consent procedures were evaluated and approved by the Ethics Committee of the Faculty of Medical Sciences of the National University of Asunción. Subjects provided written informed consent prior to entering the study.

Records of the studies conducted during the trial were entered into the Health Information System (HIS) of the Hospital de Clínicas, affiliated with the Faculty of Medical Sciences of the National University of Asunción.

Authors' contributions: The authors declare their contribution to the design and conception of the protocol, data collection and analysis, and evaluation of the final manuscript.

Conflicts of Interest: The authors declare no conflicts of interest.

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Bibliographic References

1. Read DG, Hays MT, Hershman JM. Absorption of oral thyroxine in hypothyroid and normal man. J Clin Endocrinol Metab. 1970;30(6):798-9. doi: 10.1210/jcem-30-6-798.
2. Abi-Abib RC, Vaisman M. É necessário aumentar a dose de levotiroxina em pacientes com hipotireoidismo que usam omeprazol? Arq Bras Endocrinol Metabol. 2014;58(7):731-6. doi: 10.1590/0004-2730000002997.
3. Guzman-Prado Y, Vita R, Samson O. Concomitant Use of Levothyroxine and Proton Pump Inhibitors in Patients with Primary Hypothyroidism: a Systematic Review. J Gen Intern Med 2021;36(6):1726-33. doi: 10.1007/s11606-020-06403-y.
4. Chon DA, Reisman T, Weinreb JE, et al. Concurrent Milk Ingestion Decreases Absorption of Levothyroxine. Thyroid 2018;28(4):454-7. doi: 10.1089/thy.2017.0428.
5. Benvenga S, Bartolone L, Pappalardo MA, et al. Altered intestinal absorption of L-thyroxine caused by coffee. Thyroid 2008;18(3):293-301. doi: 10.1089/thy.2007.0222.
6. Wegrzyn NM. Malabsorption of L-T4 Due to Drip Coffee: A Case Report Using Predictors of Causation. J Acad Nutr Diet. 2016;116(7):1073-5; doi: 10.1016/j.jand.2016.02.016.
7. Lilja JJ, Laitinen K, Neuvonen PJ. Effects of grapefruit juice on levothyroxine absorption. Br J Clin

Pharmacol. 2005;63(3):337-41. doi: 10.1111/j.1365-2125.2005.02433.x.

8. Wiesner A, Gajewska D, Paśko P. Levothyroxine interactions with food and dietary supplements: a systematic review. Pharmaceuticals (Basel). 2021;14(3):206. doi: 10.3390/ph14030206.
9. Benvenga S. L-T4 Therapy in the Presence of Pharmacological Interferents. Front Endocrinol (Lausanne). 2020;11:1-10. doi: 10.3389/fendo.2020.607446.
10. Dellacassa E, Bandoni A. El mate. Rev Fitoter 2001;1(4):269-78.
11. Dellacassa E, Cesio V, Vázquez A, et al. Yerba mate. Historia, uso y propiedades. Rev Asoc Quím Farm Urug. 2007;51:16-20.
12. Ríos F. Efectos de la Ilex paraguariensis (yerba mate) en el electroencefalograma y en procesos cognitivos asociados a la percepción, atención y memoria ;monografía. Montevideo: Universidad de la República; 2019. doi: 10.26438/21011.
13. Capdevila R. El tereré es patrimonio cultural de la humanidad. UNESCO; 2020. Disponible en: https://www.unesco.org/es/articles/el-terere-es-patrimonio-cultural-de-la-humanidad.
14. Singh N, Weisler SL, Hershman JM. The acute effect of calcium carbonate on the intestinal absorption of levothyroxine. Thyroid 2001;11(10):967-71. doi: 10.1089/105072501753211046.
15. Zamfirescu I, Carlson HE. Absorption of levothyroxine when coadministered with various calcium formulations. Thyroid 2011;21(5):483-6. doi: 10.1089/thy.2010.0296.
16. Sachmechi I, Reich DM, Aninyei M, et al. Effect of proton pump inhibitors on serum thyroid-stimulating hormone level in euthyroid patients treated with levothyroxine for hypothyroidism. Endocr Pract 2007;13(4):345-9. doi: 10.4158/EP.13.4.345.
17. Shakir KM, Chute JP, Aprill BS, et al. Ferrous sulfate-induced increase in requirement for thyroxine in a patient with primary hypothyroidism. South Med J 1997;90(6):637-9; doi: 10.1097/00007611-199706000-00011.
18. Belayneh A, Molla F. The Effect of Coffee on Pharmacokinetic Properties of Drugs : A Review. Biomed Res Int 2020 ;2020:7909703. doi: 10.1155/2020/7909703.
19. Lilja JJ, Laitinen K, Neuvonen PJ. Effects of grapefruit juice on the absorption of levothyroxine. Br J Clin Pharmacol 2005;60(3):337. doi: 10.1111/j.1365-2125.2005.02433.x.
20. McMillan M, Rotenberg KS, Vora K, et al. Comorbidities, concomitant medications, and diet as factors affecting levothyroxine therapy: results of the CONTROL Surveillance Project. Drugs RD. 2016;16(1):53-68. doi: 10.1007/s40268-015-0116-6.
21. Alexander EK, Pearce EN, Brent GA, et al. 2017 Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease during Pregnancy and the Postpartum. Thyroid 2017;27(3):315-89. doi: 10.1089/thy.2016.0457.
22. Colucci P, Yue CS, Ducharme M, et al. A review of the pharmacokinetics of levothyroxine for the treatment of hypothyroidism. Eur Endocrinol 2013;9(1):40-7. doi: 10.17925/EE.2013.09.01.40
23. Jonklaas J. Sex and age differences in levothyroxine dosage requirement. Endocr Pract 2010;16(1):71-9. doi: 10.4158/EP09257.OR.
24. Benvenga S, Bartolone L, Squadrito S, et al. Delayed intestinal absorption of levothyroxine. Thyroid 1995;5(4):249-53. doi: 10.1089/thy.1995.5.249.
25. Chiu AC, Sherman SI. Effects of pharmacological fiber supplements on levothyroxine absorption. Thyroid 1998;8(8):667-71. doi: 10.1089/thy.1998.8.667.
26. Van Der Deure WM, Peeters RP, Visser TJ. Molecular aspects of thyroid hormone transporters, including MCT8, MCT10, and OATPs, and the effects of genetic variation in these transporters. J Mol Endocrinol 2010;44(1):1-11. doi: 10.1677/JME-09-0042.
27. Schweizer U, Johannes J, Bayer D, et al. Structure and Function of Thyroid Hormone Plasma Membrane Transporters. Eur Thyroid J. 2014;3 (3):143-53. doi: 10.1159/000367858.
28. Heck CI, De Mejia EG. Yerba mate tea (Ilex paraguariensis): A comprehensive review on chemistry, health implications, and technological considerations. J Food Sci. 2007;72(9):R138-51. doi: 10.1111/j.1750-3841.2007.00535.x.
29. Mereles L, Caballero S, Eva C, et al. Bebidas a base de yerba mate nacional: propiedades nutricionales, estimulantes y antioxidantes. In: VI Encuentro de Investigadores de la Sociedad Científica del Paraguay; 2021; Asunción.
30. De Luis DA, Abad L, Aller R, González-Sagrado M, Dueñas A. Intoxicacíon con levotiroxina: Manifestaciones clínicas y manejo terapéutico. An Med Interna. 2004;21(1):39.
31. Tunget CL, Clark RF, Turchen SG, Manoguerra AS. Raising the decontamination level for thyroid hormone ingestions. Am J Emerg Med. 1995;13(1):9-13. doi: 10.1016/0735-6757(95)90231-7.
32. Tiara D, Masruhim MA. Ficha técnica. Samarinda (ID): Laboratorium Penelitian dan Pengembangan FARMAKA Tropis, Fakultas Farmasi, Universitas Mulawarman; 2016. p. 5-24.