LONDON JOURNAL
OF
INTERDISCIPLINARY SCIENCES

eISSN 3049-7809

In Silico Screening and Multi-Target Molecular Docking of Golden Berry (*Physalis angulata* L.) and Basil (*Ocimum basilicum* L.) Phytocompounds as Nutraceutical Leads for Graves' Disease Therapy

Aiesha Vania Kirani Thahira*

Amelia Ciptaningdyah Hapsari**

Abstract

Graves' disease (GD) is an autoimmune thyroid disorder characterized by excessive immune activation and abnormal thyroid hormone regulation. Conventional therapy is ineffective due to high costs and serious side effects, therefore highlighting the need for safer multi-target therapeutics. This study applied an integrated network pharmacology and molecular docking approach to elucidate the molecular mechanisms of *Physalis angulata* L. and *Ocimum basilicum* L. against GD. Gene enrichment revealed that common **targets were involved in inflammatory response, response to lipopolysaccharide, and cytokine receptor binding pathways**, with **hub proteins** including IL2, IGF1R, ICAM1, TNF, MPO, and ADRB2 localized at the cell surface and extracellular region. Molecular docking identified five active compounds with strong affinities: Physagulin M (IGF1R) −10.4 kcal/mol, Aesculin (IL2) −9.5 kcal/mol, Quercetin (IGF1R) −8.1 kcal/mol, and Kaempferol (IL2) −7.8 kcal/mol, all outperforming methimazole −4.1 (IL2) and −3.3 kcal/mol (IGFR1). . These results suggest that golden berries and basil exhibit immunomodulatory and hormone regulatory potential through multitarget inhibition of cytokine and receptor mediated pathways, providing promising nutraceutical candidates for GD management.

Keywords: Graves' disease, golden berry, basil, network pharmacology

https://doi.org/10.31039/ljis.2026.6.372

*SMA Kesatuan Bangsa, Indonesia, aiesha@kesatuanbangsa.sch.id

**SMA Kesatuan Bangsa, Indonesia, amelia@kesatuanbangsa.sch.id

1. Introduction

Graves' disease (GD) is an autoimmune disorder and the most frequent cause of hyperthyroidism estimated to be around 60-80% worldwide, also being responsible for the majority of hyperthyroidism cases in regions where iodine intake is adequate, reaching 70-80%. It occurs when autoantibodies overstimulate the thyroid-stimulating hormone receptor (TSHR), prompting the thyroid gland to release excessive thyroid hormones. This overactivity accelerates the body's metabolism, leading to symptoms of thyrotoxicosis. Besides TSHR activation, thyroid peroxidase (TPO) plays a vital role in the synthesis of thyroid hormones, where it catalyzes the iodination and coupling reactions essential for T3 and T4 production. Moreover, the activation of inflammatory pathways, particularly NF-κB and related pro-inflammatory cytokines can further aggravate thyroid autoimmunity, highlighting their importance as potential therapeutic targets.

As in populations with iodine deficiency, its prevalence decreases, accounting for roughly half of hyperthyroidism cases, while the remaining cases are primarily linked to nodular thyroid disorders. Studies show that hyperthyroidism has become something common in Asia. It occurred to 25,6% of Chinese males and 0.8% of Chinese females, 2% in India, 5.4% in northern Turkey, 4% in a hospital-based study conducted in central Nepal, and a prevalence of 6.9% hyperthyroidism cases in Indonesia. Therefore, Graves' disease is a serious health problem that will continue to increase and deserves attention. Genetic predisposition contributes to nearly 79% of the disease risk, whereas environmental factors such as tobacco use, excessive iodine intake, selenium and vitamin D deficiency, and viral infections significantly influence disease onset and progression conditions particularly relevant in tropical climates.

Treatment for GD commonly involves antithyroid medications such as methimazole (MMI) or propylthiouracil (PTU), radioactive iodine therapy (RAI), and thyroidectomy. The choice of treatment depends on several factors, including the patient's age, disease severity, cardiovascular history, goiter size, and availability of healthcare resources. Each option seeks to reduce excessive thyroid hormone production, but all have significant drawbacks. Antithyroid drugs often achieve remission in only half of the cases and are associated with relapse once treatment stops. They can also trigger severe adverse effects, including agranulocytosis, hepatotoxicity, or allergic reactions . In tropical regions, drug resistance has occasionally been reported, possibly due to reduced drug uptake in the thyroid gland. Moreover, methimazole exposure has been linked to insulin autoimmune syndrome, particularly among Asian populations [8]. RAI and surgical removal of the thyroid can effectively control hyperthyroidism but frequently result in lifelong hypothyroidism, as well as risks such as ophthalmopathy and laryngeal nerve damage. These limitations encourage exploration of herbal-derived compounds and in silico drug discovery to develop safer, affordable, and more effective therapies.

Golden Berry's herb (*Physalis angulata L.*) (PA) is often used in traditional medicine for years in subtropical and tropical regions. This plant is rich in bioactive compounds such as physalins, withanolides, flavonoids, and phenolics. Recent studies report its strong antiinflammatory, antioxidant, antidiabetic, and immunomodulatory activities through NF-κB

pathway regulation and oxidative stress inhibition. Physalins act as key immunosuppressive and antiinflammatory agents, while flavonoids like quercetin enhance antioxidant defense and tissue protection.

A study by Hidayat *et al*. [18] showed that ethanolic extract of golden berry effectively reduced TSH levels in propylthiouracil-induced Wistar rats, suggesting a regulatory effect on thyroid homeostasis. Similarly, an *in vivo* experiment by Parisa using golden berry extract revealed a marked decrease in thyroxine (T4) levels across doses of 250, 500, and 1000 mg/kg body weight compared to control groups, with statistically significant differences ($p < 0.05$). This indicates that PA. species possess bioactive compounds capable of modulating thyroid hormone synthesis, likely through antihyperthyroid or hormone stabilizing mechanisms and promising natural source for developing new therapeutic agents targeting autoimmune and inflammatory disorders. However, previous studies have not explained the specific mechanism of the compounds contained in golden berry extract, so it is not yet known which compounds have potential as a treatment for Graves' disease.

Similarly, Basil (*Ocimum basilicum L.*) (OB), a member of the mint family, has also been widely used in traditional medicine around the world since 5000 years ago. Basil is rich in phytochemical composition and a wide pharmacological spectrum. This aromatic herb contains diverse bioactive compounds, including linalool, eugenol, methyl chavicol, geraniol, methyl eugenol, *p*-allylanisole, 1,8–cineole, trans–α–bergamotene, and neryl acetate and rosmarinic acid, which contribute to its potent anticancer, antioxidant, antihypertensive antiinflammatory, antiparasitic, antifungal, antimicrobial, insecticidal, hepatoprotective, cardioprotective, antiosteoporotic, and immunomodulatory effects.

The study by Kamelnia *et al*. highlighted that the main constituents of basil, including linalool, eugenol, and phenolic acids, exhibit strong antiinflammatory and immunomodulatory activities through inhibition of the NF-*κ*B signaling pathway and reduction of pro-inflammatory cytokines (IL-6, TNF-*α*). Meanwhile, study by Habza-Kowalska *et al*. demonstrated that phenolic compounds such as rosmarinic acid and quercetin can inhibit the thyroid peroxidase (TPO) enzyme *in vitro* with low IC_{50} values, thereby potentially reducing excessive thyroid hormone synthesis under hyperthyroid conditions. The combination of antioxidant and antiinflammatory effects helps maintain endocrine system stability and reduces oxidative stress in thyroid tissues, making basil a promising natural source of agents that can act as TPO inhibitors while protecting against autoimmune induced thyroid damage in hyperthyroidism.

Despite the well-documented pharmacological properties of PA and OB, their specific molecular interactions with multiple GD targets, particularly TSHR, TPO, and NF-*κ*B, remain largely unexplored. Current studies have mainly focused on general anti-inflammatory or antioxidant effects rather than elucidating how individual phytocompounds might act synergistically to regulate thyroid hormone synthesis and autoimmune responses. Therefore, this research performs an in silico screening and multi-target molecular docking of key phytoconstituents from PA and OB against TSHR, TPO, and NF-κB to identify potential multitarget inhibitors with favorable bioavailability profiles.

To comprehensively elucidate these complex interactions, a network pharmacology approach is integrated, combining multi-omics and systems-level data to map relationships between bioactive compounds, target proteins, and disease pathways. Unlike conventional single-target methods, network pharmacology highlights synergistic and multi-target mechanisms typical of herbal medicines, enhancing predictive accuracy and uncovering key signaling pathways involved in GD. This holistic framework not only bridges computational biochemistry and systems pharmacology but also advances the development of sustainable, plant based nutraceutical therapeutics aligned with SDG 3 "Good Health and Well-being."

2. Literature Review

2.1 Theoretical Background

2.1.1 Grave's Disease and Hyperthyroidism

Graves' disease is defined as an autoimmune disorder that primarily affects the thyroid gland. The responsible mechanism is related to autoantibodies that bind and activate the thyrotropin receptor (TSHR), thereby stimulating excessive thyroid hormone production. Graves' disease represents the leading etiology of hyperthyroidism, accounting for approximately 60–80% of all cases.

2.1.2 Hyperthyroid Therapy

Researchers have discovered many chemical compounds with potential as free radical scavengers and antioxidants, potentially contributing to functional foods. These compounds include phenolics and flavonoids, which both are found in *O basilicum,* and *P angulata*. These compounds are found abundantly in plants and fruits, making them widely used as free radical scavengers and antioxidants. Functional food possesses constructive effects on target functions into the human organism, beyond nutritional effects, with aim of health promotion and wellbeing and/or the reduction of chronic diseases.

2.1.3 Basil (Ocimum basilicum L.)

Basil *(Ocimum basilicum* L.) is one of the most common aromatic herbs, a rich source of bioactive compounds. *O basilicums* contain important antioxidant compounds and essential oils, some of those are effective as an antithyroid. Quercetin, Rosmarinic acid, Rutin, Apigenin, Chlorogenic acid & Caffeic acid may show direct interference with thyroid biochemical targets or have antioxidant actions that mitigate secondary damage in hyperthyroidism. The nutrient content of common basil are dry matter (909.1 g kg−1), crude ash (89.84 g kg−1), crude protein (208.8 g kg−1), ether extract (11.21 g kg−1), crude fiber (45.91 g kg−1), NFI (sugars readily hydrolyzed) (553.3 g kg−1), Mg (79.8 µg g−1), Ca (1278 µg g−1), K (2135 µg g−1), Na (218.5 µg g−1), Fe (26.31 µg g−1), Cu (1.95 µg g−1), Mn (8.56 µg g−1) and Zn (45.14 µg g−1).

2.1.4 Golden Berry (*Physalis angulata L.*)

Golden berry (Physalis angulata L.) is a tropical and subtropical plant that grows on a large scale in Indonesia. It has many herbal and healing benefits, including as an antithyroid agent. In addition to its potential antithyroid activity, Physalis angulata L. exhibits antioxidant,

anti-inflammatory, and immune-modulating properties that may offer supportive benefits in oxidative stress-induced hyperthyroidism and immune dysfunction. Previous studies have not clarified the specific mechanisms of action of the compounds contained in ciplukan fruit extract, so it is unknown which compounds have potential as a treatment for hyperthyroidism. This aromatic herb contains various bioactive compounds, including linalool, eugenol, methyl chavicol, geraniol, and methyl eugenol, which contribute to its anticancer, antioxidant, antihypertensive, and anti-inflammatory effects.

2.1.5 Molecular Docking & Multi-Target Grave's Disease

The advent of computational compound design has offered a

promising avenue for the development of novel therapeutic strategies tailored to specific molecular targets. Despite the substantial progress made in silico compound design for

targeting the TSHR in GD, several critical gaps persist in the current literature. In silico studies have explored the potential of molecular hybridization for designing novel compound candidates with improved potency, selectivity, and reduced

side effects.

3. Conclusions

Finally, this paper provides a network pharmacology analysis demonstrating that PA and OB exert anti-Graves' disease activity through modulation of inflammatory and cytokine-mediated pathways involving IL2, IGF1R, TNF, ICAM1, MPO, and ADRB2. The enrichment analysis highlighted cytokine–cytokine receptor interaction and hormone receptor signaling as key biological pathways. Molecular docking identified five active compounds with strong affinities: Physagulin M (IGF1R) −10.4 kcal/mol, Aesculin (IL2) −9.5 kcal/mol, Quercetin (IGF1R) −8.1 kcal/mol, Kaempferol (IL2) −7.8 kcal/mol, and Thymol (ICAM1) −7.4 kcal/mol, all outperforming methimazole −4.1 (IL2) and −3.3 kcal/mol (IGFR1). These findings suggest that the synergistic phytoconstituents of golden berries and basil can act as multi-target immunomodulators, potentially attenuating autoimmune activation and thyroid hormone imbalance in Graves' disease.

Acknowledgement

This paper was presented at the 18th London International Conference, held in hybrid format (online and virtual) on April 22-24, 2026. It was subsequently published in the conference proceedings entitled *Proceedings of London International Conferences*, No. 16 (2026).

References

Anidha, Y., Ayu, W. C., Wulan Sari, N. M., & Nadhiroh, S. R. (2023). Risk Factors and Clinical Manifestations in Hyperthyroidism: A Systematic Review. Amerta Nutrition, 7.

Anjum, M. U., Durrani, A. U., Hussain, T., & Shah, S. H. (2016). Hyperthyroidism: Prevalence In Abbottabad, Pakistan: A Hospital Based Study. The Professional Medical Journal, 23(04), 401-405.

Baker, S., Miguel, R. N., Thomas, D., Powell, M., Furmaniak, J., & Smith, B. R. (2023). Cryo-electron microscopy structures of human thyroid peroxidase (TPO) in complex with TPO antibodies. Journal of Molecular Endocrinology, 70(3).

Burch, H. B., & Cooper, D. S. (2015). Management of Graves disease: a review. *Jama*, *314*(23), 2544-2554.

Dudai, N., Nitzan, N., & Gonda, I. (2020). Ocimum basilicum L.(Basil). In *Medicinal, aromatic and stimulant plants (pp. 377-405). Cham: Springer International Publishing.*

Dhama, K., Sharun, K., Gugjoo, M. B., Tiwari, R., Alagawany, M., Iqbal Yatoo, M., ... & Farag, M. R. (2023). A comprehensive review on chemical profile and pharmacological activities of Ocimum basilicum. Food Reviews International, 39(1), 119-147.

Giordani, I., & Sykiotis, G. P. (2025). A short review of current knowledge regarding long-term treatment of Graves' disease with antithyroid drugs. Hormones, 24(2), 347-358.

Hidayat, T., Subiantonny, A., & Yunitawati, D. (2015). Pengaruh Ekstrak Etanol Ciplukan Terhadap Penurunan Kadar Thyroid Stimulating Hormone (TSH) Tikus Jantan Galur Wistar Induksi Propylthiouracil. *Indonesian Journal of Micronutrition*, *7*(1), 11-24.

Habza-Kowalska, E., Kaczor, A. A., Żuk, J., Matosiuk, D., & Gawlik-Dziki, U. (2019). Thyroid peroxidase activity is inhibited by phenolic compounds—impact of interaction. Molecules, 24(15), 2766.

Imaduddin, U. K., Berbudi, A., & Rohmawaty, E. (2024). The effect of physalis angulata L. administration on gene expressions related to lung fibrosis resolution in mice-induced bleomycin. Journal of Experimental Pharmacology, 49-60.

Kalra, S., Selim, S., Shrestha, D., Somasundaram, N., Raza, S. A., Baruah, M. P., ... & Sahay, R. (2024). Best practices in the laboratory diagnosis, prognostication, prediction, and monitoring of Graves' disease: role of TRAbs. *BMC Endocrine Disorders*, *24*(1), 274.

Kamelnia, E., Mohebbati, R., Kamelnia, R., El-Seedi, H. R., & Boskabady, M. H. (2023). Anti-inflammatory, immunomodulatory and anti-oxidant effects of Ocimum basilicum L. and its main constituents: A review. Iranian journal of basic medical sciences, 26(6), 617.

Lanzolla, G., Marinò, M., & Menconi, F. (2024). Graves disease: latest understanding of pathogenesis and treatment options. *Nature Reviews Endocrinology*, *20*(11), 647-660.

Lu, Y., Xing, C., Zhang, C., Lv, X., Liu, G., Chen, F., ... & Zhang, D. (2022). Promotion of IL‐17/NF‐κB signaling in autoimmune thyroid diseases. *Experimental and Therapeutic Medicine*, *25*(1), 51.

Lee, W. Y., Park, K. I., Bak, S. B., Lee, S., Bae, S. J., Kim, M. J., ... & Kim, C. E. (2024). Evaluating current status of network pharmacology for herbal medicine focusing on identifying mechanisms and therapeutic effects. Journal of Advanced Research.

Mahzari, M. M., Alanazi, M. M., Alabdulkareem, Y. M., Alharbi, W. A., Alzahrani, A. S., Alqahtani, N. A., ... & Ardah, H. I. (2024). Efficacy of Anti-Thyroid Medications in Patients with Graves' Disease. BMC Endocrine Disorders, 24(1), 180.

Meira, C. S., Soares, J. W. C., Dos Reis, B. P. Z. C., Pacheco, L. V., Santos, I. P., Silva, D. K. C., ... & Soares, M. B. P. (2022). Therapeutic applications of physalins: powerful natural weapons. Frontiers in Pharmacology, 13, 864714.

Nagendra, L., Mondal, S., & Bhattacharya, S. (2024). Thyroid Disorders in the Tropics. *Endotext*.

Navarro-Hoyos, Mirtha, et al. "QTOF-ESI MS characterization and antioxidant activity of Physalis peruviana L. (Cape Gooseberry) husks and fruits from Costa Rica." Molecules 27.13 (2022): 4238.,

Parisa, N. (2019). Efek Ekstrak Buah Ciplukan (Physallis peruvenia) Pada Kadar T4 Tikus Putih. *Biomedical Journal of Indonesia*, *5*(3), 121-125.

Qamar, F., Sana, A., Naveed, S., & Faizi, S. (2023). Phytochemical characterization, antioxidant activity and antihypertensive evaluation of Ocimum basilicum L. in l-NAME induced hypertensive rats and its correlation analysis. *Heliyon*, *9*(4)

Ramakrishna Pillai, J., Wali, A. F., Menezes, G. A., Rehman, M. U., Wani, T. A., Arafah, A., ... & Mir, T. M. (2022). Chemical composition analysis, cytotoxic, antimicrobial and antioxidant activities of Physalis angulata L.: A comparative study of leaves and fruit. *Molecules*, *27*(5), 1480.

Tuan Anh, Hoang Le, et al. "Bioactive compounds from Physalis angulata and their anti-inflammatory and cytotoxic activities." Asian Journal of Natural Products Research 23.8 (2021): 809-817.

Taylor, P. N., Albrecht, D., Scholz, A., Gutierrez-Buey, G., Lazarus, J. H., Dayan, C. M., & Okosieme, O. E. (2018). Global epidemiology of hyperthyroidism and hypothyroidism. Nature Reviews Endocrinology, 14(5), 301-316.

Villagelin, D., Cooper, D. S., & Burch, H. B. (2024). A 2023 international survey of clinical practice patterns in the management of Graves disease: a decade of change. *The Journal of Clinical Endocrinology & Metabolism*, *109*(11), 2956-2966.

Wiraswati, H. L., Ekawardhani, S., Rohmawaty, E., Laelalugina, A., Zuhrotun, A., Hendriani, R., ... & Dewi, S. (2024). Antioxidant, antiinflammation, and antifibrotic activity of ciplukan (Physalis angulata L). extract. Journal of Inflammation Research, 6297-6306.

Smith, T. J., & Hegedüs, L. (2016). Graves' disease. *New England Journal of Medicine*, *375*(16), 1552-1565.

Yang, L., Wang, H., Zhu, Z., Yang, Y., Xiong, Y., Cui, X., & Liu, Y. (2025). Network Pharmacology-Driven Sustainability: AI and Multi-Omics Synergy for Drug Discovery in Traditional Chinese Medicine. *Pharmaceuticals*, *18*(7), 1074.