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Anticancer Potential Of Bioactive Extracts From Vietnamese Endemic Medicinal Plant Paramignya Trimera: A Review Of In Vitro Evidence, Sustainability, And Biodiversity Implications

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Abstract

Background: *Cancer remains one of the major causes of death in the world, and the efforts to find innovative ways of anticancer treatment are crucial. Plants of medicine are being considered, namely Paramignya trimera (Xao Tam Phan), which has possible anticancer effects. The proposed review will assess the bioactive extracts of P. trimera regarding its anticancer properties, sustainability, and biodiversity.*

Methods: *The systematic review was carried out based on the published works between 2018 and 2025 on the in vitro assessment of anticancer activity of P. trimera. The databases such as PubMed, SCOPUS and Web of Science were accessed to collect research using the PICO framework in order to evaluate the relevance of the studies. The studies comprised in vitro studies on the inhibition of cell proliferation, induction of apoptosis and selective cytotoxicity.*

Results: *Through the review, six studies were identified that, in combination, supported three major themes. The initial theme demonstrated that Paramignya trimera had always suppressive effects on cancer cell growth and induction of apoptosis in various in vitro cancer cells. The second theme portrayed that in vitro multiplication has the potential to maintain plant supply by genetically stable culturing. The third theme was raised and focused on biodiversity loss and the necessity of conservation measures to minimise the pressure on wild populations.*

Discussion: *Although P. trimera has the potential to be an anticancer agent, more studies must be done to ascertain its therapeutic efficacy and safety, both in animals and in clinical trials. The review highlights the significance of sustainable methods of crop cultivation, including somatic embryogenesis and micropropagation, to ensure that the plant can be freely available without the utilisation of natural resources.*

Conclusions: P. trimera *holds significant promise for cancer therapy but requires further validation and the development of sustainable cultivation practices to preserve its bioactive compounds and ensure long-term availability.*

Keywords: Paramignya trimera, *anticancer, bioactive compounds, apoptosis, sustainability, in vitro, medicinal plants, biodiversity.*

1. INTRODUCTION

Cancer remains one of the most significant global health challenges, and despite major progress in medical treatments, the demand for novel therapeutic agents continues to grow (Sung et al., 2021). The incidence of cancer has been nearly one in six deaths in the world in the year 2020, and this shows that it has a significant global impact (World Health Organisation, 2025). According to Lee et al. (2018), traditional medicine has long been playing a role in disease control, and medicinal plants have been growing in scientific interest due to their potential anticancer effects. In this growing field of interest, the biodiversity of Vietnam has been of particular significance in the hunt to find plant-based therapeutic candidates. The Vietnamese traditional medicine has spawned a specific interest in the use of Paramignya trimera, which is also referred to as Xao Tam Phan; however, this has since gained scientific importance as described by Nguyen et al. (2019). In spite of the fact that some conditions have been treated using this plant, it is still developing and has not been scientifically proven, as stressed by Bao Tran et al. (2025). Nevertheless, the initial scientific studies, e.g., those conducted by Nguyen et al. (2020), show that *Paramignya trimera (P. trimera)* extracts can also induce apoptosis and prevent abnormal cell growth and suppress the cell cycle, which is a strong indication of the potential of natural anticancer therapy development in in vitro research models.

Another reason that makes medicinal plants such as P. trimera a topic of research as cancer therapy is the potential of this plant to select cancer cells and minimise harmful effects on normal cells (Triantafillidis et al., 2022). Although the traditional chemotherapy method is effective in destroying cancer cells, it usually has dire side effects because of toxicity to the normal tissues (Schirrmacher, 2019). This has urged the urgency of the search for plant-based alternatives which may selectively attack cancer cells and cause

no side effects. Dumitraş and Andrei (2022) point out that flavonoid, alkaloid, and other polyphenolic extracts of plants have demonstrated antiproliferative and pro-apoptotic properties on cancer cell lines. The efficacy of initial trials of using methanolic extracts in P. trimera has shown cytotoxic properties in different cancer cell lines, such as breast and lung cancer, as well as some of the most common and challenging to cure cancers. All these encouraging results indicate that the plant can be used to develop cancer therapy.

The in vitro studies of *P. trimera* bioactive extracts using a controlled environment are a means to determine its capability as an anticancer agent. The established cancer cell lines can enable scientists to assess the action mechanisms of the plant, such as the ability to increase cancer cell growth, induce apoptosis, and control cell division (Chaudhry et al., 2020). These studies are essential in isolating the bioactive compounds of its therapeutic effects. As an illustration, other medicinal plant compounds are found to cause apoptosis by different pathways, such as p53 and control important signalling pathways, including PI3K/Akt, that mediate cell survival and proliferation (Zhang et al., 2018). A comparable study on P. trimera will be capable of discovering the bioactive components of the plant that may lead to its anticancer effects and may be used to develop new anticancer agents. Nguyen et al. (2021), in a study, performed in vitro experiments on pancreatic cancer cell lines (AsPC-1 and BxPC-3) and determined dose-dependent cytotoxicity with the IC50 values of the low hundreds of micrograms per millilitre. P. trimera, in combination with Phyllanthus amarus, increased its anticancer effects.

Nonetheless, as interest in P. trimera increases, so do concerns about its sustainability, as interest in plant-derived anticancer agents rises. Mir et al. (2021) state that excessive harvest of medicinal plants might result in loss of biodiversity and disturbance of ecosystems, along with natural habitat destruction. To reduce these issues, sustainable harvesting and in vitro methods of propagation, e.g., somatic embryogenesis, shoot organogenesis, and micropropagation, are necessary (Ahlawat et al., 2024). Such ways can support massive farming of P. trimera without disruption of the wild populations so that this rare resource remains available in the future. Ahlawat et al. (2024) also note that tissue culture methods, which have been effectively used to preserve other threatened plants, are particularly significant for medicinal plants, such as P. trimera, which are stressed by exploitation and a lack of natural resources.

Hence, Genetic stability of plants that are utilised in their propagation is vital to the mitigation that cultivated plants have the same bioactive properties as their wild counterparts. Molecular markers, including SCoT (Start Codon Targeted) markers, are typically used to measure genetic fidelity and verify that the genetics of tissue-cultured plants match the genetics of the mother plant (Biswas et al., 2022). The method not only prevents the bioactivity of the plant but also helps to come up with sustainable cultivation mechanisms that will assist the medicinal plant industry. Moreover, one should take into account the ecological effects of the harvesting of medicinal plants because inappropriate parameters of extraction may harm the ecosystems. Nevertheless, the plant growth of medicinal plants such as P. trimera under controlled conditions enables the cultivation of bioactive products without the harmful harvesting culture (Dsouza et al., 2025). This reduces the harmful effects on the environment and preserves the therapeutic value of the plant.

In general, *P. trimera* has potential anticancer effects that warrant further exploration, as it selectively targets cancer cells and exhibits low toxicity toward normal cells. Nevertheless, ecologically friendly farming is also essential to maintain biodiversity and a healthy ecosystem. The purpose of the review is to determine the bioactive extracts of this plant, their anticancer properties, and their environmental consideration in the sustainable harvesting of cancer treatment.

2. METHOD

The study began with an initial literature review to identify existing information on the anticancer potential and bioactive compounds of Paramignya trimera. This was followed by a systematic review in order to have a complete, objective synthesis of the studies. This approach was selected over the other since it is systematic and reproducible, reduces bias, and offers a rigorous analysis of the existing information (Pollock and Berge, 2018). PubMed, Scopus, and Web of Science were used to retrieve articles reporting data on the anticancer effects of P. trimera. Selection criteria and study quality were evaluated with the PICO framework (Population, Intervention, Comparison, Outcome) through in vitro studies that were associated with cell proliferation, apoptosis induction and selective cytotoxicity. Besides, the PRISMA guidelines provided transparency and consistency in reporting, and the therapeutic potential of the plant for cancer therapy were evaluated in a reliable and systematic way (see Fig. 1).

2.1 Search Strategy

The search was systematic and was conducted in PubMed, SCOPUS, and Web of Science with the inclusion of articles published in 2018-2025. The search aimed to find the studies that concentrated on the anticancer bioactivity of extracts of P. trimera, which concentrated on the in vitro models. The keywords were Paramignya trimera, anticancer, bioactive extract, apoptosis, and cancer cell lines. Inclusion criteria were limited to PICO criteria, i.e., the population studied was human cancer cell lines, the the intervention was P. trimera extracts, and the outcomes were inhibition of cancer cell proliferation or induction of cell death (see Table 1 in the Appendix). The inclusion criteria were that the studies had to be peer-reviewed and needed to be published in English, and the research must have been on in vitro methods. Studies were excluded that lacked clear data on the efficacy of anticancer agents or involved animals.

2.2 Selection Criteria

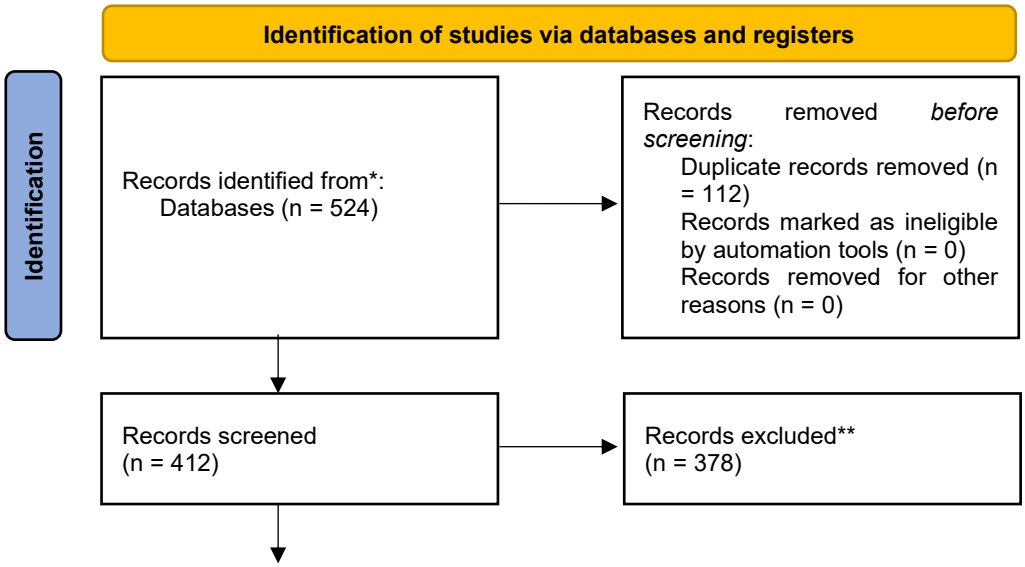
The criteria applied during the selection process were peer-reviewed articles published within the last 7 years (2018-2025) that used experimental methods to measure the anticancer activity of P. trimera extracts in human cancer cell lines. The articles were limited to quantitatively measure the effects of the plant (e.g., Half Maximal Inhibitory Concentration (IC50) values or apoptosis percentage). Research that used standard tests such as methyl thiazolyl tetrazolium assay (MTT), flow cytometry or western blotting to determine cell viability, apoptosis and other cellular processes was prioritised. The studies that did not measure the action mechanisms, e.g., apoptosis or cell cycle arrest, or studies in animal models that were not followed by in vitro confirmation, were eliminated.

2.3 Data Collection and Analysis

The chosen literature resulted in the selection of studies that were based on the qualitative and quantitative results in the field of anticancer activity of P. trimera. Measures like a group of IC50 values, apoptosis induction rate, and selective toxicity of cancer cells were transcribed. Additionally, qualitative data on bioactive compounds (i.e., flavonoids, terpenoids, and alkaloids) were collected. The information was examined with the help of thematic analysis, in which results were grouped by cancer cell lines and mechanisms of action (e.g., apoptosis, cell cycle arrest). This offered an overall insight into the anticancer potential and sustainability implications of the plant, including in vitro propagation.

3. RESULTS

The PRISMA 2020 procedure (see Fig. 1) was used for the review. The number of records that were found amounted to 524, with 112 duplicates that were deleted, and 412 records screened. Out of these, 378 were filtered out due to failure to fit the requirements. Thirty-four were considered eligible, and 28 were eliminated because of non-quantitative results or the lack of an intervention description. The number of studies incorporated into the actual synthesis was 6. These studies informed three themes that concentrated on in vitro anticancer findings, sustainability factors and the biodiversity consideration of Paramignya trimera.



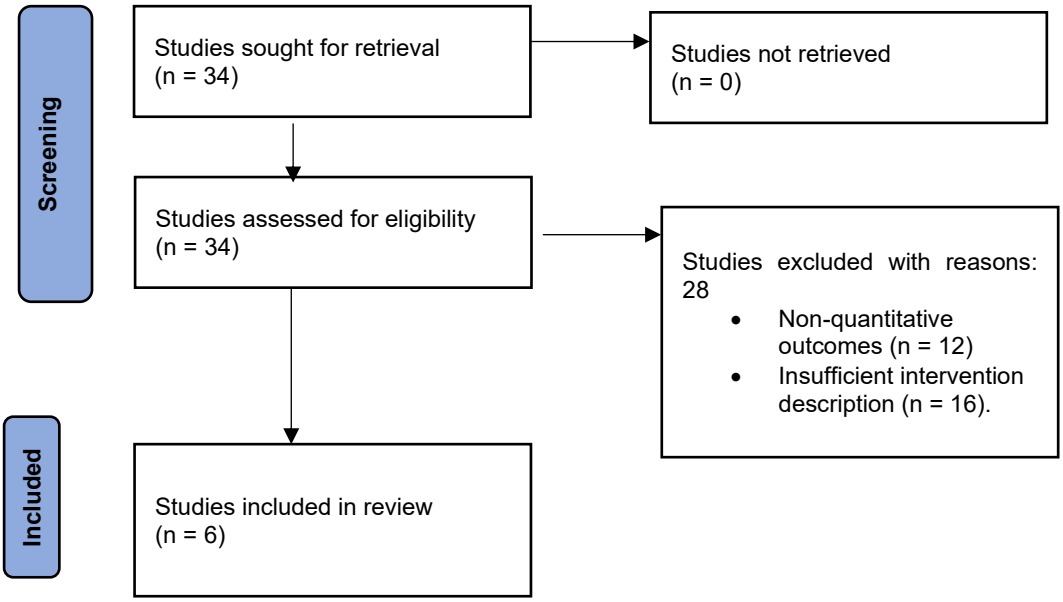


Figure 1: PRISMA Diagram

3.1 Theme 1: In Vitro Anticancer Activity of Paramignya trimera

The in vitro studies all show that *P. trimera* has quantifiable anticancer effects, but the scale and character of such effects are different among experiment designs. Nguyen et al. (2019) observed selective cytotoxicity with an IC50 of 10610 micrograms per millilitre in breast cancer stem cells, whereas in healthy fibroblasts it was minimal compared with the reference drug Doxorubicin. This selectivity shows a possible therapeutic benefit, and fluorescent microscopy further verified apoptosis as the primary process by nuclear fragmentation. The research was, however, constrained by the fact that it used two-dimensional culture only, which may not be able to replicate the complexity of tumour biology. Accordingly, although the results suggest encouraging anticancer approaches, their clinical applicability should be approached with caution. By contrast, a three-dimensional culture model of MCF7 breast cancer cells, which is closer to the conditions in tumours in vivo, was used in Nguyen Thi et al. (2018) to further develop the approach to the issue.

The comparison of the two studies demonstrates significant methodological and mechanistic information. Nguyen Thi et al. (2018) discovered that the root extract of P. trimera demonstrated lower IC50 in the three-dimensional system as compared to the two-dimensional system, which indicates a stronger antiproliferative activity at a more physiologically relevant environment. Besides, the induction of apoptosis and the total inhibition of cell invasion at a higher extract concentration were also the auxiliary materials in the evidence of its potential effectiveness. The three-dimensional results, compared with those of Nguyen et al. (2019), show that the anticancer effect of P. trimera may be underestimated in simpler models. However, the two studies have one common weakness since neither involved in vivo validation. This limits the determination of the pharmacokinetics, bioavailability and systemic toxicity. Thus, even though the two studies demonstrate the therapeutic potential of P. trimera, they also emphasise the necessity of further preclinical research in animal models to validate these promising early findings.

3.2 Theme 2: Sustainability and In Vitro Propagation of Paramignya trimera

This theme discusses the sustainability of the usage of *P. trimera* in cancer treatment by comparing two researches that discuss the problem in two scientific directions. Huynh et al. (2024) examined in vitro propagation via somatic embryogenesis and shoot organogenesis and demonstrated that the regenerated plants retained genetic fidelity, a crucial factor for the stability of bioactive compounds. This technique gives a long-lasting resolution that is an alternative to wild harvesting, as it is done by generating plants that are genetically balanced, in a controlled environment, and which exert less pressure on the natural population. Nevertheless, the study identifies that large-scale field cultivation has not been tested, even though it is of conservation value, and therefore, there is an uncertainty of whether it is economically viable, whether it is environmentally resilient, and whether it has the capacity to produce in the long term. Thus, the sustainability advantage is evident, but its scalability in practice still needs to be considered.

Conversely, Le et al. (2020) investigated the bioactivity of essential oils in P. trimera leaf extract, and they discovered that they possessed a high antimicrobial effect against Staphylococcus aureus and Candida parapsilosa, with no impact on normal cells, which has potential therapeutic applications. However, this

practice poses serious sustainability challenges, as oil production requires substantial plant biomass and can overgrow when not well managed. Le et al. (2020) point out the ecological vulnerability of the use of wild-sourced plant material, in comparison to the propagation-focused study by Huynh et al. (2024). Combining the works, it was found that although P. trimera is a useful source of medicine, its responsible exploitation should be based on the combination of biotechnological multiplication with sustainable harvesting of the resource to avoid the deprivation of the ecological system and guarantee long-term availability.

3.3 Theme 3: Biodiversity Conservation and Ethical Implications of Harvesting Paramignya trimera

This theme discusses the biodiversity consequences of Paramignya trimera's use as medicine by contrasting studies that vary in their subject of interest but all highlight the ecological and ethical issues surrounding its use. Huynh et al. (2024) focused on protecting biodiversity by in vitro propagation of epithelial cells by employing somatic embryogenesis and shoot organogenesis, as stable genomes of plants are possible to cultivate without having to harvest wild crops. Not only does this method maintain the species, but it also preserves the integrity of the bioactive compounds, which is very necessary for the consistency of the medicines. The study, however, despite providing a sustainable cultivation model, acknowledges that field-based experiments should be required to establish the long-term viability and economic viability. Consequently, the piece of work is closely related to conservation and therapeutic development but falls short of implementing it outside the lab.

Conversely, Uchida et al. (2024) investigated the thermoregulatory behaviours of ostruthin in an animal model and showed that it has a potential therapeutic implication on menopausal symptoms. Though the study does not touch on biodiversity, the results indirectly present sustainability issues since more people would be interested in ostruthin, and this may heighten natural extraction. This comparison with Huynh et al. (2024) highlights the potential for conservation-oriented studies and pharmacological development to strain wild populations unless handled ethically. Likewise, Le et al. (2025) predicted anticancer mechanisms in silico with the identification of key targets (PIK3CA, AKT1, MAPK3, and TP53) and active compounds (paratrimerin J and rutin). Although this study contributes to scientific knowledge and future laboratory studies, it does not inform on the ecological forces underlying the sources of these compounds. Analysing the three studies, it is important to note that pharmacological progress and biodiversity protection should be balanced. Hence, sustainable harvesting schemes and conservation interventions should be part of any future biomedical investigation of P. trimera so as to guarantee its future supply as a source of medicine.

4. DISCUSSION

The in vitro research on *P. trimera* has given significant information about its anticancer property, particularly the anti-proliferative capacity and apoptotic effect of the plant on cancer cells. The results of the MTT assay showed that the methanolic extract of P. trimera selectively killed breast cancer stem cells (VNBRCA1) with minimal harm to normal human fibroblasts (HF), as the outcome showed by both the MTT and flow cytometry assays (Nguyen et al., 2019). This preferential cytotoxicity and triggering of apoptosis in cancer cells highlight the potential of the plant in therapy. On the same note, Nguyen-Thi et al. (2018) established that the methanol root extract of P. trimera had a considerable effect on the proliferation of MCF-7 breast cancer cells, which had a lower IC50 in the three-dimensional tumour cell model than in the two-dimensional model. The current study emphasises the significance of implementing 3D models to have a more realistic depiction of the tumour microenvironment, which will give more physiologically relevant output. Combined, these studies show the selectivity of the plant to attack cancerous cells, which means that the plant can be used as therapy against cancer.

One major weakness of both studies, however, is the lack of in vivo validation. Although informative, in vitro models are not able to fully recapitulate the complexity of human cancers. Kaczmarzyk, Nowak-Perlak, and Woźniak (2024) insisted on the need to conduct in vivo research to verify the therapeutic effects and safety of plant-based extracts. The two articles by Nguyen et al. (2019) and Nguyen-Thi et al. (2018) do not establish animal model studies, limiting the ability to translate these studies to clinical practice. Despite the 3D model being more realistic in depicting tumours, there is still significant complexity not present in the living organism it represents. It is also required to use P. trimera in vivo to determine its anticancer efficacy, and to establish the safety and efficacy of this species in a more complicated biological system. Also, the limited number of cancer cell lines used in the in vitro studies is a strength; however, it is important to note that the findings may not be generalisable. Future research should expand the number of cancer types and cell lines evaluated to assess the generalizability of P.

trimera as an anticancer agent. In addition, examination of the long-term impacts of bioactive compounds of P. trimera and possible development of drug resistance in relation to these drugs is crucial to its sustainability as a feasible source of cancer therapy.

5. LIMITATIONS

Although the reviewed studies present useful information on the anticancer properties of Paramignya trimera, a number of constraints should be taken into consideration. In the first place, every research is based on in vitro models, which, although useful, are not able to fully reflect the complexity of human tumours. Whether these findings can be used clinically remains unknown without in vivo validation, as it is essential to shift between in vitro and in vivo models to determine the potential of plant-derived compounds in the therapeutic environment (Najmi et al., 2022). In addition, cell lines that are mostly used in the studies might not reflect the heterogeneity of tumours that occur in human patients. There are no long-term studies or clinical trials on the safety and efficacy of bioactive compounds of P. trimera in humans, and therefore, the safety and efficacy of its bioactive compounds cannot be confirmed. Also, inconsistencies in laboratory procedures may affect the reliability of results, e.g., variations in extract preparation, concentrations, and exposure periods. The other weakness is that there is a risk of bias in the choice of the cancer lines that the study can generalise the results because the studies are confined to various types of cancer, including breast and lung cancer. The necessity to use homogeneous methodologies in all studies is important to enhance the quality of findings and comparability. As Arra, Pasupala, and Anandam (2024) emphasised, animal model experiments are critical to determine the actual therapeutic potential of herbal compounds in the real world, which once again supports the need to validate the studies in vivo.

6. SUGGESTION

Future studies on P. trimera should aim at filling the gap between in vitro studies and clinical uses. It is necessary to conduct in vivo studies using an animal model to determine the efficacy and safety of the plant in a more complex multi-organism system. Long-term research should also be included in these studies to determine the side effects of the bioactive compounds of P. trimera. Moreover, there will be a need to conduct clinical trials involving human subjects to establish the therapeutic value of P. trimera in the actual situation. As stressed by Sorkin et al. (2020), clinical trials are a vital process to achieve an efficient translation of in vitro findings to viable treatment options.

Moreover, standardised methodologies should be used in future studies to enhance the comparability and reliability of results. These involve setting standard operating procedures for preparing extracts and dosages, and for determining the duration of treatment. Considering the good bioactivity of P. trimera, one can also consider determining the possible synergistic relationship between the extract of this plant and conventional cancer treatment forms. Additionally, sustainability should be one of the principal concerns, and the future viability of large-scale production and sustainable sourcing should be investigated to make sure that P. trimera can be utilised as a renewable source of cancer treatment without causing harm to biodiversity. The consideration of these points will play a significant role in the exploration of the full therapeutic potential of P. trimera and the development of its clinical use.

7. CONCLUSIONS

In conclusion, *P. trimera* has substantial potential in anticancer due to its specificity in targeting cancer cells and causing cell death in them. Although some encouraging in vitro findings were achieved, its clinical applicability is yet to be determined because, although promising results have been reported, there is no in vivo validation of its usage. There is also a need to have standardised procedures of research. Moreover, sustainable procurement and mass cultivation are essential to maintain the bioactive functions of the plant, as well as to guarantee biodiversity. The consideration of these areas will contribute to the advancement of P. trimera toward clinical application and to the maximisation of its curative effect.

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APPENDIX

Table 1: Study Table

Authors (Year)	Country of Origin	Study Design	Objective	Population (N)	Gender and Age	Intervention	Outcome	Results of Digital Literacy Assessment	Quality Assessment
Nguyen et al.	Vietnam	In vitro	Cytotoxicity of methanolic	VNBRCA1, Human	Not specified	Methanolic extract of P. trimera	Apoptosis induction,	IC50 = 106±10 µg/mL for	High

(2019)			extract of P. trimera on breast cancer stem cells (VNBRCA1)	fibroblasts (HF)			selective cytotoxicity	VNBRCA1, apoptosis induction in VNBRCA1 cells	
Le et al. (2025)	Vietnam	In silico	Evaluate bioactivity of P. trimera extract in lung cancer	N/A (in silico)	N/A	In silico screening of phytochemicals	Bioactivity against lung cancer pathways	Predicted targets: PIK3CA, AKT1, MAPK3, MAPK1, TP53, RELA	Moderate
Nguyen-Thi et al. (2018)	Vietnam	In vitro (3D model)	Anti-cancer effect of methanol root extract of P. trimera on MCF-7 breast cancer cells	MCF-7 breast cancer cells	Not specified	Methanol root extract	Inhibition of cell proliferation, apoptosis, and invasion	IC50 = 168.9±11.65 µg/mL in 3D model, apoptosis induction	High
Huynh et al. (2024)	Vietnam	In vitro	In vitro propagation of P. trimera via somatic embryogenesis	P. trimera plant explants	Not applicable	Somatic embryogenesis and shoot organogenesis	In vitro propagation for conservation	Successful propagation with genetic fidelity	High
Le et al. (2020)	Vietnam	In vitro	Bioactivity of essential oils from P. trimera leaves	Not specified	Not specified	Essential oils from P. trimera	Cytotoxicity and antimicrobial activity	Strong inhibition against Staphylococcus aureus, no cytotoxicity on normal cells	Moderate
Uchida et al. (2024)	Japan	Animal model (rats)	Effects of ostruthin (found in P. trimera) on thermoregulation	Ovariectomized rats	Not specified	Ostruthin (TREK agonist)	Body temperature regulation, effect on thermoregulatory behavior	Increased body temperature in ovariectomized rats	Moderate