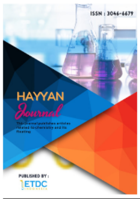

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Integrative Mapping of Phytochemistry, Pharmacology, Green Extraction, and Bioeconomics Peperomia pellucida (L.) Kunth: Systematic Literature Review

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ABSTRACT

This study aims to integrate scientific evidence on phytochemistry, pharmacology, green extraction, and bioeconomics *of Peperomia pellucida* (L.). Kunth through the *Systematic Literature Review* approach. The research was conducted by searching the Scopus database for articles using keywords related to *Peperomia pellucida*, phytochemicals, pharmacology, extraction, toxicology, antioxidants, antibacterial activity, and antidiabetic activity. Of the initial 89 articles, the selection process across identification, screening, eligibility, and inclusion yielded 34 articles for narrative analysis. The study found that *P. pellucida* contains various bioactive compounds, including flavonoids, alkaloids, tannins, saponins, phenols, terpenoids, steroids, lignans, phenylpropanoids, essential oils, dillapiole, quercetin, apigenin, stigmasterol, and fucosterol. The compound exhibits antioxidant, anti-inflammatory, antidiabetic, antibacterial, antihypertensive, anticancer, gastroprotective, neuroprotective, antiarthritis, antimalarial, and wound-healing activities. Extraction techniques such as maceration, solvent fractionation, MAE, IL-MAE, NADES, fermentation, drying, and gamma irradiation have been shown to affect compound content, biological activity, safety, and extract quality. This study concludes that *P. pellucida* has the potential to be developed as an ingredient in herbs, functional foods, phytopharmaceuticals, cosmetics, topical products, bioaccharicides, and bioeconomic commodities, but still requires standardization, safety validation, and further research.

Keywords: *Peperomia pellucida*, phytochemistry, pharmacology, green extraction, bioeconomics, *systematic literature review*

I. INTRODUCTION

Peperomia pellucida (L.) Kunth or Chinese betel is one of the tropical herbal plants that has received scientific attention due to its history of traditional use and potential as a raw material for modern herbal products. Previous research has shown that this plant grows widely in tropical and subtropical regions and is used empirically to treat inflammation, skin lesions, indigestion, diabetes, hypertension, pain, fever, eye disorders, and other metabolic complaints. *P. pellucida* has a strong ethnopharmacological basis, as it has been reported to exhibit antimicrobial, cytotoxic, antioxidant, antidiabetic, fracture-healing, and anti-hypercholesterolemia activities (Alves et al., 2019). However, the study also shows that some research is still limited to general phytochemical screening and has not fully identified active compounds in depth. This plant has been used in various countries, including Indonesia, the Philippines, India, Nigeria, and Brazil, but its use as a raw material for commercial herbal medicines remains suboptimal (Ahmad, Yanuar, Mulia, & Mun, 2017). This condition indicates a major problem: the significant potential of *P. pellucida* has not been balanced by a scientific synthesis that integrates aspects of phytochemistry, pharmacology, extraction techniques, safety, and economic prospects (Ahmad et al., 2023). In other words, the existing literature has shown that these plants are promising, but the evidence remains scattered across various research foci. Therefore, a research study entitled "Integrative Mapping of Phytochemistry, Pharmacology, Green Extraction, and Bioeconomics *Peperomia pellucida* (L.) Kunth: Systematic Literature Review" is important for developing a more systematic and critical map of knowledge.

In terms of phytochemistry, *P. pellucida* is reported to contain various secondary metabolites, such as polyphenols, flavonoids, alkaloids, tannins, saponins, steroids, terpenoids, phenylpropanoids, lignans, secolignans, essential oils, as well as specific compounds such as dillapiole, quercetin, apigenin, apigetrin, phytol, vitexin, stigmasterol, fucosterol, and pheophorbide. These plant bioactive compounds exhibit immunomodulatory, antibacterial, anti-inflammatory, antiglycemic, analgesic, and antioxidant activities (Tuan & Men, 2024). Lam et al., (2022) extended pharmacological studies to eye diseases by discussing the MAPK and NF-κB pathways (Lam, Har, et al., 2022), while Lam et al., (2024) demonstrated anti-inflammatory activity in ARPE-19 cells via the NF-κB and PPAR-γ pathways (Lam et al., 2024). Abraham and Varkey (2026) attributed the methanol extract *of P. pellucida* to antioxidant, antidiabetic, anticancer, antibacterial, and wound-healing activity (Abraham & Iwin C. Varkey, 2026). Agung (2020) placed this plant in the context of estrogenic activity and anti-osteoporosis potential by studying phenylpropanoid compounds, lignans, quercetin, stigmasterol, apigenin, and apigetrin (Agung et al., 2020). Bialangi (2018) demonstrated antimalarial potential by isolating stigmasterol and fucosterol (Bialangi et al., 2018), while Salnus (2026) reinforced this evidence by identifying GC-MS and antibacterial activity associated with dillapiole (Salnus et al., 2026). In addition, other research expand the pharmacological spectrum of these plants in the direction of antidiabetics (Men et al., 2022), anti-inflammatory (Fakayode et al., 2021), antiarthritis (Uwaya et al., 2024), pulmonary fibrosis protection (Johanes AF et al., 2025), gastroprotective (Pertiwi et al., 2022), and neuroprotective (Ancy & Sumithra, 2024). Thus, an important reason for this study is the need to read the pharmacological activity *of P. pellucida* not as a separate claim, but as a consequence of the diversity of phytochemicals and the differences in the test methods used.

In addition to phytochemistry and pharmacology, research on *P. pellucida* has also led to important developments in extraction and processing techniques. Solvent polarity and liquid-liquid fractionation strongly determine the phytochemical profile, biological activity, and toxicity of extracts (Lam, Ghuan, et al., 2022). Ahmad (2017) developed *ionic liquid-based microwave-assisted extraction, or IL-MAE,* to obtain polyphenols more efficiently, quickly, and environmentally friendly (Ahmad, Yanuar, Mulia, & Mun, 2017). Hashim (2020) showed that temperature and time parameters in microwave-assisted extraction affect the yield and total phenolic content of *P. pellucida* leaf extract (Hashim et al., 2020). The direction of green extraction through the use of natural deep eutectic solvent or NADES, which has the potential to increase extraction efficiency and initial safety (Ahmad et al., 2017; Saini et al., 2025). Gamma irradiation can maintain ACE inhibitor activity and TLC profile, although it affects total flavonoids, total phenolics, and antioxidant activity (Adhitia et al., 2017). Fermentation and drying methods can alter the phenolic content, flavonoid levels, antioxidant and anti-inflammatory activities, and consumer acceptance of *P. pellucida herbal* tea (Xiang et al., 2021). The findings suggest that the quality, safety, and economic value of herbal extracts are strongly influenced by the processing of raw materials. Therefore, the relationship between extraction techniques, standardization, and bioeconomics is one of the important focuses of this study.

This study aims to integrate scientific evidence on the phytochemistry, pharmacology, green extraction, and bioeconomics *of P. pellucida,* based on the available literature. The first objective is to identify the main groups of phytochemical compounds reported and explain their association with the plant's pharmacological activity. The second objective is to analyze how extraction methods, solvent types, fractionation, fermentation, drying, irradiation, MAE, IL-MAE, NADES, and modern formulations affect the content of bioactive compounds, biological activity, safety, and standardization of extracts. The third objective is to evaluate the opportunities and challenges of developing *P. pellucida* as a raw material for herbal products, functional foods, phytopharmaceuticals, cosmetics, bioaccharicides, and bioeconomic commodities. In relation to the existing literature, this study does not stand as a repetition of the previous review, but as a systematic synthesis that connects the research results. The formulation of the problem in this study is: what are the main phytochemical compounds that have been identified in *P. pellucida,* and how they relate to pharmacological activities; how extraction and processing methods affect the quality, safety, and standardization of extracts; and what are the opportunities and challenges of the development *of P. pellucida* as a raw material for herbal products with economic value. The three formulations of the problem show that this research focuses on integrating knowledge rather than just on an inventory of plant benefits. Thus, this research is expected to provide a conceptual basis for the development of *P. pellucida* as a potential medicinal plant, a source of bioactive metabolites, an object of green extraction innovation, and an economically valuable herbal commodity.

II. METHODS

This study uses a Systematic Literature Review (SLR) design with a descriptive-qualitative approach to map the development of studies on phytochemicals, pharmacology, green extraction, and bioeconomics of *Peperomia pellucida* (L) Kunth. The SLR design was chosen because the main purpose of this research is not to conduct laboratory experiments but to systematically identify, select, assess, and synthesize relevant scientific articles. The subject or sample of the research is a journal article that discusses *Peperomia pellucida* from the perspectives of phytochemistry, pharmacology, extraction, toxicology, antioxidants, antibacterial activity, antidiabetic activity, and the potential for the development of herbal products. The database used is Scopus, with search keywords: "*Peperomia pellucida* phytochemistry", "*Peperomia pellucida* pharmacology", "*Peperomia pellucida* extraction", "*Peperomia pellucida* toxicology", "*Peperomia pellucida* antioxidant", "*Peperomia pellucida* antibacterial", "*Peperomia pellucida* antidiabetic", and "*Peperomia pellucida*". Based on the initial search results, 89 articles were obtained from the Scopus database. The articles are then filtered through the stages of identification, screening, feasibility, and inclusion, as shown in the PRISMA diagram for this study. In addition, the distribution of search results by year shows that publications on *P. pellucida* have increased significantly in recent years, especially in 2017, 2022, and 2025, indicating that this topic remains relevant and evolving. The selection of articles focuses on literature that addresses three research formulations: phytochemical content, the influence of extraction methods, and the bioeconomic opportunities of this plant.

The research instruments included a list of search keywords, inclusion and exclusion criteria, PRISMA flowcharts, and data extraction tables. The inclusion criteria for this study are articles that discuss *Peperomia pellucida* directly, are available as journal articles, have an accessible abstract, have a valid DOI, and are relevant to phytochemical, pharmacological, extraction, toxicological, safety, or economic outlook themes. Exclusion criteria include duplicate articles, articles outside the year range set in the filter, articles without abstracts, articles without DOIs, DOIs that are not recognized by CrossRef, and articles that do not fit the focus of the study. Of the initial 89 articles, 32 were removed due to duplication, 9 were eliminated based on year criteria, 8 were excluded for journal tier suitability, and 1 was removed because it lacked an abstract for screening. After that stage, 39 articles entered the screening process, and all of them were retrieved. At the eligibility stage, 39 articles were fully assessed; 3 were removed because they lacked a DOI, and 2 were removed because their DOIs were not recognized by CrossRef. Thus, the final number of articles used in the review is 34. This flow is important so that the literature selection process can be replicated by other researchers with the same database, keywords, and screening criteria.

Data collection is carried out through several successive stages. The first stage is to search the Scopus database for articles using predetermined keyword combinations. The second stage is the recording of all initial search results based on the year of publication, keywords, article title, author, and topic suitability. The third stage is the removal of duplicate and non-compliant articles. The fourth stage is to read the title and abstract to ensure the article actually discusses *P. pellucida* and is relevant to the research focus. The fifth stage is the assessment of the article's feasibility based on the availability of DOIs, the traceability of the DOI, and the relevance of the article's content to the main variables of the research. The sixth stage is data extraction from selected articles, including the author's name, year of publication, research purpose, method, type of extract or solvent, phytochemical compounds, pharmacological activities, main results, safety aspects, and potential economic development. The last stage is preparing a synthesis based on the main themes that emerge from the selected articles. The themes include the richness of secondary metabolites, biological activity, the influence of extraction techniques, safety, standardization, and downstream opportunities of herbal products. The scope aligns with previous literature, which shows that *P. pellucida* has four key areas: phytochemistry, pharmacology, extraction techniques, and economic prospects.

The analysis method used is narrative thematic analysis. Data from selected articles are not analyzed quantitatively; instead, they are classified by themes and conceptual relationships among research results. Articles discussing bioactive compounds are grouped by phytochemical themes. Articles that discuss antioxidant, anti-inflammatory, antidiabetic, antibacterial, anticancer, gastroprotective, neuroprotective, antiarthritis, and other activities are included in the pharmacological theme. Articles discussing maceration, fractionation, microwave-assisted extraction, ionic liquid, NADES, fermentation, drying, and gamma irradiation are analyzed in the theme of green extraction and processing. Meanwhile, articles showing opportunities for the development of herbal teas, functional foods, phytopharmaceuticals, cosmetics, wound healing, SNEDDS, bioacaricide, or bioprospecting are included in the theme of bioeconomics. The results of each theme were then compared to identify patterns, gaps, consistency in findings, and the direction of research development. The analysis also considers the level of evidence, for example, whether the results are still in the form of phytochemical screening, in vitro tests, in vivo tests, molecular docking, or product formulations. In this way, the research can be replicated as other researchers can follow the same data source, keywords, selection criteria, PRISMA stages, extraction tables, and analysis categories. The final results of the analysis were used to answer research questions and to compile an integrative map of *Peperomia pellucida's position* as a source of bioactive compounds, a modern herbal candidate, a green-extraction innovation, and a potential bioeconomic commodity.

Research Questions

The research questions in this systematic literature review were formulated to guide the identification, selection, extraction, and synthesis of relevant evidence on *Peperomia pellucida* (L.) Kunth. The questions were designed to capture three major analytical domains: phytochemical and pharmacological evidence, extraction and processing methods, and the bioeconomic potential of the plant. RQ1 focuses on identifying the major phytochemical compounds reported in *P. pellucida* and examining their relationship with pharmacological activities. RQ2 investigates how extraction and processing methods influence bioactive compound content, biological activity, extract safety, and standardization. RQ3 explores the opportunities and challenges in developing *P. pellucida* as a raw material for economically valuable herbal products based on the available scientific evidence. These research questions served as the analytical framework for organizing the literature synthesis and ensuring that the review remained focused on both scientific evidence and potential downstream applications.

Table 1. Research Questions and Analytical Focus of the Systematic Literature Review

Code	Research Question	Analytical Focus of the SLR
RQ1	What are the main phytochemical compounds that have been identified in *Peperomia pellucida* (L.) Kunth, and how are these compounds related to its pharmacological activities?	Phytochemistry and pharmacology
RQ2	How do extraction and processing methods influence the bioactive compound content, biological activity, safety, and extract standardization of *Peperomia pellucida* (L.) Kunth?	Extraction techniques and extract quality
RQ3	What are the opportunities and challenges in developing *Peperomia pellucida* (L.) Kunth as a raw material for economically valuable herbal products based on the available scientific evidence?	Economic prospects and downstream product development

III. RESULTS AND DISCUSSION

Synthesis of Research Results

The database used is Scopus (accessed on May 25, 2025, at 8:00 PM West Indonesian Time), with search keywords: "*Peperomia pellucida phytochemistry*", "*Peperomia pellucida pharmacology*", "*Peperomia pellucida extraction*", "*Peperomia pellucida toxicology*", "*Peperomia pellucida antioxidant*", "*Peperomia pellucida antibacterial*", "*Peperomia pellucida antidiabetic*", and "*Peperomia pellucida*". The entire screening and selection process is presented in Figure 1 through the PRISMA flow diagram. From the initial search, 89 articles were identified. Before the screening stage, 32 articles were removed due to duplication. A total of 9 articles were excluded because they were not in accordance with the range of years used in the selection process. A total of 8 articles were issued due to journal tier suitability. 1 article was excluded during screening because it lacked an abstract. After that stage, 39 articles were screened, and none were released. A total of 39 articles were then searched for full text, and none were unsuccessful. At the eligibility stage, 39 articles were assessed; 3 were removed because they lacked a DOI, and 2 were removed because their DOIs were not recognized by CrossRef. Thus, the final number of studies included in the synthesis is 34 articles.

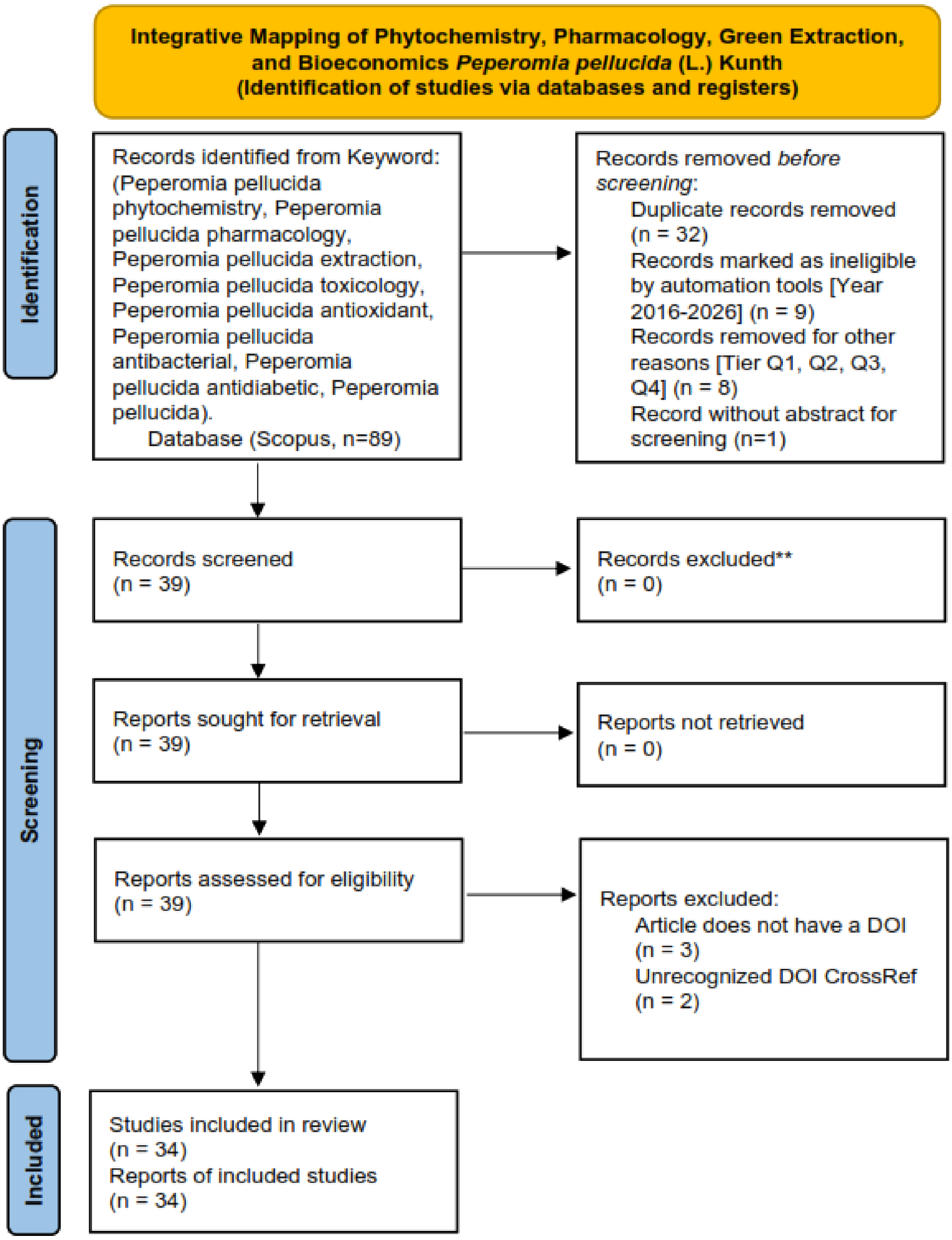

Figure 1. Prisma flow diagram of the Article Screening and Selection Process

The annual distribution of the initial articles identified through the Scopus keyword search is presented in Figure 2. The distribution of articles by year shows that publications on *Peperomia pellucida* spread from 1983 to 2026. The search results showed 1 article in 1983, 1 in 2000, 1 in 2001, 3 in 2002, 1 in 2004, and 1 in 2006. In 2010, 2 articles were found, while in 2013, 1 article was found. The number of publications increased in 2017 to 16 articles, then in 2018 to 4, and in 2019 to 4. In 2020, there were 6 articles; in 2021, 6; and in 2022, 13. In 2023, there will be 3 articles; in 2024, 5; in 2025, 15; and in 2026, 6. The highest number, according to the graph, was in 2017 with 16 articles, followed by 2025 with 15 articles and 2022 with 13 articles. The data are used to provide an initial mapping of the publication's progress before the articles are filtered to the final number of studies synthesized. The total number on the search results graph is 89, corresponding to the number of initial articles identified in the Scopus.

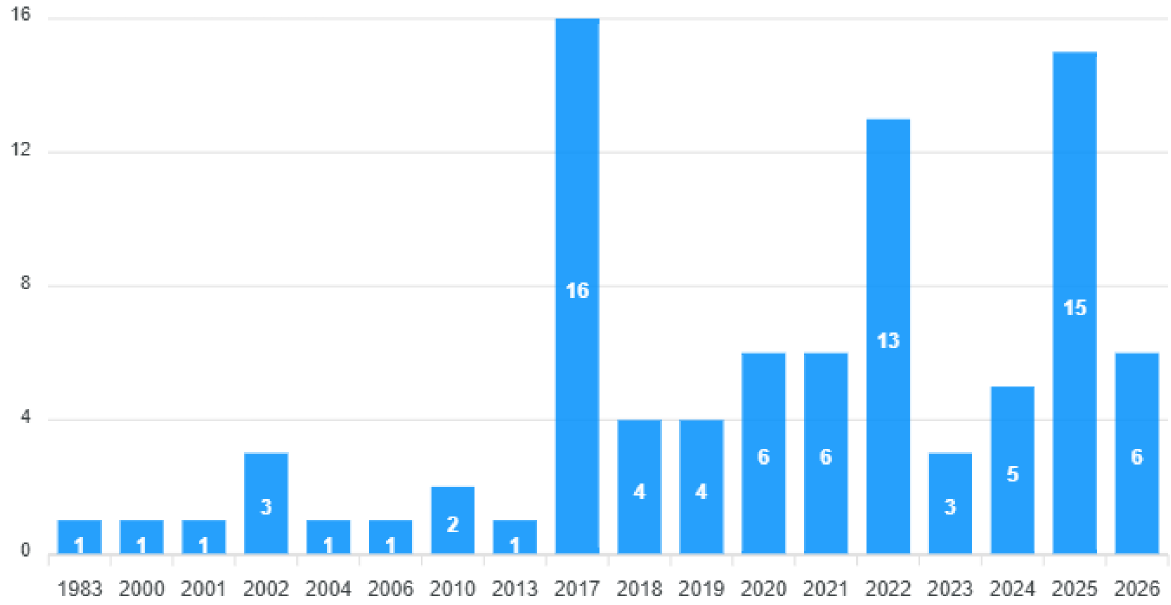

Figure 2. Annual Distribution of Articles Identified Through the Scopus Keyword Search

The thematic keywords and dominant concepts derived from the included articles are visualized in Figure 3 through a keyword cloud. The results of the thematic synthesis of the included articles show several key data groups. In the phytochemical group, the studies reviewed reported the presence of alkaloids, flavonoids, sterols, tannins, reducing sugars, amino acids, saponins, triterpenoids, carbohydrates, phenols, azulene, carotenoids, depsides, quinones, steroids, essential oils, lignans, secolignans, and phenylpropanoids. Some of the specific compounds reported include dillapiole, β-caryophyllene, carotol, ellagic acid, pellucidin A, phytol, vitexin, 2,4,5-trimethoxystyrene, 9-octadecenoic acid methyl ester, pheophorbide-a methyl ester, quercetin, stigmasterol, apigenin, apigetrin, apiol, fucosterol, and caryophyllene. In the pharmacology group, the activities found included antioxidants, anti-inflammatories, antidiabetics, antiglycations, antibacterials, antimicrobials, antihypertensives, antiangiogenics, estrogenics, anticancers, wound healers, antimalarials, neuroprotectives, gastroprotectives, antiarthritis, antifibrosis, and acaricides. Some of the test models recorded include DPPH, ABTS, *reducing power*, total antioxidant capacity, α-amylase, α-glucosidase (Hidayati et al., 2023), ACE inhibition, COX-2 inhibition, E-SCREEN assay, MTT assay, scratch assay, ELISA, GC-MS, HPTLC, HPLC, NMR, molecular docking, ARPE-19 cell test, L929 fibroblast test, MCF-7 cell test, *Drosophila* model, and animal models. In terms of safety, the data included normal cell toxicity, mild toxicity in animal models, brine shrimp lethality assay, acute toxicity, subchronic toxicity, and observations of blood parameters and liver function. In the extraction aspect, the data found included maceration, liquid-liquid fractionation, methanol solvent, ethyl acetate, n-hexane, chloroform, n-butanol, water, petroleum ether, ionic liquid-based microwave-assisted extraction, microwave-assisted extraction, natural deep eutectic solvent, ultrasonic extraction, fermentation, drying, freeze drying, microwave drying, and gamma irradiation.

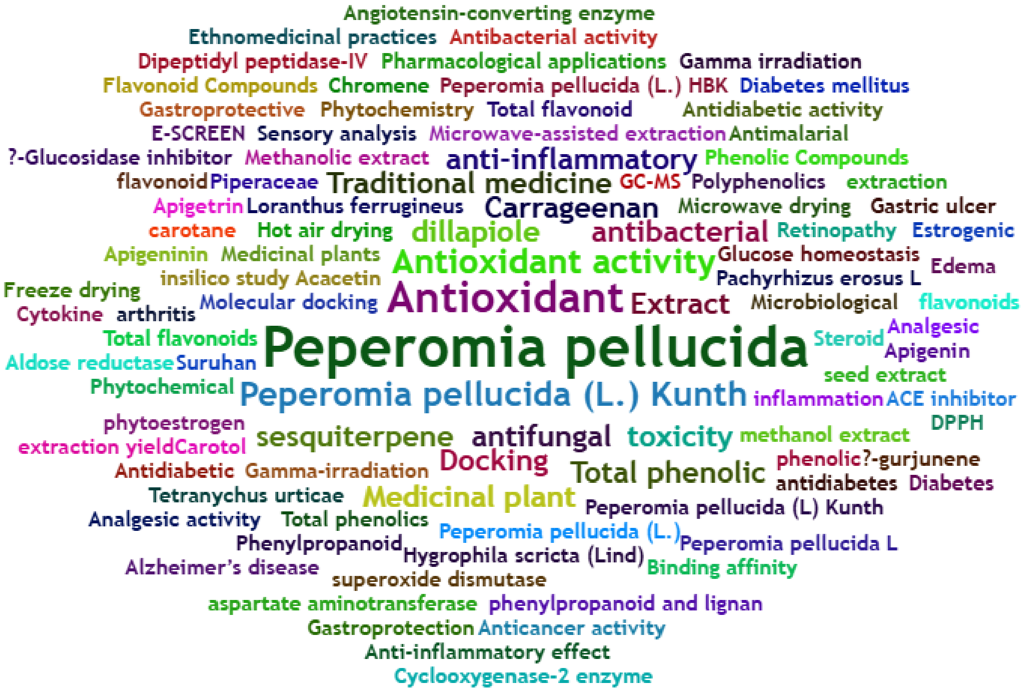

Figure 3. Thematic Keyword Cloud of Phytochemical, Pharmacological, Toxicological, and Extraction Studies on *Peperomia pellucida*

The main thematic categories and key data extracted from the included studies are summarized in Table 2. The synthesis was organized into five major themes, namely phytochemicals, pharmacology, extraction and processing, safety, and bioeconomics. The phytochemical theme includes major secondary metabolites and specific compounds reported in previous studies, while the pharmacological theme summarizes the biological activities associated with *Peperomia pellucida*. The extraction and processing theme describes the methods and technologies used to obtain or modify plant extracts. The safety theme covers toxicity-related evaluations, including cell-based and animal-based toxicity assessments. Meanwhile, the bioeconomic theme highlights the potential downstream applications of *P. pellucida* in herbal products, functional foods, phytopharmaceuticals, cosmetics, topical formulations, and bioacaricide development.

Table 2. Thematic Synthesis of Key Findings from Included Studies on *Peperomia pellucida*

Theme Synthesis	**Key Data Found**
Phytochemicals	Alkaloids, flavonoids, tannins, saponins, phenols, terpenoids, steroids, lignans, essential oils, dillapiole, quercetin, apigenin, stigmasterol, fucosterol
Pharmacology	Antioxidant, anti-inflammatory, antidiabetic, antibacterial, antihypertensive, anticancer, wound healing, antimalarial, neuroprotective, gastroprotective, antiarthritis
Extraction and processing	Maceration, solvent fractionation, IL-MAE, MAE, NADES, ultrasonic extraction, fermentation, drying, gamma irradiation
Security	Cell toxicity test, animal toxicity, BSLA, acute toxicity, subchronic toxicity
Bioeconomics	Herbal teas, functional foods, supplements, phytopharmaceuticals, cosmetics, topical products, SNEDDS, bioacaricides, microbial bioprospecting

In the extraction result group, several studies recorded key numerical data related to yield, polyphenol content, biological activity, and initial safety. Ahmad (2025) reported optimal conditions of IL-MAE using [bmim]BF4 with a microwave power of 30%, an extraction time of 18.5 minutes, an ionic liquid concentration of 0.79 mol/L, and a liquid-solid ratio of 10.72 mL/g, with a total polyphenol of 31.1725 mg GAE/g (Ahmad, Mulia, et al., 2025). Another study with EMIMBr reported optimal conditions of 30% microwave power, 10 min extraction time, a liquid-to-solid ratio of 14 mL/g, and an ionic liquid concentration of 0.7 mol/L, yielding a total polyphenol content of 13,750 µg GAE/g (Ahmad, Yanuar, Mulia, Mun, et al., 2017). Hashim (2020) reported that the best MAE conditions were 145°C for 15 minutes (Hashim et al., 2020). Ahmad (2025) reported a 1:3 glucose-citric acid NADES with a total phenolic content of 114.59 mg GAE/g sample, as well as the optimal MAE condition at 50% microwave power, 5 min time, 5:1 NADES ratio, and solvent-sample ratio 6:1 ml/g, with a TPC of 138.29 ± 2.21 mg GAE/g sample (Ahmad, Hikmawan, et al., 2025). Saini (2025) reported that NADES produced an extraction yield of 17.39 ± 0.03%, DPPH activity of 83.31 ± 0.03%, and LC50 BSLA of 1597.62 µg/mL (Saini et al., 2025). Adhitia (2017) reported that gamma irradiation up to 10 kGy did not alter ACE inhibitor activity or the TLC profile, but did affect total flavonoids, total phenolics, and antioxidant activity (Adhitia et al., 2017). Tuan (2024) report that fermentation decreases total phenolic, flavonoid, and antioxidant activity, but increases anti-inflammatory potential (Tuan & Men, 2024). The data are presented as the main results of the extraction and processing groups without further assessment of the advantages of each method.

In the bioactivity and application group, the main results were obtained from phytochemical tests, enzyme tests, cell tests, animal tests, and formulation tests. Teruna (2022) reported that the m*ethanol extract of P. pellucida* at concentrations of 1.5 mg/mL and 3 mg/mL, and the ethyl acetate fraction of 4 mg/mL were non-toxic to ARPE-19 cells and exhibited cytoprotective effects on high glucose and AGE conditions (Teruna et al., 2022). Kartika (2021) reported that extracts obtained with n-hexane, ethyl acetate, and ethanol at 0.1 µg/mL showed partial agonist effects, whereas water extracts showed full agonist effects (Kartika et al., 2021). Abraham and Varkey (2025) reported the activity of the DPPH methanol extract, with an IC50 of 75.4 µg/mL, an antibacterial inhibition zone of 15–17 mm, non-toxicity up to 125 µg/mL in L929 fibroblast cells, and support for cell migration in a scratch assay (Abraham & Varkey, 2025). They also reported an IC50 of 48.5 µg/mL for LDH in the MCF-7 breast cancer cell assay(Abraham & Varkey, 2025). Bialangi (2018) reported IC_{50} antimalarial stigmasterol of 5.24 ppm and fucosterol of 0.85 ppm (Bialangi et al., 2018). Ardiono (2025) reported 22 pure Actinomycetes isolates from the rhizosphere of *P. pellucida*, with the two main isolates, RKS-0.3-13 and RKS-0.4-04, active against *Escherichia coli*, *Staphylococcus aureus*, and *Candida albicans* (Ardiono et al., 2025). Hartati (2025) reported an SNEDDS formulation with a globule size of 11.29 ± 0.88 nm, zeta potential -10.33 mV, PDI 0.35 ± 0.29, as well as the highest blood glucose reduction of around 82% at a combined ratio of 1:1 (Hartati et al., 2025). Salnus (2025) reported 43 bioactive compounds via GC-MS, dillapiole of 41.77%, N,N'-diacridin-9-yl-hydrazine of 7.44%, caryophyllene 6.94%, antioxidant activity of IC50 of 4.30 µg/mL, and the largest antibacterial inhibition zone against *Staphylococcus aureus* of 14 mmv (Salnus et al., 2026).

Discussion

The findings of this study show that the literature on *Peperomia pellucida* (L.) Kunth has evolved from a simple ethnomedical study into a multidisciplinary effort encompassing phytochemistry, pharmacology, green extraction (Ahmad, Yanuar, Mulia, & Mun'im, 2017), toxicology, formulation, and bioeconomics. Based on the SLR selection process, 89 articles were identified from Scopus and then underwent duplicate removal, screening, feasibility assessment, and DOI validation, resulting in 34 studies included in the review. This number suggests that *the literature on P. pellucida is* sufficient to be systematically synthesized, although not all studies have the same depth or strength of evidence. The literature reviewed shows that these plants are no longer merely understood as wild plants or traditional herbs, but are now recognized as a source of bioactive metabolites and as candidates for use as raw materials in modern herbal products. This is in line with the findings of Alves (2019) which position *P. pellucida* as a plant with a strong ethnopharmacological basis but that still requires critical evaluation of the quality of the evidence, extraction methods, the validity of pharmacological assays, and potential applications. These findings are important because SLR research is not enough to simply collect efficacy claims; it must also sort out the relationships among chemical evidence, biological evidence, safety, and product development opportunities. Thus, the initial significance of this study lies in its ability to compile a more complete map of knowledge from studies previously scattered across their respective focuses. The main contribution of this study is to make clear that *P. pellucida* has scientific and economic potential, but its development should be read gradually, evidence-based, and should not jump directly from traditional claims to clinical claims.

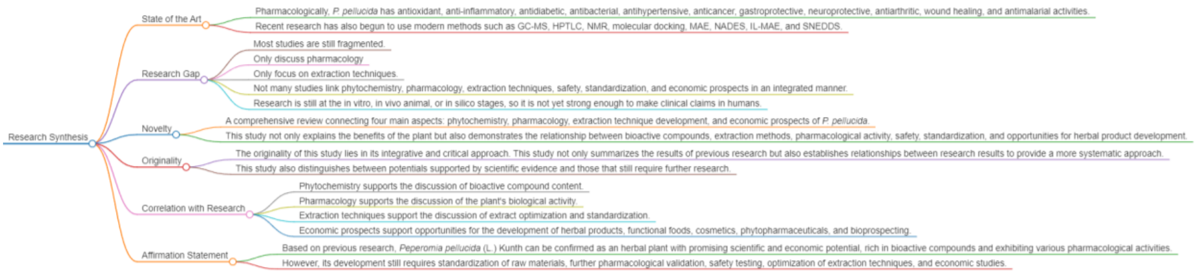

Figure 4. Research Synthesis Map of *Peperomia pellucida* (L.) Kunth

The research synthesis map illustrates the logical structure of this review, beginning with the current state of research on *Peperomia pellucida* (L.) Kunth, followed by identified gaps, novelty, originality, and its connection with the study focus. The figure 4 shows that although previous studies have reported various pharmacological activities and modern analytical or extraction methods, the existing evidence remains fragmented and has not fully integrated phytochemistry, pharmacology, extraction techniques, safety, standardization, and economic prospects. Therefore, this study offers an integrative synthesis that connects these dimensions to provide a more systematic understanding of the scientific and bioeconomic potential of *P. pellucida*.

To answer RQ1, the main findings show that *P. pellucida* has a very diverse group of phytochemical compounds, including alkaloids, flavonoids, sterols, tannins, reducing sugars, amino acids, saponins, triterpenoids, carbohydrates, phenols, azulene, carotenoids, depsida, quinones, steroids, lignans, phenylpropanoids, secolignans, and essential oils. Xiang (2021) report that the group of compounds exhibits immunomodulatory, antibacterial, anti-inflammatory, antiglycemic, analgesic, and antioxidant potential (Xiang et al., 2021). These findings are important because they show that the pharmacological activity *of P. pellucida* cannot be explained by a single compound, but rather by a combination of compounds that can act synergistically, additively, or differently depending on the solvent and extraction method used. In this context, the phytochemical content not only provides descriptive information but also serves as a rational basis for the biological activities reported in various studies. Phenolics and flavonoids are widely associated with antioxidant and anti-inflammatory activities, while alkaloids, saponins, tannins, terpenoids, steroids, and essential oil components contribute to antibacterial, antidiabetic, antihypertensive, wound-healing, estrogenic, and antimalarial activities. Kartika (2021) research strengthens the link between specific compounds and biological receptor activity by identifying phenylpropanoids and lignans associated with estrogenic activity (Kartika et al., 2021). The research of Bialangi (2018) also expanded the scope of phytochemicals by showing that the stigmasterol and fucosterol of *P. pellucida* have antimalarial activity (Bialangi et al., 2018). Thus, the answer to RQ1 is that the phytochemistry *of P. pellucida* is multidimensional and is the main foundation for the breadth of its pharmacological activity.

The findings of RQ1 also show that the link between phytochemistry and pharmacology is stronger when research uses a mechanistic approach, rather than just initial screening. Ahmad (2023) discuss the roles of compounds such as β-caryophyllene, carotol, dillapiole, ellagic acid, pellucidin A, phytol, and vitexin in the MAPK and NF-κB pathways involved in inflammatory eye disease (Ahmad et al., 2023). Ifora (2023) then provided more specific evidence that the methanol extract and ethyl acetate fraction *of P. pellucida* are non-toxic to ARPE-19 cells at certain concentrations and can suppress inflammatory markers in response to high glucose and AGEs (Ifora et al., 2023). The compounds dillapiole, 2,4,5-trimethoxystyrene, 9-octadecenoic acid, and pheophorbide A-methyl ester also showed affinity for NF-κB p65 and PPAR-γ proteins vi*a molecular docking*. This suggests that some studies have moved from empirical claims to cellular, molecular, and computational validation. Abraham and Varkey strengthened the relationship by discovering antioxidant, antibacterial, antidiabetic, anticancer, and wound-healing activities in methanol extracts rich in bioactive compounds. Salnus (2025) provided cutting-edge evidence by identifying 43 bioactive compounds, with dillapiole as the dominant component, and demonstrating antibacterial activity against several pathogenic bacteria (Salnus et al., 2026). The significance of these results is that *P. pellucida* can be considered a source of multipotent bioactive metabolites, but its pharmacological claims must be associated with the type of extract or fraction, dose, test model, and the compound identified. Thus, the contribution of this research to the field of natural materials science and herbal pharmacy is to establish a clearer relationship between phytochemical content and the direction of plant biological activity.

To answer RQ2, the research findings show that extraction and processing methods greatly affect the bioactive compound content, biological activity, safety, and standardization of *P. pellucida extract*. Men (2025) showed that liquid-liquid fractionation with solvents of different polarities resulted in variations in yield, compound profile, biological activity, and toxicity (Men et al., 2025). The fractions of chloroform, ethyl acetate, and n-butanol are reported to be rich in phenolics, tannins, saponins, and alkaloids, although their yields are low. Phenolics and saponins are positively correlated with antioxidant, anti-inflammatory, and antiglycation activity, while hexane fractions show high anti-inflammatory potential. The fractions of ethyl acetate, water, and hexane also show relatively strong antiglycation effects. These findings show that no single extraction method can be considered superior for all compound targets and biological activities. This is important because developing herbal products requires matching activity targets, marker compounds, solvents, and extraction methods. In other words, extraction is not just a technical stage, but a determining factor in pharmacological quality and product standardization.

The RQ2 findings also show that the development of *P. pellucida* extraction techniques has led to more modern and environmentally friendly methods. Ahmad (2017) developed *ionic liquid-based microwave-assisted extraction, or IL-MAE*, to improve the efficiency of polyphenol acquisition from *P. pellucida* (Ahmad, Yanuar, Mulia, & Mun, 2017). This approach is important because it optimizes parameters such as microwave power, extraction time, ionic liquid concentration, and liquid-to-solid ratio, so that the extraction process no longer relies on less scalable conventional experiments. Hashim (2020) show that *microwave-assisted extraction* is influenced by temperature and time, so extraction parameters must be controlled to achieve optimal phenolic content (Hashim et al., 2020). Ahmad (2017) and Saini (2025) expand the direction of green extraction through the use of natural deep eutectic solvent or NADES (Ahmad, Yanuar, Mulia, & Mun'im, 2017; Saini et al., 2025). Saini (2025) showed that NADES can produce high extraction yields, antioxidant activity, and initial safety, as assessed by BSLA (Saini et al., 2025). Tuan (2024) show that fermentation and drying methods also affect total phenolics, flavonoids, antioxidant activity, anti-inflammatory activity, and consumer acceptance (Tuan & Men, 2024). Adhitia (2017) show that gamma irradiation can maintain ACE inhibitor activity and the TLC profile while altering the phenolic composition, flavonoid content, and antioxidant activity (Adhitia et al., 2017). Thus, the results of RQ2 confirm that green extraction and post-harvest processing are important components in the development of *P. pellucida* as a consistent and economically valuable herbal raw material.

The significance of the results in RQ2 lies in the shift in the perspective of herbal extracts. In medicinal plant research, extracts are often treated as the end product, even though the findings in this SLR suggest that extracts are the product of complex methodological decisions. Solvent type, polarity, temperature, time, fractionation, fermentation, drying, irradiation, and extraction technology can alter the compound's profile and the biological activity observed. Tran Thanh Men and colleagues showed that different fractions, such as hexane, dichloromethane, ethyl acetate, and the aqueous fraction, produce different alkaloids, phenolics, flavonoids, antioxidant activity, anti-inflammatory activity, α-glucosidase inhibition, and antibacterial activity. The ethyl acetate fraction shows prominent activity in several parameters, including antioxidant and anti-inflammatory activities. This suggests that the claim about the "benefits *of P. pellucida*" cannot be separated from the question of "what extract was used, made with what solvent, and tested on what model". The scientific significance is that this study clarifies the need to standardize extracts as a prerequisite for the development of phytopharmaceuticals, functional foods, cosmetics, and other bioeconomic products. Contributing to the scientific field by providing a basis for the argument that green extraction is not only an environmental issue but also directly related to phytochemical quality, reproducibility, safety, and the added value of products. Thus, this study places extraction techniques as a bridge between phytochemical science and the commercialization of herbal products.

To answer RQ3, the research findings suggest that *P. pellucida* has broad bioeconomic development opportunities, but still faces scientific and technological challenges. In terms of opportunities, these plants have the potential to be developed into herbal teas, functional foods, antioxidant supplements, phytopharmaceutical candidates, topical wound-healing products, cosmetic ingredients, anti-osteoporosis agents, antidiabetic ingredients, nanoemulsion formulations, plant-based biopesticides, and rhizosphere microbial bioprospecting sources. Tuan (2024) point to opportunities for the development of herbal tea (Tuan & Men, 2024), while Men (2025) point out that *P. pellucida* has potential as a food and herbal medicine because it contains polyphenols, tannins, flavonoids, saponins, alkaloids, and terpenoids (Men et al., 2025). The study also reported no acute or chronic toxicity that impaired liver function or blood parameters in general in animal models, although there remains a note of caution against long-term use due to possible effects on the hematopoietic system. Hartati et al. showed that *P. pellucida* can be developed through SNEDDS technology in combination with antidiabetic extracts. Pertiwi (2022) demonstrate the potential of a combination of gastroprotective products (Pertiwi et al., 2022), while Abraham and Varkey (2025) demonstrate the potential of topical products for antibacterial activity and wound healing (Abraham & Varkey, 2025). Ardiono (2025) open up rhizosphere bioprospecting opportunities through *Actinomycetes* isolates (Ardiono et al., 2025), while Oliveira (2017) show agroindustrial opportunities through essential oils with acaricide activity (Oliveira et al., 2017). Thus, RQ3's answer is that *P. pellucida* has cross-sectoral economic opportunities, but its development requires stronger validation, standardization, safety, and production viability.

The significance of the RQ3 results is that this study expands the way in which the economic value of medicinal plants is assessed. The economic value *of P. pellucida* lies not only in the claim that this plant is "efficacious", but in its ability to be developed into an evidence-based product chain. If this crop is intended as a functional food, the key aspects are safety of consumption, nutritional stability, post-harvest processing, and consumer acceptance. If directed as a phytopharmaceutical or as a candidate active ingredient for herbal medicines, the key aspects include marker compounds, extract standardization, mechanism of action, toxicity testing, and preclinical-to-clinical validation. If directed as a cosmetic or topical product, then the important aspects are skin safety, formulation stability, effectiveness against wounds or infections, and consistency of active ingredients. If it is directed as a bioacrichide or agroindustrial product, then the important aspects are environmental toxicity, essential oil stability, field effectiveness, and production costs. If it is directed at microbial bioprospecting, then the important aspects are the isolation of microorganisms, molecular identification, metabolite production, antimicrobial activity, and the potential development of antibiotics or biological agents. Thus, the contribution of this research is to position the bioeconomics *of P. pellucida* as a multidimensional agenda grounded in the integration of phytochemicals, pharmacology, extraction, safety, and product technology. This contribution is important because it can help the next researcher determine the most rational development path, rather than just mentioning potential in general.

The available evidence suggests that *Peperomia pellucida* (L.) Kunth has promising bioeconomic potential, although current findings should be regarded as indicators of early-stage development rather than proof of economic feasibility. Its bioeconomic relevance is reflected in several proxy indicators, including product diversification opportunities, extraction productivity, technological readiness, safety evidence, formulation feasibility, consumer acceptance, and value-chain positioning. The reviewed studies indicate potential applications in herbal teas, functional foods, antioxidant supplements, phytopharmaceuticals, topical wound-healing products, cosmetics, antidiabetic formulations, plant-based biopesticides, and microbial bioprospecting. Economic-related indicators reported in the literature include extract yield, phenolic content, antioxidant activity, processing efficiency, formulation performance, and preliminary safety data, all of which support the possibility of generating higher-value products from *P. pellucida* biomass. However, most studies remain at the laboratory, preclinical, or proof-of-concept stage, while critical bioeconomic indicators such as production costs, supply-chain stability, cultivation productivity, market demand, price competitiveness, regulatory requirements, and techno-economic feasibility are still largely absent. Therefore, although *P. pellucida* demonstrates considerable cross-sectoral development potential, future research should integrate phytochemical standardization, safety validation, scalability assessment, market analysis, and cost–benefit evaluation to establish its true bioeconomic viability and commercialization prospects.

Table 3. Proposed Bioeconomic Indicators for *Peperomia pellucida* Development

Development pathway	**Scientific evidence available**	**Key bioeconomic indicators needed**	**Readiness level**
Herbal tea and functional beverage	Effects of processing on bioactive compounds and consumer acceptance	Raw-material supply, production cost, shelf life, market acceptance	Early stage
Functional food and antioxidant supplement	Rich in bioactive compounds with antioxidant activity	Standardization, safety, production cost, market demand	Preliminary
Phytopharmaceutical/herbal medicine	Multiple preclinical pharmacological activities reported	Clinical validation, regulation, development cost	Low commercial readiness
SNEDDS and advanced formulations	Promising formulation performance and antidiabetic potential	Scalability, stability, manufacturing cost	Proof-of-concept
Topical and cosmetic products	Antioxidant, antibacterial, and wound-healing potential	Safety testing, stability, regulatory compliance	Moderate potential

Anti-osteoporosis products	Estrogenic-related compounds identified	Safety, efficacy validation, market feasibility	Early stage
Bioacaricide/agroindustrial products	Essential oils show acaricidal activity	Yield, field efficacy, production cost	Early stage
Microbial bioprospecting	Rhizosphere Actinomycetes show antimicrobial activity	Fermentation scalability, IP potential, commercialization	Discovery stage
Green extraction products	Improved extraction efficiency using advanced methods	Process cost, scalability, environmental assessment	Technology development stage
Standardized herbal raw materials	Phytochemical and biological activity data available	Cultivation yield, supply chain, quality control	Foundational stage

These indicators suggest that the bioeconomic value of *P. pellucida* should be assessed across the entire value chain. Current studies mainly provide scientific evidence, such as bioactive content, biological activity, extraction performance, and safety data. However, stronger bioeconomic evaluation requires additional indicators, including production costs, supply-chain reliability, scalability, market demand, regulatory requirements, and techno-economic feasibility. Future research should therefore complement biological studies with quantitative economic assessments to determine the commercial viability of each development pathway.

Compared with previous literature, this study contributes by compiling a synthesis that is more integrative than those that focus on only one specific aspect. Some of the previous research focused on phytochemistry, some on pharmacology, some on extraction, and partly on specific product applications. The advantage of SLR is that it integrates all these findings into a single framework that shows the relationships among compound content, extraction methods, biological activity, safety, and downstream opportunities. This relationship is important because pharmacological evidence would be weak without an understanding of phytochemistry, and the economic outlook would be unrealistic without extraction technology and product standardization. Previous literature has also shown that most evidence remains in the preclinical, in vitro, in vivo animal, or in silico stages, so it is not yet sufficient to support direct clinical claims. By stating the limits of this level of evidence, this study makes a critical contribution so that the development of *P. pellucida* does not fall into excessive claims. In addition, this study confirms that green extracts, such as IL-MAE, MAE, and NADES, are not only technically relevant but also contribute to increasing the bioeconomic potential of plants. Thus, the scientific contribution of this research lies in the integrative mapping and sharpening of research direction, rather than merely repeating the narrative of plant benefits.

Compared with previous reviews, the novelty of this study lies not in being the first review on *Peperomia pellucida*, but in offering an updated and integrative SLR framework. Alves et al. (2019) mainly reviewed the chemistry and biological activities of *P. pellucida*, Ahmad et al. (2023) discussed phytochemistry, pharmacology, extraction engineering, and economic prospects, while Lam et al. (2022) focused more specifically on phytochemical extraction, bioactivity, and health-related applications. The present study extends these works by systematically connecting phytochemical composition, pharmacological activity, green extraction and processing, safety, standardization, and bioeconomic readiness in one analytical framework.

The main contribution of this review is its effort to move beyond a general inventory of plant benefits. It links bioactive compounds with pharmacological evidence, relates extraction methods to extract quality and standardization, and evaluates downstream opportunities using bioeconomic indicators such as product readiness, scalability, safety evidence, formulation feasibility, and the need for techno-economic assessment. Therefore, this review provides a more operational map for identifying research gaps and prioritizing rational development pathways for *P. pellucida* as a potential herbal, pharmaceutical, cosmetic, agroindustrial, and bioprospecting resource.

Table 4. Positioning of the Present Review Compared with Previous Reviews on *Peperomia pellucida*

Review article	**Main focus**	**Limitation/gap**	**Novelty of the present study**
Alves et al. (2019)	Chemistry and biological activities of *P. pellucida*	Limited integration with green extraction, standardization, and downstream product development	Extends the discussion by linking phytochemistry, pharmacology, extraction methods, safety, and bioeconomic readiness
Ahmad et al. (2023)	Phytochemistry, pharmacology, extraction engineering, and economic prospects	Economic discussion remains more prospective and less indicator-based	Adds a structured SLR synthesis and introduces bioeconomic indicators such as scalability, product readiness, safety evidence, and techno-economic needs
Lam et al. (2022)	Phytochemical extraction, bioactivity, and health-related applications	More focused on specific pharmacological and extraction aspects	Broadens the analysis by integrating multiple domains, including green extraction, product standardization, and value-chain-oriented development
Present review	Integrative mapping of phytochemistry, pharmacology, green extraction, safety, and bioeconomics	—	Provides an updated decision-oriented framework to identify research gaps and prioritize rational development pathways for *P. pellucida*

The implications of this research can be seen on several levels. At the academic level, this study provides a literature map that can be used as a basis for further research on the isolation of active compounds, validation of mechanisms of action, standardization of extracts, and safety testing. At the pharmaceutical level of natural ingredients, this study emphasizes the need to link marker compounds, such as dillapiole, quercetin, apigenin, stigmasterol, fucosterol, and others, with specific biological activities. At the level of extraction technology, this study shows that green extraction methods should be prioritized because they are more efficient, sustainable, and have potential industrial applications. At the product development level, this study provides guidance for developing *P. pellucida* as herbal teas, functional foods, supplements, phytopharmaceuticals, cosmetics, topical products, nanoemulsion formulations, bioacharicides, or microbial bioprospecting sources. At the economic level, this study shows that the bioeconomy of herbal plants must be built from a value chain that includes raw materials, extraction, standardization, safety, formulation, regulation, and markets. The practical implication is that researchers and product developers need to choose specific product targets, as each target requires different quality parameters and safety evidence. The methodological implication is that subsequent SLR research could use the same category to evaluate other herbal plants. Thus, this study is not only useful for understanding *P. pellucida* but can also serve as an integrative mapping model for the study of other tropical medicinal plants.

The limitations of this study also need to be clearly explained so that the conclusions produced remain proportional. First, the data sources for this research were limited to articles obtained from the Scopus database, and the selection process resulted in 34 final studies, so that relevant articles outside the database were not included in the synthesis. Second, the selection criteria exclude articles without DOIs and those with DOIs that are not recognized by CrossRef, so some substantially relevant literature may not be further analyzed. Third, this synthesis uses a narrative-thematic approach, so the results do not yield quantitative estimates such as those from meta-analysis. Fourth, the variety of methods in the articles studied is quite large, ranging from phytochemical screening, GC-MS, NMR, HPTLC, enzyme tests, cell tests, and animal tests to molecular docking and SNEDDS formulations, so comparisons between studies cannot always be made directly. Fifth, most available studies are still in the preclinical stage, in vitro, in vivo, or in silico, so the results cannot be compared with clinical evidence in humans. Sixth, bioeconomic data in the literature is still more in the form of development potential than market analysis, production costs, supply chains, regulations, and mature industrial feasibility. Seventh, variations in plant parts, growing locations, solvents, processing methods, and test parameters make the results across studies difficult to interpret. Thus, these limitations do not weaken the value of the research but suggest that the results of the SLR should be understood as a strong initial knowledge map to guide further research.

Overall, this discussion shows that the research results have clear scientific and practical significance. For RQ1, this study confirms that the strength of *P. pellucida* lies in the diversity of its phytochemicals, which are associated with various pharmacological activities. For RQ2, this study shows that extraction and processing methods are determinants of extract quality, biological activity, safety, and standardization. For RQ3, this study shows that the bioeconomic prospects of *P. pellucida are* broad, but can only be realized if supported by evidence on pharmacology, extraction technology, safety, formulation, and production feasibility. This research is important because it bridges the previously fragmented literature into a more systematic synthesis framework. His scientific contribution lies in integrative mapping that connects plants, compounds, methods, activities, security, and downstream opportunities. Its practical contribution is to provide direction for researchers, the herbal industry, and product developers to determine the focus of *P. pellucida* development more realistically. Thus, *P. pellucida* can be considered a source of bioactive compounds and a potential herbal commodity, but still requires further validation before it is developed into a safe and effective commercial product. The conclusion of this discussion is that older research helps clarify *P. pellucida's position* as an object of study in natural materials, which is not only scientifically interesting but also relevant to green extraction and biodiversity-based bioeconomics.

IV. CONCLUSION

This systematic literature review concludes that *Peperomia pellucida* (L.) Kunth has strong potential as a medicinal and bioeconomic plant. The reviewed studies show that it contains diverse bioactive compounds, including flavonoids, alkaloids, tannins, saponins, phenols, terpenoids, steroids, lignans, essential oils, dillapiole, quercetin, apigenin, stigmasterol, and fucosterol. These compounds are associated with antioxidant, anti-inflammatory, antidiabetic, antibacterial, antihypertensive, anticancer, neuroprotective, gastroprotective, antiarthritic, antimalarial, and wound-healing activities. Extraction and processing methods, such as maceration, solvent fractionation, MAE, IL-MAE, NADES, fermentation, drying, and gamma irradiation, were found to influence bioactive content, biological activity, safety, and extract quality. In addition, *P. pellucida* has potential for development into herbal teas, functional foods, supplements, phytopharmaceuticals, cosmetics, topical products, nanoemulsion formulations, bioacaricides, and microbial bioprospecting sources. This review contributes by integrating phytochemical, pharmacological, extraction, safety, and bioeconomic evidence into a unified research framework.

Future research should focus on validating the main active compounds of *P. pellucida* through isolation, characterization, and mechanism-of-action studies. The relationship between marker compounds, extract types, dosage, and pharmacological effects also needs to be clarified. Further toxicity studies, including acute, subchronic, and chronic evaluations, are required before product development. Green extraction techniques such as NADES, IL-MAE, and MAE should be further optimized for stability, cost, energy efficiency, and industrial feasibility. In addition, studies on market potential, regulation, raw-material supply, standardization, consumer acceptance, and human clinical trials are needed to support the responsible development of *P. pellucida* as a safe and sustainable bioeconomic commodity.

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