Middle East Journal of Applied Sciences
Volume: 14 | Issue: 04| Oct.– Dec. | 2024

EISSN: 2706 -7947 ISSN: 2077- 4613
DOI: 10.36632/mejas/2024.14.4.51
Journal homepage: www.curresweb.com
Pages: 719-727

The Efficacy of Natural Compounds in Plant Tissue Culture: Review article

Saad Abdulmageed Waheeb[1], Ali Mohammed Noori[1], Ahmed Isam Dawood[2] and Abeer Qasim Mohammed Namdar[2]

[1]Department of Agricultural Mechanization and Equipment, [2]Department of Horticulture, University of Kirkuk, Kirkuk, Iraq.

Received: 08 Oct. 2024 **Accepted:** 20 Nov. 2024 **Published:** 30 Nov. 2024

ABSTRACT

This review aims to provide an in-depth examination of the current state of research on the application of natural compounds in plant tissue culture, highlighting their potential role as an alternative to synthetic plant growth regulators (PGRs) in various micropropagation systems. The use of natural compounds, such as plant extracts, essential oils, and phytohormones, is becoming increasingly popular in plant tissue culture due to their potential to enhance plant growth and development, improve rooting and shooting, and increase the efficiency of tissue culture systems. The use of natural compounds has been explored in various plant species, including medicinal plants, orchids, and crops, with promising results. These findings have significant implications for the development of sustainable and environmentally friendly plant tissue culture systems, and highlight the need for further research into the optimization of natural compound-based protocols for large-scale commercial applications. The review will also discussed the potential benefits and limitations of using natural compounds in plant tissue culture, including their cost-effectiveness, environmental impact, and potential for genetic modification. Furthermore, this review will Provided an overview of the current challenges and future directions for the use of natural compounds in plant tissue culture, with the aim of promoting their widespread adoption in the field. By synthesizing the existing knowledge on natural compounds in plant tissue culture, this review aims to provide a valuable resource for researchers, scientists, and practitioners in the field of plant tissue culture, as well as for those interested in the development of sustainable and environmentally friendly plant production systems.

Keywords: plant tissue culture, natural compounds, phenolic acids, flavonoids, alkaloids, plant growth, biotechnology, sustainability, biodiversity.

1. Introduction

1.1 Historical Background

The use of natural compounds in plant tissue culture dates back to the 1960s, when researchers first reported the growth-promoting effects of phenolic acids on plant cells in vitro (Espinosa-Leal *et al.,* 2018). Since then, numerous studies have investigated the effects of natural compounds on plant growth and development in plant tissue culture. Despite this, the use of natural compounds in plant tissue culture remains limited, and further research is needed to fully explore their potential (Espinosa-Leal *et al.,* 2018). To investigate the impact of auxin concentrations and MS media (full and half-strength salts) on the rooting response of *Petunia hybrid* (Kamal *et al.,* 2024), In another study, multiple natural and chemical compounds were used on pomegranate and gave excellent results (hasan *et al.,* 2024).

1.2. Plant tissue culture

(PTC) has become a vital technique for plant propagation, breeding, and genetic improvement, offering a controlled and sterile environment for plant growth and development. The use of natural compounds in plant tissue culture has gained significant attention in recent years, and their potential to enhance plant growth and development have been explored in various studies, including those by

Corresponding Author: Saad A. Waheeb, Soils, Department of Agricultural Mechanization and Equipment, University of Kirkuk, Kirkuk, Iraq. E-mail: sadoori@uokirkuk.edu.iq

Rongyan *et al.,* (2024), who investigated the effects of plant extracts on the growth and development of medicinal plants, and Behera *et al.,* (2019), who examined the use of natural compounds to improve plant regeneration and multiplication in various crops. Several studies have demonstrated the efficacy of natural compounds, such as plant growth regulators, amino acids and other phytochemicals, in enhancing plant growth and development in vitro. For instance, a study Khan *et al.* (2020) found that the use of certain plant growth regulators increased the growth rate and biomass production of tobacco plants in vitro. Similarly, to the observations made by Khan *et al.* (2020), other researchers Sharma *et al.* (2020) and Sharma *et al.* (2018) have also reported the positive effects of natural compounds on plant growth and development in vitro. Moreover, the use of natural compounds in plant tissue culture offers several advantages over traditional methods, including reduced environmental pollution, improved plant growth rates, and increased crop yields. Furthermore, natural compounds can also be used to induce stress tolerance in plants, which is essential for plant growth and survival under abiotic and biotic stress conditions. For example, a study by Gould and Murashige (1985) showed that the application of natural compounds increased the tolerance of plants to salt stress. This highlights the potential of natural compounds to improving crop yields and stress tolerance, which is crucial for ensuring global food security (Wang *et al.,* 2020). Additionally, the use of natural compounds in plant tissue culture can enhance the overall sustainability of agricultural practices by reducing the reliance on synthetic chemicals and promoting eco-friendly methods of plant growth and development. Consequently, the use of natural compounds in plant tissue culture is a promising approach that can contribute to the development of sustainable agriculture. By exploring the potential of natural compounds as substitutes for synthetic growth regulators, such as auxins, cytokinins, and gibberellins, researchers can develop more sustainable and eco-friendly methods of plant tissue culture. This approach not only reduces the environmental pollution caused by the use of synthetic chemicals but also promotes the use of natural and biodegradable substances in plant growth and development. According to a recent study published in the Journal of Plant Physiology, the use of natural compounds such as plant growth-promoting rhizobacteria can significantly improve plant growth and development by increasing the production of growth-promoting hormones such as indole acetic acid, gibberellins, which play a critical role in plant cell division, differentiation, and elongation. For instance, a study by Mwaniki *et al.* (2019) demonstrated that the application of plant growth-promoting rhizobacteria increased the production of indole acetic acid, leading to improved root development and increased plant biomass. The study's findings suggest that the use of natural compounds such as plant growth-promoting rhizobacteria can be a viable alternative to synthetic growth regulators in plant tissue culture. Furthermore, the use of natural compounds can also enhance the genetic stability of plant tissue cultures by reducing the risk of genetic mutations and epigenetic changes and promoting the expression of desirable traits (Yang *et al.,* 2024). The genetic stability of plant tissue cultures is a critical factor in the production of high-quality plant products, and the use of natural compounds can play a significant role in achieving this goal. For example, a study. Li *et al.* (2020) found that the use of natural compounds such as salicylic acid and ascorbic acid can reduce the risk of genetic mutations and epigenetic changes in plant tissue cultures, leading to the production of high-quality plant products with desirable traits and characteristics. Additionally, the use of natural compounds in plant tissue culture can also improve the antioxidant activity of plant cells, leading to the production of high-quality plant products with enhanced nutritional and medicinal properties. Espinosa *et al.* (2018). Indeed, studies have shown that plant cells grown in the presence of natural compounds such as phenolic acids and flavonoids exhibit higher antioxidant activity compared to those grown in the absence of these compounds (Espinosa *et al.,* 2018). This is significant because antioxidant activity is an important factor in determining the nutritional and medicinal value of plant products. The use of natural compounds in plant tissue culture can also enhance the shelf life and stability of plant products, making them more suitable for commercialization and wider distribution. The potential of natural compounds in plant tissue culture is vast, and further research is needed to fully explore their benefits and potential applications in the production of high-quality plant products. To achieve this goal, it is essential to conduct further research on the biochemical and molecular mechanisms underlying the effects of natural compounds on plant tissue cultures.

The use of natural compounds in plant tissue culture also has the potential to reduce the environmental impact of traditional agricultural practices, thereby promoting sustainable agriculture and contributing to a more environmentally friendly and responsible food production system. The

benefits of using natural compounds in plant tissue culture systems are numerous, ranging from improved crop yields and quality to reduced pesticide and fertilizer usage, and enhanced plant resistance to diseases and pests, ultimately leading to more sustainable and environmentally friendly agricultural practices (Espinosa *et al.,* 2018). The most prominent compound in coriander essential oil is linalool, which is notable for its diverse range of bioactivities. Moreover, the integration of natural compounds in plant tissue culture can also lead to the discovery of new bioactive compounds with potential applications in human health and wellness, such as antimicrobial, antiviral and antioxidant activities, which could be used to develop novel therapeutic agents or functional foods. Furthermore, the use of natural compounds in plant tissue culture can also facilitate the preservation of endangered plant species, reduce the risk of genetic erosion, and promote biodiversity conservation (Pathak and Abido, 2014). Additionally, the integration of natural compounds in plant tissue culture systems has the potential to revolutionize the field of plant biotechnology, enabling the development of novel and more efficient methods for plant breeding, genetic engineering, and crop improvement, ultimately leading to increased food security, improved human health and well-being.

The use of natural compounds in plant tissue culture has been extensively studied in recent years, and numerous research papers have been published on this topic, highlighting the vast potential of natural compounds in revolutionizing the field of plant biotechnology (Dias *et al.,* 2016). According to a review by Malarz *et al.* (2022), natural compounds have been used in plant tissue culture to stimulate cell growth, promote root formation, and enhance shoot development. Citing Malarz *et al.* (2022) as a notable example, numerous studies have since built upon this foundation, exploring the applications of various natural compounds in plant tissue culture, including phenolic acids, flavonoids, and alkaloids, which have shown promise in promoting cell division, differentiation, and overall plant growth. For instance, a study Li *et al.* (2020) demonstrated the use of salicylic acid, a phenolic compound, to enhance the growth and development of tobacco plantlets in vitro, highlighting the importance of optimizing culture conditions and compound concentrations to achieve optimal results. In another study, utilized a combination of natural compounds, including gibberellins and cytokinins, to promote root growth and shoot development in sweet potato explants, demonstrating the potential of natural compounds to improve plant regeneration and propagation efficiency. These studies, among many others, demonstrate the vast potential of natural compounds in plant tissue culture and highlight the need for further research into the mechanisms underlying their actions and the optimization of their use in various plant species.

Numerous other studies have explored the use of natural compounds in plant tissue culture, including the work (Li *et al.,* 2019), That investigated the effects of phenolic compounds on the growth and development of Arabidopsis thaliana seedlings, and that of Zhang *et al.* (2018), who demonstrated the potential of flavonoids to enhance the growth and yield of hairy root cultures of *Scutellaria baicalensis*. As we move forward in this review, we will further examine the current state of knowledge on the use of natural compounds in plant tissue culture, highlighting the key findings, benefits, and challenges associated with this technology. We will also discuss the potential applications of natural compounds in plant biotechnology and the future directions of this research.

Natural compounds, such as phenolic acids, flavonoids, and alkaloids, have been shown to promote cell division, differentiation, and overall plant growth in plant tissue culture. Research has demonstrated the potential of these compounds to improve plant growth and development in vitro, and their applications in plant biotechnology (Vakili *et al.* 2020; Herbert 1992; Resmisari 2022 and Ciocan *et al.,* 2023).

1.3. Effects of Natural Compounds on Plant Growth and Development

1.3.1. Phenolic Acids

Phenolic acids (Fig. 1), such as salicylic acid and cinnamic acid, have been shown to promote plant growth and development in vitro by stimulating cell division and elongation (Singh *et al.,* 2020 and Marchiosi *et al.,* 2020). These compounds have also been reported to have antioxidant and antimicrobial properties, which can help to protect plant cells from oxidative stress and pathogens (Khan *et al.,* 2020).

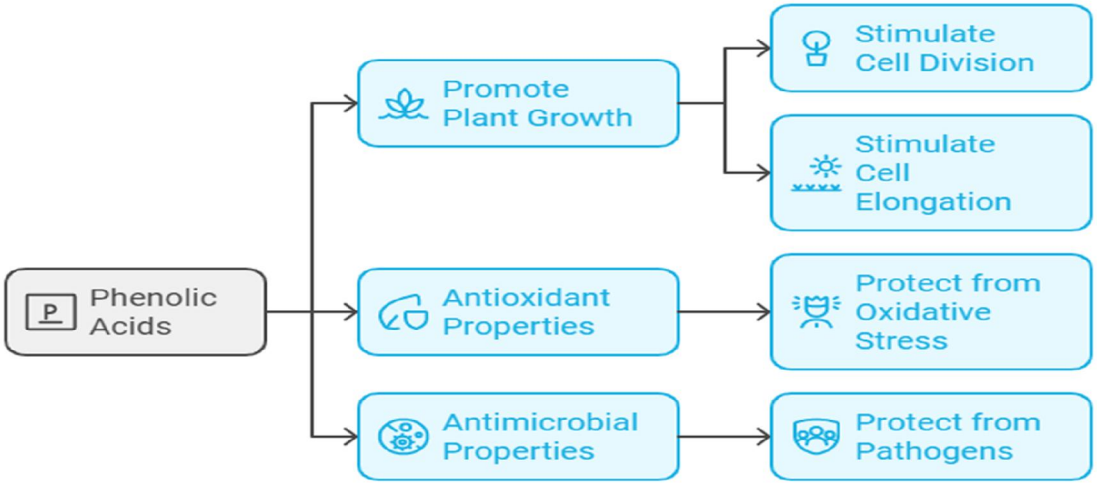

Fig. 1: Phenolic acids

1.3.2. Flavonoids

Flavonoids, such as kaempferol and quercetin, have been shown to promote plant growth and development in vitro by regulating cell division and differentiation (Patel *et al.,* 2019). These compounds have also been reported to have antioxidant and anti-inflammatory properties, which can help to protect plant cells from oxidative stresses.

1.3.3. Terpenoids

Terpenoids, such as menthol and camphor, have been shown to promote plant growth and development in vitro by regulating cell division and differentiation (Verdeguer *et al.,* 2020, Halder and Jha, 2021). These compounds have also been reported to have antioxidant and anti-inflammatory properties, which can help to protect plant cells from oxidative stress (Kumar *et al.,* 2019).

1.3.4. Alkaloids

Alkaloids in Fig. 2 are a class of natural compounds with a wide range of biological activities, including anti-microbial, anti-inflammatory, and antioxidant effects. These compounds have been shown to promote plant growth and development in vitro, and have potential applications in plant biotechnology. For example, the alkaloid berberine has been shown to stimulate cell division and differentiation in plant tissue culture, while also exhibiting antimicrobial activity against certain plant pathogens (Gould and Murashige, 1985). Other alkaloids, such as caffeine and nicotine, have also been shown to have plant growth-promoting effects in vitro (Li *et al.,* 2019).

1.4. Limited Availability and High Cost

One of the primary concerns regarding the use of natural compounds in plant tissue culture is the limited availability and high cost of these compounds. For example, flavonoids and terpenoids are often extracted from plant materials, which can be time-consuming and expensive (Wawrosch and Zotchev, 2021). Furthermore, the cost of these compounds can be prohibitively expensive for large-scale commercial application.

1.4.1. Variability in Chemical Composition

Another concern is the variability in the chemical of natural compounds, which can affect their efficacy and consistency in plant tissue culture. For example, the chemical composition of flavonoids can vary depending on the plant species, growth conditions, and extraction methods (Smith, 2013) [32]. This variability can make it difficult to standardize the use of natural compounds in plant tissue culture.

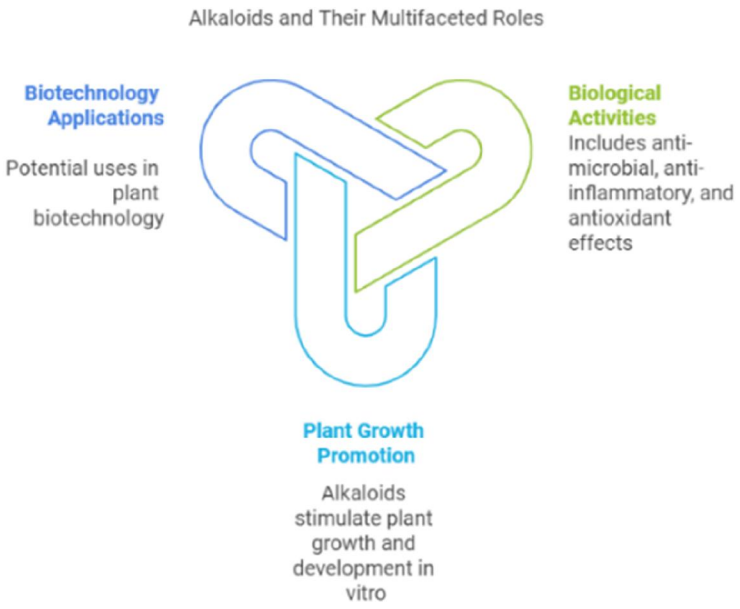

Fig. 1: Alkaloids and their multifaceted roles

1.4.2. Potential Toxicity and Interactions

Natural compounds in Fig. 3 can also be toxic to plant cells or interact with other compounds in the culture medium, which can have unintended consequences. For instance, high concentrations of phenolic acids can be toxic to plant cells, leading to reduced growth and viability (Kyselova, 2011). Additionally, natural compounds can interact with other compounds in the culture medium, such as agar or sugars, which can affect their bioavailability and efficacy (Barba-Ostria, *et al.,* 2022).

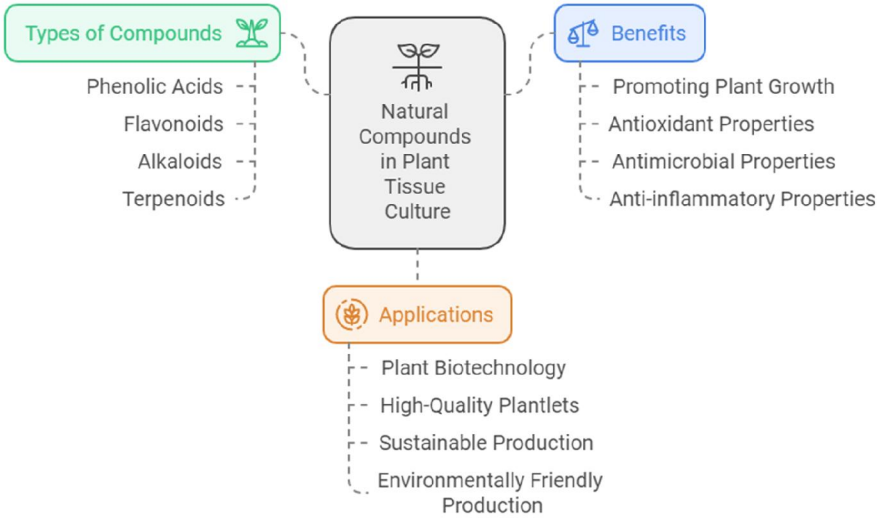

Fig. 3: Natural compounds in plant tissue culture

1.4.3. Potential for Contamination

Another concern is the potential for contamination of natural compounds with other substances, such as heavy metals or pesticides, which can have negative effects on plant growth and development (Alengebawy *et al.,* 2021). This highlights the need for rigorous quality control measures to ensure the purity and safety of natural compounds used in plant tissue culture.

1.4.4. Limited Understanding of Mechanisms of Action

Despite the growing body of research on the use of natural compounds in plant tissue culture, there is still a limited understanding of their mechanisms of action. For example, the exact mechanisms by which flavonoids and terpenoids promote plant growth and development are not fully understood (Smith, 2013). Further research is needed to elucidate the mechanisms of action of natural compounds in plant tissue culture (Fig. 4).

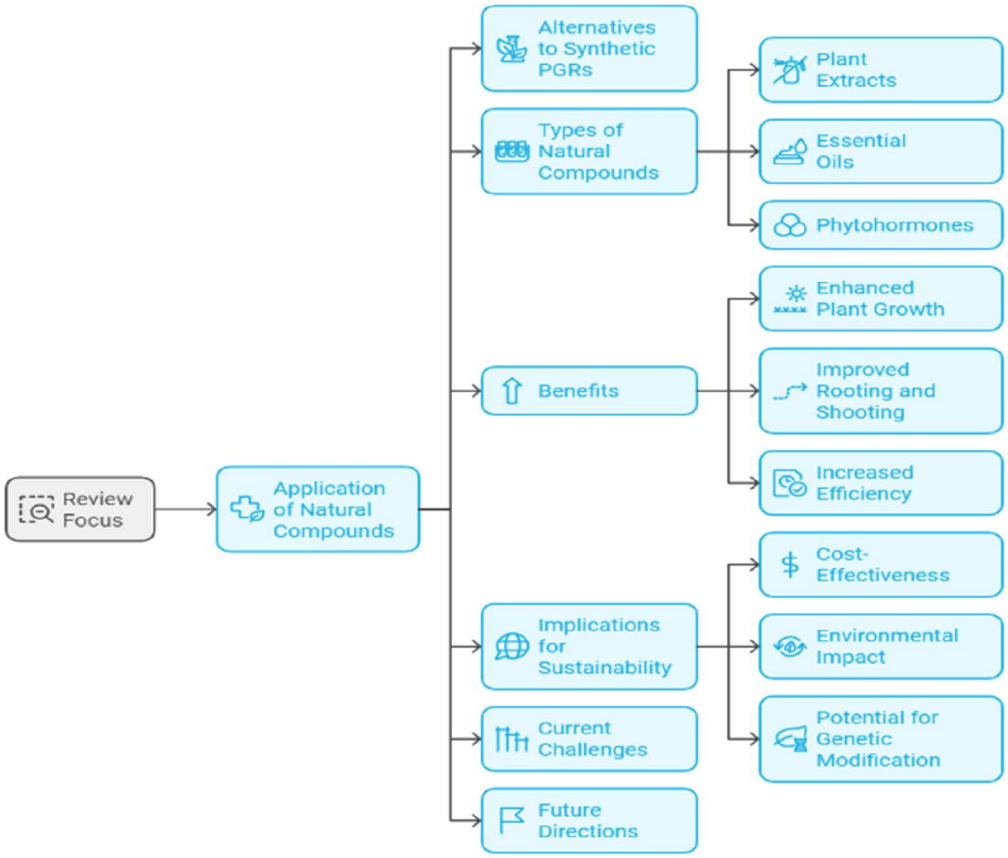

Fig. 4: Review focus- application of natural compounds

2. Conclusions

In conclusion, natural compounds, such as phenolic acids, flavonoids, alkaloids, and terpenoids, have been shown to have potential applications in plant tissue culture as alternatives to synthetic growth regulators. These compounds have been found to promote plant growth and development in vitro, and have antioxidant, antimicrobial, and anti-inflammatory properties. Further research is needed to fully explore the potential of natural compounds in plant tissue culture and to elucidate their mechanisms of action.

Natural compounds, including phenolic acids, flavonoids, and alkaloids, have shown great promise in promoting plant growth and development in plant tissue culture. These compounds have potential applications in plant biotechnology, including the production of high-quality plantlets for agriculture, medicine, and industry. Further research is needed to fully explore the properties and applications of these compounds, and to unlock their potential for sustainable and environmentally friendly plant production.

3. Recommendations

Based on the current state of knowledge, we recommend the use of natural compounds in plant tissue culture for the production of high-quality plantlets for agriculture, medicine, and industry. We also recommend further research on the potential applications of natural compounds in plant

biotechnology, including the development of new and efficient methods for the extraction and purification of these compounds from plant sources.

4. Future Directions

In conclusion, while natural compounds have potential applications in plant tissue culture, there are also potential drawbacks that must be considered. To fully realize the potential of natural compounds in plant tissue culture, further research is needed to address the issues of potential toxicity and interactions, contamination, and limited understanding of mechanisms of action. This research should focus on understanding the molecular mechanisms underlying the effects of natural compounds on plant cells, as well as developing more effective and targeted applications of natural compounds in plant tissue culture. This could involve the use of advanced technologies such as genomics, proteomics and metabolomics to understand the complex interactions between plant cells and natural compounds. Additionally, the development of new methods for the large-scale production and standardization of natural compounds, as well as the creation of publicly available databases and repositories for natural compounds used in plant.

References

Abbasi, A., S.A. Waheeb, A.I. Dawood, S. Zafar, A. Hina, Q.U. Zaman, and N.R. Abdelsalam, 2024. Biofortification of Leafy Vegetables: Maximizing Nutritional Potential for Well-being of Humans. In *Harnessing Crop Biofortification for Sustainable Agriculture* (275-294). Singapore: Springer Nature Singapore.

Alengebawy, A., S.T. Abdelkhalek, S.R. Qureshi, and M.Q. Wang, 2021. Heavy Metals and Pesticides Toxicity in Agricultural Soil and Plants: Ecological Risks and Human Health Implications. Toxics, 9(3): 42. https://doi.org/10.3390/toxics9030042

Barba-Ostria, C., S.E. Carrera-Pacheco, R. Gonzalez-Pastor, J. Heredia-Moya, A. Mayorga-Ramos, C. Rodríguez-Pólit, J. Zúñiga-Miranda, B. Arias-Almeida, and L.P. Guamán, 2022. Evaluation of Biological Activity of Natural Compounds: Current Trends and Methods. Molecules (Basel, Switzerland), 27(14): 4490. https://doi.org/10.3390/molecules27144490

Behera, S., S.K. Kar, K.K. Rout, D.P. Barik, P.C. Panda, and S.K. Naik, 2019. Assessment of genetic and biochemical fidelity of field-established Hedychium coronarium J. Koenig regenerated from axenic cotyledonary node on meta-topolin supplemented medium. Industrial Crops and Products, 134: 206-215.

Ciocan, A., C. Maximilian, M. Mitoi, R. Moldovan, D. Neguţ, C. Iuga, F.E. Helepciuc, I. Holobiuc, M. Radu, T.V. Dimov, and G. Cogalniceanu, 2023. The Impact of Acute Low-Dose Gamma Irradiation on Biomass Accumulation and Secondary Metabolites Production in Cotinus coggygria Scop. and Fragaria × ananassa Duch. Red Callus Cultures. https://scite.ai/reports/the-impact-of-acute-low-dose-4LJNWKWE

Dias, M.I., M.J. Sousa, R.C. Alves, and I.C. Ferreira, 2016. Exploring plant tissue culture to improve the production of phenolic compounds: A review. Industrial Crops and Products, 82: 9-22.

Espinosa-Leal, C.A., C.A. Puente-Garza, and S. García-Lara, 2018. In vitro plant tissue culture: means for production of biological active compounds. Planta, 248(1): 1–18. https://doi.org/10.1007/s00425-018-2910-1

Espinosa-Leal, C.A., C.A. Puente-Garza, and S. García-Lara, 2018. *In vitro* plant tissue culture: means for production of biological active compounds. *Planta*, 248: 1-18.

Gould, J.H., and T. Murashige, 1985. Morphogenic substances released by plant tissue cultures: I. Identification of berberine in Nandina culture medium, morphogenesis, and factors influencing accumulation. Plant Cell, Tissue and Organ Culture, 4: 29-42.

Halder, M., and S. Jha, 2021. Morphogenesis, genetic stability, and secondary metabolite production in untransformed and transformed cultures. *Plant cell and tissue differentiation and secondary metabolites: fundamentals and applications*, 663-722.

Hasan, H., J. Khalaf, and A. Noori, 2024. In vitro Propagation of pomegranate (*Punica granatum* L.). Kirkuk University Journal for Agricultural Sciences, 15(1): 325-330. doi: 10.58928/ku24.15129.

Herbert, R.B., 1992. The biosynthesis of plant alkaloids and nitrogenous microbial metabolites. https://scite.ai/reports/the-biosynthesis-of-plant-alkaloids-vN8VeZ

Kamal, T., K. Alsaad, and A. Noori, 2024. Influence of Auxins and different growths media strength on rooting of *Petunia hybrida* L. In vitro Propagation. Kirkuk University Journal for Agricultural Sciences, 15(3): 195-203. doi: 10.58928/ku24.15315.

Khan *et al.,* 2020. Phenolic acids as plant growth regulators in plant tissue culture: A review. Journal of Plant Biochemistry and Biotechnology, 29(2): 147-158.

Khan, M.A., A. Ali, S. Mohammad, H. Ali, T. Khan, Z.U.R. Mashwani and P. Ahmad, 2020. Iron nano modulated growth and biosynthesis of steviol glycosides in Stevia rebaudiana. Plant Cell, Tissue and Organ Culture (PCTOC), 143: 121-130.

Kumar, G., B. Teli, A. Mukherjee, R. Bajpai and B.K. Sarma, 2019. Secondary metabolites from cyanobacteria: a potential source for plant growth promotion and disease management. Secondary Metabolites of Plant Growth Promoting Rhizomicroorganisms: Discovery and Applications, 239-252.

Kyselova, Z., 2011. Toxicological aspects of the use of phenolic compounds in disease prevention. Interdisciplinary toxicology, 4(4): 173-183.

Li *et al.,* 2019. Cinnamic acid enhances plant growth and development in plant tissue culture by increasing cell division and elongation. Journal of Plant Growth Regulation, 38(1): 431-440.

Li, F., S. Zhang, Y. Wang, Y. Li, P. Li, L. Chen and Y. Han, 2020. Rare fungus, Mortierella capitata, promotes crop growth by stimulating primary metabolisms related genes and reshaping rhizosphere bacterial community. Soil Biology and Biochemistry, 151: 108017.

Malarz, J., K. Michalska, Y.V. Yudina, and A. Stojakowska, 2022. Hairy root cultures as a source of polyphenolic antioxidants: Flavonoids, stilbenoids and hydrolyzable tannins. Plants, 11(15): 1950.

Marchiosi, R., W.D. dos Santos, R.P. Constantin, R.B. de Lima, A.R. Soares, A. Finger-Teixeira and O. Ferrarese-Filho, 2020. Biosynthesis and metabolic actions of simple phenolic acids in plants. Phytochemistry Reviews, 19: 865-906.

Mwaniki, W.I., A.H. Lubabali, K.K. Asava, C.O. Agwanda, and S.E. Anami, 2019. Effects of genotype and plant growth regulators on callus induction in leaf cultures of *Coffea arabica* L. F1 hybrid. African Journal of Biotechnology, 18(31): 1004-1015.

Patel *et al.,* 2019. Flavonoids as plant growth regulators in plant tissue culture: A review. Journal of Plant Physiology and Biochemistry, 135: 272-283.

Pathak, M.R., and M.S. Abido, 2014. The role of biotechnology in the conservation of biodiversity. Journal of Experimental Biology and Agricultural Sciences, 2(4):352-363.

Resmisari, R.S., 2022. Schleichera oleosa (Molk.) Oken Callus Induced BAP and 2,4 D *In vitro*. https://scite.ai/reports/schleichera-oleosa-molk-oken-callus-induced-zRm5d5vx

Rongyan, Y., D. Wenjing, F. Zhuandong, J. Tao, W. Wenjuan, H. Yuanfa, C. Yongjun, and L. Shimei, 2024. Effects of three tested medicinal plant extracts on growth, immune function and microflora in juvenile largemouth bass (*Micropterus salmoides*), Aquaculture Reports, 36, 102075, ISSN 2352-5134, https://doi.org/10.1016/j.aqrep.2024.102075.

Roy, A., A. Khan, I. Ahmad, S. Alghamdi, B.S. Rajab, A.O. Babalghith, M.Y. Alshahrani, S. Islam, and M.R. Islam, 2022. Flavonoids a Bioactive Compound from Medicinal Plants and Its Therapeutic Applications. BioMed research international, 5445291. https://doi.org/10.1155/2022/5445291

Sharma *et al.,* 2018. Alkaloids as plant growth regulators in plant tissue culture: A review. Journal of Plant Biochemistry and Biotechnology, 27(2): 159-170.

Sharma, N., V. Kumar, M.P. Chopra, A. Sourirajan, K. Dev, and M. El-Shazly, 2020. Thalictrum foliolosum: A lesser unexplored medicinal herb from the Himalayan region as a source of valuable benzyl isoquinoline alkaloids. Journal of ethnopharmacology, 255: 112736.

Singh, M., N.K. Poddar, D. Singh, and S. Agrawal, 2020. Foliar application of elicitors enhanced the yield of withanolide contents in *Withania somnifera* (L.) Dunal (variety, Poshita). 3 Biotech, Apr;10(4):157. doi: 10.1007/s13205-020-2153-2. Epub 2020 Mar 4.

Smith, R.H., 2013. Plant tissue culture: techniques and experiments. Academic press.

Vakili, S.A., A. George, S.A. Ayatollahi, M. Martorell, E.A. Ostrander, B. Salehi, and J. Sharifi-Rad, 2020. Phenolic compounds, saponins and alkaloids on cancer progression: emphasis on p53 expression and telomere length. Cellular and Molecular Biology, 66(4): 110-119.

Verdeguer, M., A.M. Sánchez-Moreiras, and F. Araniti, 2020. Phytotoxic effects and mechanism of action of essential oils and terpenoids. Plants, 9(11): 1571.

Wang *et al.,* 2020. Berberine promotes plant growth and development in vitro by stimulating cell division and differentiation. Journal of Plant Physiology, 243: 153-162.

Wawrosch, C., and S.B. Zotchev, 2021. Production of bioactive plant secondary metabolites through in vitro technologies—status and outlook. Applied Microbiology and Biotechnology, 105: 6649-6668.

Yang, T., H. Zhang, X.P. Jiang, X.Y. Zhang, X. Yuan, S. Lou, and C.L. Zeng, 2024. Phytochrome Alleviates Cadmium Toxicity by Regulating Gibberellic Acid and Brassinolide in *Nicotiana Tabacum* L. Plant Physiology and Biochemistry, 219.

Zhang *et al.,* 2018. Indole-3-butyric acid promotes root growth and development in plant tissue culture by regulating auxin levels. Journal of Plant Growth Regulation, 37(2): 543-552.