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Production of plant pharmaceutical compounds in laboratory: (Article review)

Emad Hamdi Jassim[1] and Sanaria A. Alallaq [2]

Institute of Genetic Engineering and Biotechnology for Postgraduate Studies, 1 .University of Baghdad, Baghdad, Iraq
Department of Biology, College of Science for women, University of Baghdad, 2 .Baghdad, Iraq

Corresponding author: sanariaaa_bio@csw.uobaghdad.edu.iq

Abstract:

Plant pharmaceutical compounds, which play a major role as renewable sources of medicinal compounds. These compounds that medicinally very important for many aspects such us modern medicine discovery and the therapy of numerous diseases. Therefore, there is an urgent need to manufacture plant-derived on a commercial scale using unconventional methods to reach the needs of the pharmaceutical. This review article highlights the current advancements and future approaches for the production of medicinal compounds using different techniques like plant cell, tissue and organ culture and genetic engineering represents a transformative approach to reach the growing demand for these valuable compounds. It is also summarizing the advanced in vitro culture techniques, such as micropropagation and bioreactor systems, provide controlled environments that improve the yield and quality of medicinal compounds. All these modern techniques overcome the limitations of both seasonal and environmental changes which is associated with regular agriculture. In this article, we also reviewed the progress of metabolic genetic engineering techniques which has optimizes the production of pharmaceutical compounds by enabling very precise manipulation of biosynthetic pathways.

Keywords: *Plant pharmaceutical, pharmaceutical compounds, pharmaceutical techniques*

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أنتاج المركبات الدوائية النباتية مختبريا (مراجعة مقالة).

أ.م.د.عماد حمدي جاسم ، أ.م.د. سناريا عباس العلاق

معهد الهندسة الوراثية والتقنيات الأحيائية للدراسات العليا/ جامعة بغداد/ بغداد /العراق

قسم علوم الحياة / كلية العلوم للبنات / جامعة بغداد/ بغداد /العراق

لخلاصة

تلعب المركبات الصيدلانية النباتية دورًا محوريًا كمصادر متجددة للأدوية. وتكتسب هذه المركبات أهمية طبية بالغة في جوانب عديدة، منها اكتشاف الأدوية الحديثة وعلاج العديد من الأمراض. لذا، ثمة حاجة ملحة لتصنيعها على نطاق تجاري باستخدام أساليب غير تقليدية لتلبية احتياجات القطاع الصيدلاني. تسلط هذه المقالة الضوء على التطورات الحالية والأساليب المستقبلية لإنتاج المركبات الصيدلانية باستخدام تقنيات مختلفة مثل زراعة الخلايا والأنسجة والأعضاء النباتية، والهندسة الوراثية التي تمثل نهجًا ثوريًا لتلبية الطلب المتزايد على هذه المركبات القيّمة. كما تلخص المقالة تقنيات الزراعة المتقدمة في المختبر، مثل أنظمة الإكثار الدقيق والمفاعلات الحيوية، التي توفر بيئات مضبوطة تُحسّن من إنتاجية وجودة المركبات الصيدلانية . تتغلب هذه التقنيات الحديثة على قيود التغيرات الموسمية والبيئية المرتبطة بالزراعة التقليدية. في هذه المقالة، استعرضنا أيضًا التقدم المحرز في تقنيات الهندسة الوراثية الأيضية التي حسّنت إنتاج المركبات الصيدلانية من خلال تمكين التلاعب الدقيق للغاية بالمسارات الحيوية.

الكلمات المفتاحية: *المستحضرات الصيدلانية النباتية، المركبات الصيدلانية، التقنيات الصيدلانية .*

1. Introduction

Plants have ability to synthesize several organic compounds called secondary metabolites (SM). These molecules playing key roles in plants protection against biotic or abiotic stresses for plant survival Verpoorte, *et al*., (2020); Akbar *et al*., (2024); Isah, T (2019) and Stevenson, *et al*., (2017). These (SMs) also contribute to plant –plant as well as plant–pollinator interactions, enhancing ecological success Akbar *et al*., (2024) and Isah, T (2019) . Due to their diverse bio activities, (SMs) have substantial applications in pharmaceuticals, agriculture, and industrial sectors. For instance, alkaloids are widely used in cancer treatments, while flavonoids and phenolics are recognized for their antioxidant and antimicrobial properties Isah, T. (2019) and Satyam *et al*., (2025). However, the traditional extraction of these valuable compounds from natural sources presents several challenges, including low yield, seasonal variability, and the over harvesting of rare plant species, leading to ecological concerns Mungwari *et al*., (2024) and Nguyen *et al*., (2023). The micropropagation techniques has emerged as a promising solution for the sustainable production of (SMs). This important technique involves cultivating different parts of plant body in controlled *in vitro* conditions, enabling the production of desired metabolites independent of climatic or seasonal factors Murthy *et al*., (2020) and Debnath *et al*., (2022). Among the advantages of micropropagation techniques is its ability to overcome supply constraints, enhance metabolite yield, and conserve endangered plant species by reducing the need for wild harvesting, all this with low cost, Shera *et al*., (2024) and Petrova *et al*., (2024). Recently (Gao *et al*., 2025) showed advancements in biotechnological tools which have further revolutionized the field. The incorporation of elicitors biotic or abiotic agents that stimulate (SM) synthesis has shown significant success in enhancing elite plants yield. Moreover, genetic engineering approaches, such as the over expression of biosynthetic pathway genes, have enabled the optimization of (SM) production in plant cultures Reshi *et al*., (2023). These approaches not only enhance metabolite production but also provide insights into the underlying biosynthetic pathways Jain *et al*., (2023). The objective of this review is to provides a comprehensive overview of micropropagation techniques tools, coupled with modern biotechnological advancements, holds great promise as a sustainable and scalable approach to meet the growing demand for (SM). This an innovative technology offers a viable alternative to traditional extraction methods, with potential applications in pharmaceuticals, nutraceuticals, and (SM) production.

2. Applications of Plant-derived Pharmaceutical Compounds

Phytochemicals, have been essential role in medicine, agriculture as well as in the food industry for periods. These bioactive molecules serve as crucial resources for drug development, pest control, and functional food enhancement. Bhowmick and Prabhakar, 2023.

2.1 Pharmaceuticals

It has been known that many discovered drugs are sourced from medicinal and aromatic plants Chaachouay and Zidane (2024). The use of phytochemicals forms the basis for numerous modern drugs due to their diverse therapeutic properties:

Anticancer Agents: Recently, Rakholiya and collaborators showed that Paclitaxel, derived from the bark of the Pacific yew (*Taxus brevifolia*), is a critical drug used in chemotherapy for treating various cancers, including breast and ovarian cancer Sati *et al*., (2024). Similarly, vinblastine and vincristine, alkaloids from *Catharanthus roseus*, are well known as pharmaceutical agents (Pan *et al*., 2020).
Antimicrobial Agents: It has been known that plants cover a wide range of secondary metabolites, which have been antimicrobial characteristics, like tannins, alkaloids, and flavonoids (Rakholiya *et al*., 2025).
Cardiovascular Medications: It has been shown by Boakye *et al*., (2019), that digoxin which obtained from *Digitalis purpurea*, is used to manage heart failure and arrhythmias by increasing cardiac contractility.
Antimalarial Drugs: Recently, it was shown that Artemisinin, a sesquiterpene lactone from *Artemisia annua*, remains unique compound of the most active actions against malaria, particularly in combination therapies (Zheng *et al*., 2024) .
Cardiovascular Medications: Recently, Khandelwal and collaborators showed that Digoxin, obtained from *Digitalis purpurea*, was use to manage heart failure and arrhythmias by increasing cardiac contractility Khandelwal *et al*., (2024).

2. 2 Agriculture

Plant-derived secondary metabolites are also utilized extensively in agriculture as natural pesticides, herbicides, and growth regulators:

Biopesticides: In a recent report, Hezakiel, and collaborators reported that Neem oil, extracted from the neem tree (*Azadirachta indica*), is an eco-friendly insecticide widely used for pest control causing of its wide-ranging effectiveness and biodegradability Hezakiel *et al*., (2024).

Herbicides: Herbicides: Sorghum (*Sorghum bicolor*) produced the Sorgoleone, as a secondary metabolite. That act as a normal alternate artificial herbicide and has a robust herbicidal activity (de Oliveira *et al*., 2024).

2.3 Food Industry

Phytochemicals show a critical effect in enhancing the nutritional value and safety of food products:
Antioxidants: It has been shown by Zahra *et al*., (2024) that polyphenols and flavonoids, such as quercetin and catechins found in fruits, vegetables, and tea, provide antioxidant benefits that promote health and prevent oxidative stress-related diseases.

Natural Colorants: Recently, Magalhães *et al*., (2024) have reported that some compounds such as betalains from beets and anthocyanins from berries were use as natural food dyes, offering additional value and safe alternatives to synthetic additives while delivering health benefits. Ivan Luzardo-Ocampo *et al*., (2021) showed that anthocyanin-based colorants have been used in products such as yogurt and fruit juices.

3. Plant Tissue Culture for Pharmaceutical Production

It is a critical tool for producing pharmaceutical compounds, offering a controlled environment for the biosynthesis of secondary metabolites. The primary techniques employed in this field comprise callus culture, cell suspension culture, and bioreactor systems for economic production (Bapat *et al*., 2023).

3.1. Callus Culture

It is well known that calli act as totipotent cells which capable of synthesizing secondary metabolites under controlled conditions Bojko *et al*., (2024). Recently, it was shown that the production of valuable compounds like vinblastine from *Catharanthus roseus* and berberine from *Coptis japonica* could be using as callus culture Kiran *et al*., (2024). [In addition, high levels of other secondary metabolites were observed when callus cultivation was successfully carried out by other researchers in the same direction Jassim ;(2018) and Jassim *et al*., (2021), also the production of harmine and harmaline alkaloids from *P. harmalain* Mutasher and Attiya ; (2019). The production of flavonoids in *Salvadora persica* callus was also enhanced by the use of chitosan and titanium dioxide nanoparticles from *Fusarium oxporum* Jasim and Habeeb (2024) ; Abed and Jassim (2024). Furthermore, it was shown that the callus of *Hyoscyamus Niger* L. contains higher concentrations of tropane alkaloids (hyoscyamine, scopolamine and atropine) than the leaves of the parent plant. Although callus culture provides a versatile platform for metabolite production, challenges such as somaclonal variation and reduced metabolite accumulation over time require optimization Murthy *et al*., (2014) and Titova *et al*., (2024).

3.2. Cell Suspension Culture

It is established by transferring fragile callus tissue to liquid media under constant agitation. This method allows for uniform exposure to nutrients and oxygen, resulting in higher growth rates and metabolite yields compared to solid media systems. Cell suspension culture has been successfully utilized to produce active compounds like shikonin from *Lithospermum erythrorhizon* and taxol from *Taxus chinensis*. Additionally, elicitation with biotic (yeast extract) or abiotic (UV light) agents has been shown to further enhance metabolite synthesis Zhao *et al*., (2014). However, maintaining cell viability and genetic stability during prolonged cultivation is a key consideration.

3.3. Bioreactor Systems

For industrial-scale manufacturing, bioreactor systems provide the scalability and controlled environment necessary for efficient secondary metabolite synthesis. Several bioreactor designs, like wave, airlift and stirred tank, have been employed depending on the specific requirements of plant cell cultures. For example, paclitaxel production in *Taxus* species has been optimized using stirred-tank bioreactors under controlled nutrient and aeration conditions Kumar *et al*., (2021). Bioreactors also allow for the integration of stimulants, like methyl jasmonate (MeJA), to enhance metabolite production. The use of bioreactors mitigates environmental and supply challenges associated with traditional extraction methods, providing a sustainable solution for pharmaceutical production.

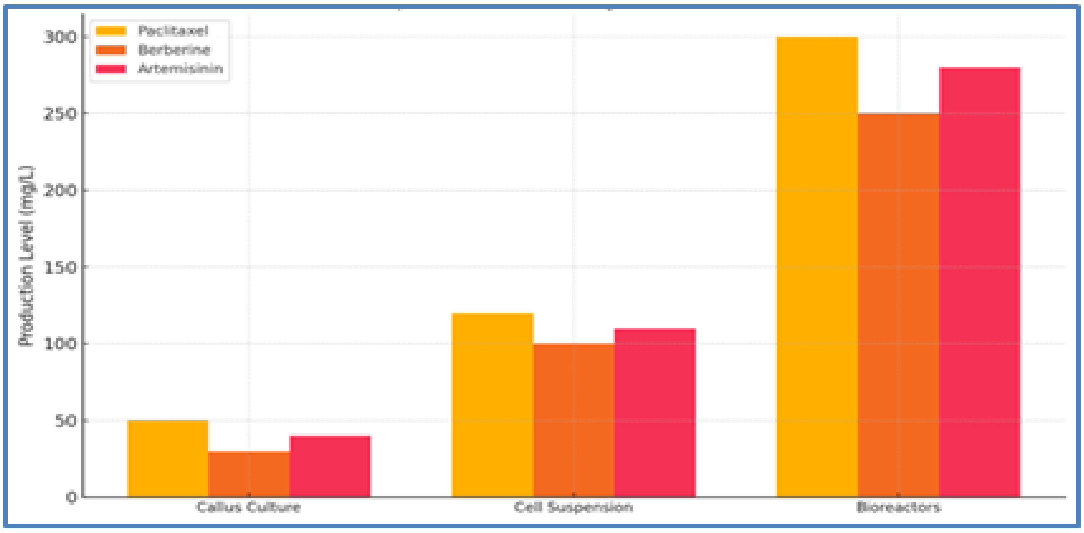

Figure 1. Comparison of some active compounds across different methods.

Interestingly, We compares the production levels of three key secondary metabolites-Paclitaxel, Berberine, and Artemisinin-across three *in vitro* production methods Fig.1. : Callus culture, cell suspension culture, and bioreactors. In this comparative the Bioreactors registered the highest efficiency in producing of all the three metabolites due to their scalability and optimized conditions Qaderi *et al*., (2023).

4.Factors Affecting on Secondary Metabolites Manufacturing In *Vitro*

The creation of secondary metabolites *in vitro* was influence by various physical, chemical, biological, and technical factors. Improving these limits is important to increase the yield and quality of metabolites for pharmaceutical and industrial applications.

4.1. Physical Factors

Light: Several studies showed that light intensity, quality, and photo-period significantly impact secondary metabolite biosynthesis. For example, blue and red wavelengths have been shown to stimulate phenolic and flavonoid production in some plant cultures, while UV light acts as an elicitor for stress-induced metabolite synthesis Georgiev *et al*., (2007).

Temperature: It is well known that the optimal temperature ranges (20–25°C for most plant species) are crucial for enzymatic activities involved in biosynthesis. In contrast, the deviations from this range can inhibit metabolite accumulation or lead to the formation of undesired compounds Gabriella *et al*., (2002).

pH: Similar to temperature, the pH of the culture medium affects enzyme functionality and nutrient uptake. An optimal pH range of 5.5–6.0 is often maintained to maximize metabolite production Mosa *et al*., (2022).

Aeration and Agitation: It has been shown by several researchers that proper oxygen supply and medium agitation ensure homogeneity, enhance cell respiration, and improve metabolite yield. However, excessive aeration can cause shear stress in sensitive cell cultures, Fig.2. Al Aboud *et al*., (2024).

4.2. Chemical Factors

Nutrient Composition: previous studies have reported that the concentration of macronutrients (e.g., nitrogen, phosphate) and micronutrients (e.g., iron, zinc) in the culture medium affects secondary metabolite pathways. For example, reduced nitrogen levels enhance alkaloid production in *Catharanthus roseus Jeyasri et al*., (2023).

Plant Growth Regulators (PGRs): It is well known that auxins (e.g., indole-3-acetic acid) and cytokinins (e.g., kinetin) influence callus induction and metabolite biosynthesis. The auxin-to-cytokinin ratio must be carefully optimized for each plant species and metabolite Murthy *et al*., (2014).

4.3. Biological Factors

Genotype: It has been reported that the genetic makeup of the plant material determines the ability to produce specific metabolites. Selecting high-yielding genotypes is critical for in vitro applications Murthy *et al*., (2022).

Elicitors: Some studies present that the biotic elicitors (fungal or bacterial extracts) and abiotic elicitors (e.g., UV radiation, MeJA activate defense pathways, enhancing metabolite production. For example, MeJA enhances taxol production in Taxus cell cultures Ayiecho *et al*., (2025). Therefore, in this radar chart we summarize the relative impact of different factors such as light, temperature, pH, aeration, and elicitors on secondary metabolite production *In vitro*. Among these factors, elicitors which showed the highest impact, underlining their critical role in stimulating bio synthetic pathways Fig.2.

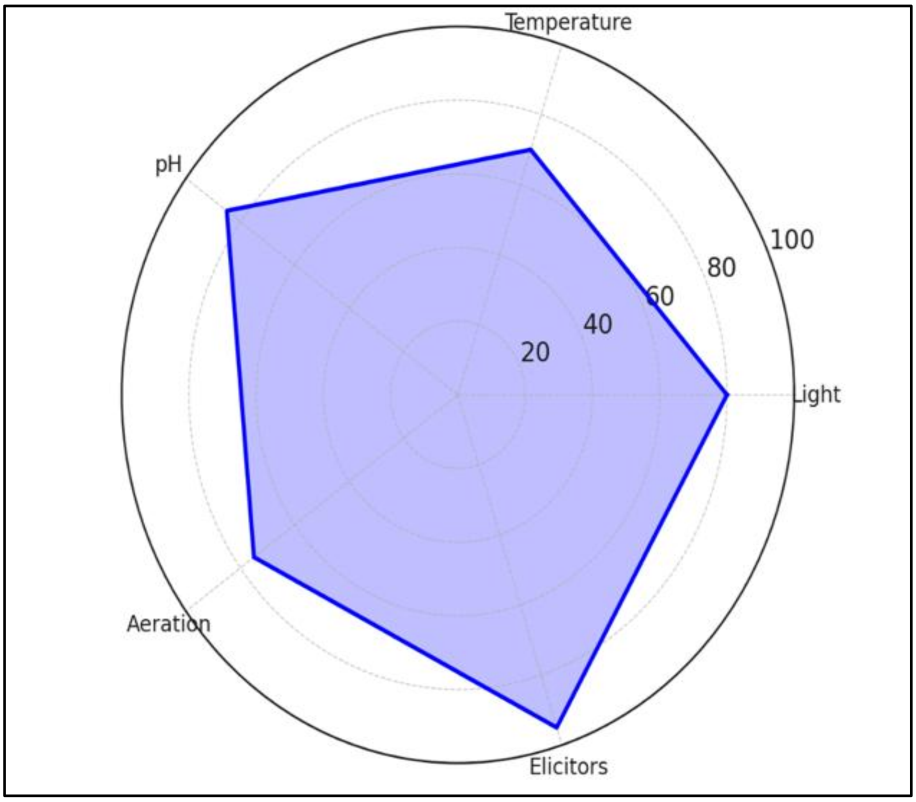

Figure 2. Impact of different factors on *in vitro* secondary metabolite production

4.4. Technical Factors

Culture Type: Many studies showed that the choice between the plant tissue culture like callus culture, cell suspension culture, or organ culture is determined by the target metabolite. For instance, anthraquinones are better synthesized in cultures of *Rubia tinctorum* root (Huang *et al*., 2022).

Subculture Frequency: It has been reported that regular sub culturing is required to maintain cell viability and productivity. However, prolonged sub culturing may cause soma clonal variation, leading to changes in metabolite profiles Yuqing *et al*., (2024).

5. Icrement of Secondary Metabolite via Genetic Engineering

It is well known that genetic engineering has arisen as a influential implement for enhancing the production of secondary metabolites in plants. By directly manipulating biosynthetic pathways, it is possible to increase the yield, quality, and diversity of valuable compounds. Two key approaches in this domain are gene cloning and the development of transgenic plants and cells.

5.1. Gene Cloning

It has been reported that gene cloning involves isolating and transferring genes accountable for the creation of specific secondary metabolites into host systems to improve production. This important technique enables the exact manipulation of metabolic pathways, often leading to enhanced metabolite accumulation.

Biosynthetic Pathway Optimization: It is well known that by identifying and overexpressing key genes in anabolic pathways, the production of target metabolites can be significantly increased. For example, the up- regulate expression of the tyrosine aminotransferase gene in *Coptis japonica* enhanced berberine production, a valuable alkaloid with antimicrobial properties (Paddon *et al*., 2013).

Introduction of Regulatory Genes: It has been reported that regulatory genes, such as factors of transcription, regulator the expression of whole pathways. Overexpression of transcription factors like WRKY or MYB has been shown to boost the production of flavonoids and terpenoids in plant cultures (Hansen *et al*., 2007).

Heterologous Expression Systems: Several studies showed that gene cloning has also enabled the production of plant secondary metabolites in microbial hosts like *Escherichia coli* or *Saccharomyces cerevisiae*. For example, the biosynthesis of artemisinin, a potent antimalarial compound, was successfully reconstructed in yeast cells Zhou *et al*., (2020).

5.2. Transgenic Plants and Cells

It is well known that transgenic technology involves the stable integration of strange genes into plant genomes to produce high levels of desired secondary metabolites. This approach has been widely applied to both whole plants and plant cell cultures.

Metabolic Engineering in Plants: Several studies showed that transgenic plants have been developed to produce higher levels of secondary metabolites by introducing or overexpressing specific biosynthetic genes. For instance, transgenic *Nicotiana tabacum* plants engineered with the *glucosinolate* biosynthetic pathway exhibited enhanced production of these sulfur-containing compounds with anticancer properties Guillon *et al*., (2006).

Edit of CRISPR/Cas9 Gene: In recent years, the advent of genome editing tools like CRISPR/Cas9 has allowed for precise modifications of biosynthetic pathways. By knocking out genes encoding competitive enzymes or repressors, plants can redirect resources towards the synthesis of target metabolites Guillon *et al*., (2006) and Ahmadikhah *et al*., (2025) .

Hairy Root Cultures: Recently, Ahmad and collaborators showed that transformed root culture produced by infecting the roots of higher plants with *Agrobacterium rhizogenic*. They showed that this strategy was use for small- and large-scale production, with high efficiency, genetic and biochemical stability, and a plant hormone-independent growth approach. These bacteria mediated transformation results in hairy root cultures that produce secondary metabolites at higher levels. These transformed roots was genetically stable and have been widely used to enhance the production of compounds like withanolides in *Withania somnifera* Ahmad *et al*., (2024).

6.Conclusions

Plant cell, tissue, and organ culture is a valued technique for producing secondary metabolites of medical importance. In current time, most in vitro production strategies have been used due to the knowledge of the secondary metabolite pathway and its regulation in commercially valuable plants. Advances in plant tissue culture, genetic engineering, and bioreactor techniques have revolutionized the in vitro production of plant-derived pharmaceutical compounds, providing a supportable and accessible resolution to the challenges of old-fashioned plant cultivation, and at a lower cost.

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