

Thyroid-gut axis: the relationship between gut microbiota and hypothyroidism

Eje tiroides-intestino: la relación entre la microbiota intestinal y el hipotiroidismo

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Abstract: Objective: Systematically review recent scientific literature regarding the relationship between gut microbiota and hypothyroidism. **Methods:** A bibliographic search was conducted in PubMed and Frontiers databases using descriptors "gut microbiota", "hypothyroidism", "thyroid diseases", and "Mendelian randomization". Articles from the last two years directly addressing this relationship were included. **Results:** Eight studies were selected, demonstrating a significant association between gut microbiota alterations and the development or worsening of hypothyroidism. Reductions in short-chain fatty acid-producing bacteria, specific metabolites directly affecting thyroid function, and causal associations confirmed by robust studies were observed. **Conclusion:** There is a significant interaction between gut microbiota and hypothyroidism, indicating that dietary interventions targeting microbiota modulation could positively influence thyroid health, thus warranting further clinical research.

Keywords: Gut microbiota; Hypothyroidism; Dysbiosis; Metabolism; Nutrition.

Resumen: Objetivo: Revisar sistemáticamente la literatura científica reciente sobre la relación entre la microbiota intestinal y el hipotiroidismo. **Métodos:** Se realizó una búsqueda bibliográfica en las bases de datos PubMed y Frontiers utilizando los descriptores "microbiota intestinal", "hipotiroidismo", "enfermedades tiroideas" y "aleatorización mendeliana". Se incluyeron artículos de los últimos dos años que abordaban directamente esta relación. **Resultados:** Se seleccionaron ocho estudios que demostraron una asociación significativa entre las alteraciones de la microbiota intestinal y el desarrollo o agravamiento del hipotiroidismo. Se observaron reducciones en bacterias productoras de ácidos grasos de cadena corta, metabolitos específicos que afectan directamente la

función tiroidea, y asociaciones causales confirmadas por estudios robustos. **Conclusión:** Existe una interacción significativa entre la microbiota intestinal y el hipotiroidismo, lo que sugiere que las intervenciones dietéticas dirigidas a la modulación de la microbiota podrían influir positivamente en la salud tiroidea. Estos hallazgos respaldan la necesidad de realizar más investigaciones clínicas.

Palabras clave: Microbiota intestinal; Hipotiroidismo; Disbiosis; Metabolismo; Nutrición.

1 INTRODUCTION

Hypothyroidism is a commonly diagnosed clinical condition that affects millions of people worldwide. It is characterized by reduced production of thyroid hormones, which are essential for metabolism and the maintenance of various bodily functions. In recent years, the importance of gut microbiota has been widely discussed in the scientific literature, particularly regarding its role in the proper functioning of the thyroid gland, leading to the emergence of the thyroid-gut axis concept. A better understanding of this interaction may open new therapeutic avenues and significantly improve the clinical management of hypothyroidism.

Recent reviews have highlighted that imbalances in gut microbiota, known as dysbiosis, are associated with the development or worsening of thyroid diseases, especially hypothyroidism. Research indicates that intestinal bacteria can interfere with the absorption and metabolism of medications used to treat this condition and directly influence thyroid hormone synthesis through the modulation of specific metabolites (JIANG et al., 2022; VIRILI et al., 2024). Moreover, studies based on robust methodologies, such as Mendelian randomization, have corroborated the relevance of these associations (SHI et al., 2024; LIU et al., 2024).

Despite these advances, significant gaps remain in the precise understanding of the mechanisms involved in the microbiota-thyroid interaction, including the accurate identification of bacterial metabolites and their real influence on the clinical manifestations of hypothyroidism. Several studies still present divergent or limited results in terms of specificity and causality, reinforcing the continuous need for additional research to clarify these critical aspects.

In this context, the present study aims to conduct a systematic review of recent scientific literature to critically analyze the existing relationships between gut microbiota and hypothyroidism. Specifically, it seeks to synthesize current findings, identify emerging trends, and discuss controversial points regarding this interaction, thereby contributing to the foundation of future research and more effective clinical strategies for the prevention and treatment of hypothyroidism associated with microbiota alterations.

2 MATERIALS AND METHODS

This study was conducted through a systematic review of recent scientific literature, aiming to explore the existing relationships between gut microbiota and hypothyroidism, with emphasis on the interaction known as the thyroid-gut axis. To achieve this, a comprehensive bibliographic search was carried out in indexed scientific databases to collect updated information on the association between these two components.

The bibliographic search included scientific articles published in the last two years in internationally recognized electronic databases, such as PubMed and Frontiers. Specific descriptors were used, including the terms "gut microbiota", "hypothyroidism", "thyroid diseases", and "Mendelian randomization". These terms were selected to ensure that the search results were directly relevant to the main objective of the study.

The inclusion criteria encompassed clinical studies, systematic reviews, and observational studies that specifically addressed the relationship between gut microbiota alterations and thyroid dysfunctions, with a particular focus on hypothyroidism. Conversely, articles written in languages other than English or those that did not directly address the proposed theme were excluded.

After the initial screening and application of the inclusion and exclusion criteria, eight articles were selected for detailed analysis. Among these, studies using specific methodologies such as Mendelian randomization to investigate causal associations between gut microbiota and hypothyroidism were highlighted (SHI et al., 2024; LIU et al., 2024; XIE et al., 2023). In addition, systematic reviews that analyzed the interaction between microbiota and thyroid functions were included, providing a more integrated view of the topic (STRAMAZZO et al., 2023; VIRILI et al., 2024).

Furthermore, studies that addressed specific metabolites produced by the gut microbiota and their direct implications on thyroid gland functions were analyzed, significantly contributing to the understanding of the mechanisms involved in the microbiota-thyroid interaction (JIANG et al., 2022; MENDOZA-LEÓN et al., 2023).

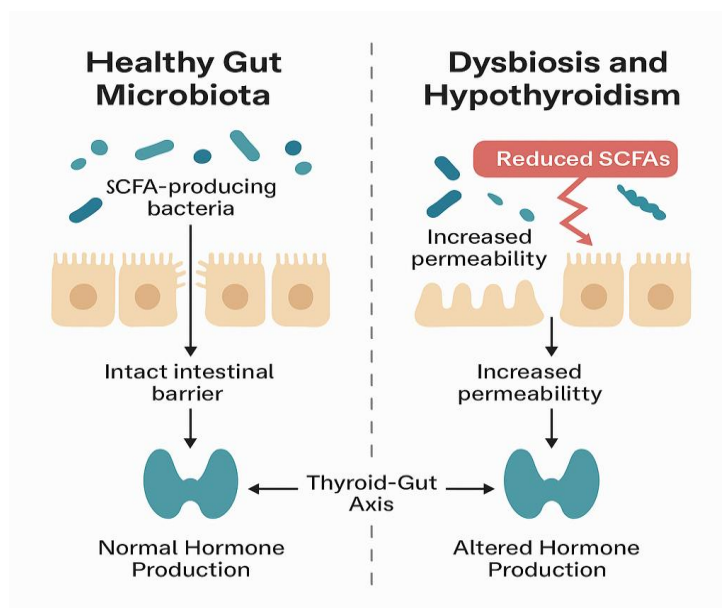
Due to the bibliographic review nature of this study, there was no need for Research Ethics Committee (REC) approval. The analysis of the results was conducted qualitatively, allowing a detailed interpretative approach to the connections evidenced in the recent scientific literature.

3 RESULTS

The systematic review identified eight relevant studies published in the last two years. Among these, investigations employing advanced methodologies such as Mendelian randomization stood out, having established causal associations between gut microbiota and hypothyroidism. Several studies revealed specific alterations in gut bacteria associated with hypothyroidism, including the reduction

of short-chain fatty acid (SCFA)-producing bacteria (MENDOZA-LEÓN et al., 2023). **Figure 1** visually compares the state of a healthy gut microbiota with that of dysbiosis, highlighting their effects on intestinal permeability and thyroid hormone production.

Figure 1: Healthy Gut Microbiota vs. Dysbiosis and Hypothyroidism.



In addition, recent systematic reviews confirmed the strong association between intestinal dysbiosis and functional alterations of the thyroid gland, particularly in relation to the metabolism and absorption of thyroid hormones (STRAMAZZO et al., 2023; VIRILI et al., 2024). **Table 1:** Illustrates the frequency of the main bacterial alterations associated with hypothyroidism identified in the reviewed studies, highlighting the most frequently involved bacteria in the dysbiosis observed in these patients.

Table 1. Characteristics of the studies included in the review

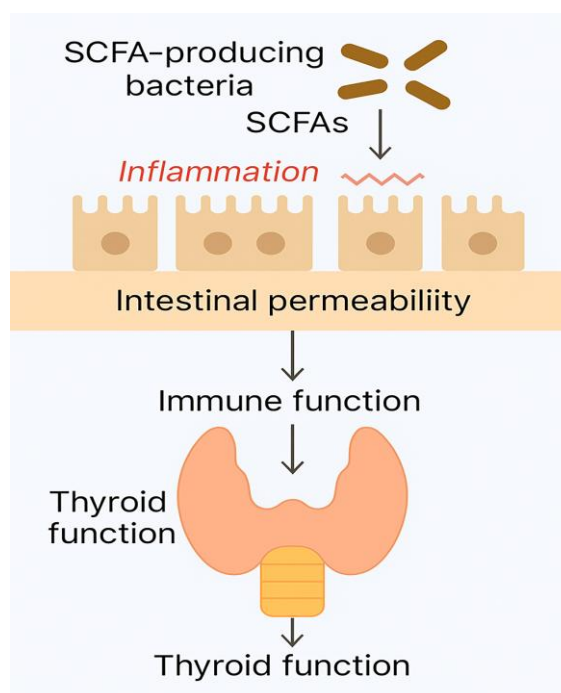
Author	Year	Study Type	Main Findings
Jiang et al.	2022	Review	Influence of bacterial metabolites on thyroid function
Shi et al.	2024	Mendelian Randomization	Causal association between gut microbiota and hypothyroidism
Liu et al.	2024	Mendelian Randomization	Causal association of gut microbiota and autoimmune hypothyroidism
Mendoza-León et al.	2023	Observational	Reduction of SCFA-producing bacteria in hypothyroidism

*SCFA: Short-chain fatty acids.

The analysis also highlighted that specific microbial metabolites may play critical roles in modulating thyroid function, particularly through the regulation of intestinal inflammation and permeability (JIANG et al., 2022; SHI et al., 2024). Findings from these studies suggest that dietary interventions aimed at modulating the microbiota could yield beneficial effects on thyroid health.

Figure 2: Demonstrates the role of short-chain fatty acids (SCFAs) produced by gut bacteria in protecting the intestinal barrier and maintaining proper thyroid function.

Figure 2: Mechanism of SCFA action in intestinal barrier protection and thyroid function.



4 DISCUSSION

This study aimed to evaluate recent literature on the relationship between gut microbiota and hypothyroidism, in order to clarify potential mechanisms and propose future directions for research and clinical practice.

The reviewed findings consistently demonstrate that alterations in gut microbiota are associated with hypothyroidism. Particularly notable is the role of metabolites produced by intestinal bacteria, such as short-chain fatty acids (SCFAs), which directly influence thyroid function (MENDOZA-LEÓN et al., 2023).

These results are supported by other studies that identified direct connections between changes in gut microbiota and thyroid disorders, suggesting a significant bidirectional interaction within the thyroid-gut axis (VIRILI et al., 2024). **Figure 3:** The thyroid-gut axis is characterized by hormonal, immunological, and metabolic communication pathways between the gut microbiota and the thyroid gland, contributing to the organism's functional balance.

Figure 3: Conceptual model of the thyroid-gut axis.

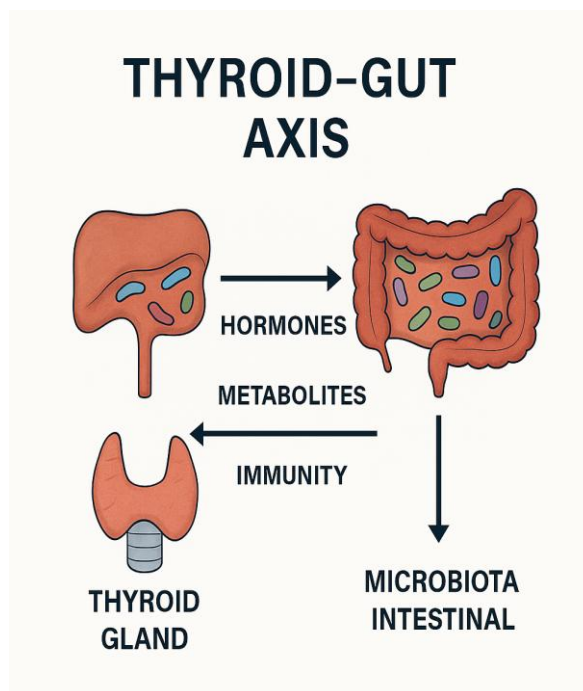


Table 2: Summarizes the causal relationships established by the reviewed studies, highlighting the bidirectional interaction and the main biological pathways involved in the influence of gut microbiota on thyroid function.

Table 2. Main bacterial metabolites related to thyroid function

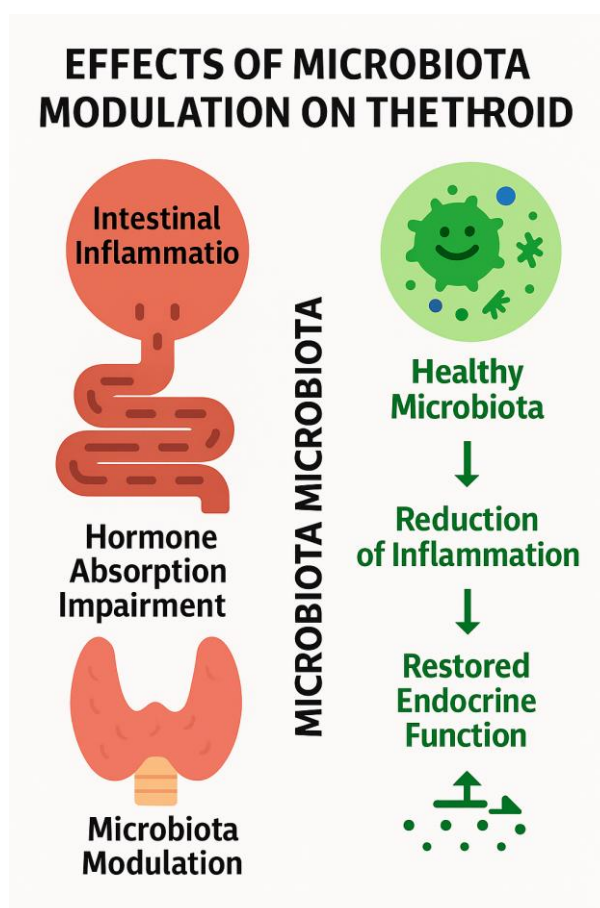
Metabolite	Thyroid Function Impact
Short-chain fatty acids (SCFAs)	Modulate intestinal inflammation and permeability, influencing thyroid autoimmunity
Propionic acid	Directly influences thyroid hormone synthesis
Butyric acid	Positive impact on intestinal barrier and potential reduction of hypothyroidism-related inflammation

In clinical practice, understanding these relationships may assist in the early identification of patients at increased risk of hypothyroidism through microbiota analysis. Specific nutritional interventions could be developed to correct dysbiosis, aiming to prevent or alleviate disease-related symptoms.

It is important to emphasize that maintaining a healthy balance of gut microbiota may also enhance the therapeutic efficacy of thyroid medications, positioning microbiota modulation as a

promising complement to traditional approaches. **Figure 4:** Graphically summarizes the effects of microbiota modulation on intestinal inflammation, hormone absorption, and the endocrine function of the thyroid gland.

Figure 4: Effects of microbiota modulation on inflammation, hormone absorption, and thyroid function.



On the other hand, drastic dietary changes or interventions intended to alter gut microbiota require careful evaluation of potential risks and benefits, especially considering individual variability in treatment responses.

Moreover, it is not yet clearly established whether gut microbiota manipulation offers benefits superior or equivalent to current conventional therapies, highlighting the need for additional high-quality methodological studies.

Healthcare professionals should remain attentive to emerging evidence and consider evaluating and modulating gut microbiota as a potential complementary strategy in the management of hypothyroidism.

Finally, it is essential to acknowledge the limitations of this study, including the small number of available articles and the methodological heterogeneity among them. These limitations should be considered when interpreting the results and designing future research in this field.

5 CONCLUSION

This literature review clearly demonstrated a significant association between gut microbiota and hypothyroidism, highlighting the potential therapeutic role of microbiota modulation in the clinical approach to this condition. However, there is still a need for additional studies to deepen the understanding of the mechanisms involved and to more precisely clarify causal relationships. Current evidence suggests that targeted nutritional interventions may become important complementary tools in the treatment and clinical management of hypothyroidism, thereby justifying future investigations in this promising field.

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