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Potential of Phytochemical Compounds from Natural Products as Anticancer Agents: A Systematic Literature Review

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Abstract
Cancer is one of the leading causes of death worldwide, necessitating the development of more effective and safe anticancer therapies. Phytochemical compounds from natural sources hold great potential due to their diverse biological activities. This study aims to assess the potential of phytochemical compounds as anticancer agents through a systematic literature review of fifteen scientific articles selected based on specific inclusion criteria and analyzed qualitatively. The results indicate that compounds such as flavonoids including quercetin, polyphenols, alkaloids, and terpenoids have anticancer activity through inhibition of cell proliferation, induction of apoptosis, and inhibition of angiogenesis and metastasis, mediated by molecular pathways such as p53, nuclear factor kappa B, and caspases. In addition, approaches such as nanoformulation and combination therapy can improve the efficacy and bioavailability of the compounds. These findings indicate that phytochemical compounds have the potential to be safer and more effective anticancer agents, and require further research for clinical development.

Keywords: Phytochemistry; Anticancer; Natural products; Molecular mechanisms; Systematic review

INTRODUCTION

Cancer remains one of the leading causes of death worldwide, and its incidence continues to increase year after year (Naeem et al., 2022). Commonly used treatment methods, such as chemotherapy, radiotherapy, and surgery, are not yet fully optimal due to frequent serious side effects, the risk of drug resistance, and a lack of specificity toward cancer cells (Naeem et al., 2022). Therefore, alternative therapeutic approaches that are more effective and offer a higher level of safety are needed. One emerging strategy is the use of natural ingredients, particularly phytochemicals, which are known to possess diverse biological activities (Elrayess & El-Hak, 2025).

Phytochemical compounds, including flavonoids, polyphenols, alkaloids, and terpenoids such as quercetin, have been widely reported to have potential as anticancer agents (Ramdhiani & Amin, 2025). Their mechanisms of action are diverse, including inhibiting cancer cell proliferation, inducing apoptosis, and suppressing angiogenesis and metastatic spread. These effects are related to the compounds' ability to influence various important molecular pathways, such as p53, nuclear factor kappa B (NF-κB), and the caspase pathway (Ramdhiani & Amin, 2025; Naeem et al., 2022). Furthermore, their antioxidant activity also plays a role in reducing oxidative stress that contributes to cancer development (Hançer, 2026). Innovations such as nanotechnology-based formulations and combination therapies have also been

developed to increase the effectiveness and bioavailability of these compounds (Budiarto et al., 2025; Fakudze et al., 2026).

METHOD

This study employed a systematic literature review method to assess the potential of phytochemical compounds derived from natural materials as candidate anticancer agents. Data collection was conducted through a search of various scientific articles in electronic databases, such as PubMed, ScienceDirect, Scopus, and Google Scholar, using the keywords phytochemicals, anticancer, flavonoids, molecular docking, nanoformulation, and natural products (Amin, Fariidah, et al., 2025).

The literature sources used consisted of 15 scientific articles selected according to the research topic. All articles are listed in a study comparison table and cover several research approaches, including reviews, molecular docking, in silico, in vitro, and meta-analyses. These articles discuss various active compounds from natural ingredients, such as flavonoids, alkaloids, quercetin, curcumin, EGCG, acetogenin, gingerol, and natural ingredient-based nanoformulations that have anticancer activity against various targets and cancer cell models (Elrayess & El-Hak, 2025; Ramdhiani & Amin, 2025).

The literature selection process was conducted using predetermined inclusion and exclusion criteria. Inclusion criteria included articles discussing the anticancer activity of natural compounds, available in full text, and published in both Indonesian and English. Conversely, articles that did not align with the research focus, had incomplete data, or did not explain the mechanism or anticancer activity were excluded from the analysis.

Next, data from the 15 selected articles were analyzed qualitatively by grouping information based on research methods, natural source, type of bioactive compound, cancer target or model, and anticancer activity testing parameters. The analysis results were then compiled descriptively in the form of descriptions and comparative tables to provide a systematic overview of the potential of phytochemical compounds as anticancer agents (Naeem et al., 2022)..

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RESULTS AND DISCUSSION

Flavonoids as Anticancer Agents: A Review of Medicinal Chemistry and Biological Activities

Flavonoids are a group of phytochemical compounds widely studied in the development of anticancer agents because they exhibit diverse biological activities in inhibiting cancer cell growth. These compounds are known to suppress cell proliferation by influencing cell cycle regulation and can induce apoptosis in various types of cancer cells. Furthermore, flavonoids also play a role in inhibiting angiogenesis, the process of new blood vessel formation that is essential for tumor growth and development (Ramdhiani & Amin, 2025).

Molecularly, flavonoid activity is related to its ability to modulate various cellular signaling pathways, such as p53, PI3K/Akt, MAPK, and nuclear factor kappa B (NF-κB) (Ramdhiani & Amin, 2025). These pathways play a crucial role in regulating the balance between cell proliferation and death. Activation of p53 by flavonoids can trigger apoptosis, while inhibition of the NF-κB pathway contributes to suppressing the inflammatory process associated with cancer development. Furthermore, flavonoids can also increase the activity of antioxidant enzymes, which function to reduce cell damage caused by oxidative stress (Naeem et al., 2022).

When compared with previous research, these findings consistently demonstrate that flavonoids have a multi-target mechanism of action. This advantage makes flavonoids more potent than therapeutic agents that focus solely on a single target (Elrayess & El-Hak, 2025). However, several studies have also revealed

limitations with flavonoids, particularly related to low bioavailability and rapid metabolism in the body, necessitating the development of further strategies to improve their therapeutic effectiveness (Ramdhiani & Amin, 2025).

Literature Review: Molecular Docking of Indonesian Phytochemicals to Therapeutic Targets of Four Types of Cancer

This study examines the potential of phytochemical compounds derived from Indonesian plants as candidate anticancer agents through a molecular docking approach. The analysis results indicate that various bioactive compounds, such as flavonoids, alkaloids, and terpenoids, have the ability to interact with target proteins that play a role in the cancer development process (Bioaktif & Kanker, 2025). These targets include enzymes and receptors that regulate the proliferation and survival of cancer cells. This study covers several major cancer types, including breast, lung, colon, and leukemia. Based on the simulation results, binding affinity values indicate that several compounds have strong potential as inhibitors of the studied therapeutic targets.

At the molecular level, the molecular docking approach provides insight into the interaction patterns between phytochemical compounds and the active site of target proteins. Compounds with lower binding energies tend to form more stable complexes (Amin, Fariidah, et al., 2025), thus potentially being more effective in inhibiting the function of the protein. The types of interactions involved include hydrogen bonds, hydrophobic interactions, and van der Waals forces, which collectively determine the stability of the ligand-protein complex. Therefore, the results of docking analysis can be used as an initial step in the process of identifying candidate compounds with the potential to be developed into anticancer drugs.

Exploration of the Potential of Natural Compounds as Anti-Lung Cancer Candidates through a Molecular Docking Approach: A Literature Review

The study results indicate that various natural compounds have the potential to be anti-lung cancer candidates based on a molecular docking approach. Compound groups such as flavonoids, alkaloids, and terpenoids have been reported to interact with target proteins that play a role in lung cancer development, including growth factor receptors and enzymes involved in cell proliferation (Nisa et al., 2025). The binding affinity values from the simulation results indicate that several compounds have good ability to bind to the active site of the protein, thus potentially inhibiting biological activities that support the growth of lung cancer cells.

Molecularly, the interaction between natural compounds and target proteins is demonstrated through the formation of hydrogen bonds, hydrophobic interactions, and van der Waals forces, which contribute to the stability of the ligand-protein complex. Lower bond energies indicate stronger and more stable interactions, thus increasing the compound's potential as an inhibitor. Furthermore, some compounds also have the ability to target more than one protein, indicating multitarget properties in inhibiting lung cancer development. This characteristic offers advantages because it can reduce the risk of therapy resistance.

The Role of Computational Medicinal Chemistry in Identification of Anti-Cancer Agents through Molecular Docking of Natural Compounds

The study results indicate that computational medicinal chemistry plays a crucial role as a strategic initial approach in the discovery of natural-based anticancer drugs. Through molecular docking (Amin, Fariidah, et al., 2025), various natural compounds can be screened based on their ability to interact with biological targets involved in cancer development. Compared with experimental methods, which tend to

be time-consuming and expensive, this approach allows for a more rapid evaluation of many compounds to identify the most potent candidates before further testing.

During the analysis phase, this method not only assesses the strength of the interaction between the ligand and the target protein but also provides information on the orientation and stability of the formed bond. This evaluation includes parameters such as bond energy, the position of the ligand in the active site, and the type of interaction that occurs. Furthermore, computational medicinal chemistry is also capable of predicting pharmacokinetic properties, such as absorption, distribution, metabolism, and excretion, thus assisting in screening compounds that are not only active but also possess characteristics suitable for drug development (Amin, Fariidah, et al., 2025). Thus, this approach provides greater value than simply identifying biological activity.

Evaluation of the Anticancer Potential of Moringa Leaf Compounds through Medicinal Chemistry

Studies have shown that Moringa oleifera leaves contain various phytochemical compounds with potential anticancer properties, such as flavonoids, alkaloids, and other phenolic compounds (Amin, Rusiyana, et al., 2024). These compounds are known to have biological activity in inhibiting cancer cell growth and inducing programmed cell death (apoptosis). Furthermore, Moringa leaf extract also has high antioxidant activity, which plays a role in suppressing free radical formation and protecting cells from damage that can trigger carcinogenesis.

The medicinal chemistry approach provides an understanding of how the active compounds in Moringa leaves interact with biological targets related to cancer. Through analysis of the relationship between structure and activity, these compounds are thought to be able to disrupt the function of proteins involved in the proliferation and survival of cancer cells (Amin, Rusiyana, et al., 2024). Furthermore, assessing pharmacokinetic properties is also a crucial aspect in determining the potential for compound development, such as their absorption and distribution within the body. This demonstrates that the medicinal chemistry approach focuses not only on biological activity but also on the compounds' suitability as drug candidates (Amin, Rusiyana, et al., 2024).

Potential of Quercetin Compound as an Anti-Breast Cancer Agent through Molecular Docking Approach

The study results indicate that quercetin has potential as an anti-breast cancer candidate based on a molecular docking approach (Amin, Wihdatunnisa, et al., 2024). This compound is known to interact with various target proteins that play a role in breast cancer development, including hormone receptors and enzymes that regulate cell proliferation. The binding affinity values from the simulation results indicate that quercetin has a strong interaction ability with the active site of the protein, thus potentially inhibiting biological activities that support cancer cell growth.

From a mechanistic perspective, the interaction between quercetin and target proteins is characterized by the formation of various types of bonds, such as hydrogen bonds and hydrophobic interactions, which contribute to the stability of the ligand-protein complex (Amin, Wihdatunnisa, et al., 2024). Furthermore, quercetin is also able to adjust its structural orientation within the active site of the protein, thereby increasing its inhibitory effectiveness. This approach provides an initial insight into quercetin's potential in targeting molecular pathways involved in breast cancer (Amin, Wihdatunnisa, et al., 2024).

1. Review of Natural Anticancer Products

   Studies have shown that natural products are a crucial resource for discovering new anticancer compounds with a wide range of chemical structures. Natural products derived from plants, microorganisms, and marine organisms are known to contain secondary metabolites with cytotoxic

activity against cancer cells (Elrayess & El-Hak, 2025). Various studies have shown that these compounds can inhibit tumor growth through their effects on cell viability, differentiation, and the ability of cancer cells to survive in unstable environmental conditions.

In terms of mechanisms, natural products generally work not only on a single pathway but are able to simultaneously affect multiple biological targets (Naeem et al., 2022). Some compounds can disrupt the redox balance in cancer cells, while others play a role in regulating gene expression related to the cell cycle and responses to cellular stress. Furthermore, interactions with regulatory proteins also contribute to indirectly inhibiting tumor development. This demonstrates the characteristics of natural products as multi-target agents with the potential to provide broader therapeutic effects.

Compared with synthetic therapies, the use of natural products offers the advantage of diverse chemical structures and the potential for synergistic effects between compounds. However, challenges include compositional variability and limitations in maintaining consistent quality. Several studies also emphasize the importance of standardization and further testing to ensure safety and effectiveness. Therefore, despite their significant potential, the development of natural products as anticancer agents requires an integrated approach between basic research and technological innovation (Elrayess & El-Hak, 2025).

In Silico Study of Compounds Contained in Mangosteen (Garcinia mangostana L.) Peel as Breast Anticancer Agents

The results of the study indicate that computational medicinal chemistry has an important role as a strategic initial approach in the discovery of natural-based anticancer drugs, especially in mangosteen rind (Garcinia mangostana L.). Through molecular docking methods, various xanthone compounds were screened based on their ability to interact with biological targets such as the 1QKM, 1X7J, and 6QGG receptors involved in breast cancer development. Compared with experimental methods that tend to be time-consuming and expensive, this computational approach allows for a faster evaluation of 31 secondary metabolite compounds to identify the most potential candidates before further laboratory testing.

In the analysis stage, this method not only assesses the strength of the interaction between the ligand and the target protein through the binding affinity value, but also provides in-depth information regarding the orientation and stability of the formed bond. The evaluation includes parameters such as the position of the ligand on the active site of the 1X7J receptor and the type of amino acid residue interaction, where the compounds Toxyloxanthone A, 8-Deoxygartanin, and Demethylcalabaxanthone show better stability than their natural ligands. In addition, computational medicinal chemistry is able to predict pharmacokinetic properties through ADMET profiles and Lipinski's rules, which help screen compounds based on safety aspects such as toxicity levels and absorption capabilities in the body.

This study emphasizes the integration of medicinal chemistry and molecular dynamics simulations in the process of drug discovery from natural products. This approach not only focuses on affinity values but also considers fluctuations in protein-ligand structures over time to dynamically determine their effectiveness. This demonstrates the broad role of computational medicinal chemistry as a bridge between early drug discovery and development, by identifying obstacles such as hepatotoxicity in certain compounds before they enter the development phase. Although providing comprehensive data, the results of this study still require validation through experimental testing to confirm the biological activity of the mangosteen peel compounds..

Antioxidant and Anticancer Potentials of Apple Peel and Fruit Extracts: A Combined Docking and Chemical Composition Study

This study shows that apples have a very rich phenolic compound content, especially in the skin compared to the flesh. The most dominant compound is chlorogenic acid, followed by catechin, epicatechin, rutin, and quercetin (Hançer, 2026). The extraction process for these compounds is greatly influenced by the type of solvent, with methanol and ethanol being more effective than water in producing higher phenolic levels. Furthermore, differences in the location where the apples are grown also affect the amount of active compounds produced.

The antioxidant capacity of apple extract has been shown to be closely related to its total phenolic content, based on ABTS and DPPH assays. Apple peel exhibits stronger antioxidant activity than the fruit flesh, as it acts as a natural barrier against environmental stress. Cytotoxicity tests also indicate that apple extract has anticancer potential, as evidenced by its ability to inhibit the growth of HT-22 nerve cells and C6 glioma cells. This effect is dose- and treatment-dependent, with higher doses and longer incubation times (Hançer, 2026) indicating greater cell death.

Based on computer analysis, active compounds in apples, such as rutin and chlorogenic acid, have a good ability to interact with targets that play a role in cancer development. Of the two, chlorogenic acid is thought to be more easily absorbed by the body. Overall, the results of this study indicate that Hünkar apples have potential as a natural therapeutic agent and support the consumption of whole fruit for maximum health benefits (Hançer, 2026).

Medicinal Chemistry Approach in Optimizing Bioactive Compounds from Natural Ingredients as Anticancer Drug Candidates

Based on a literature review, bioactive compounds derived from natural materials show great potential as anticancer drug candidates because they work through various important biological mechanisms. These mechanisms include triggering apoptosis and suppressing the cell cycle, as well as modulating various signaling pathways such as PI3K/Akt, MAPK, and ferroptosis. The main advantage of natural compounds over conventional therapies lies in their multi-target nature, allowing them to attack cancer cells through multiple mechanisms simultaneously. This has the potential to increase the effectiveness of therapy while reducing the risk of drug resistance, which is common in chemotherapy.

Some of the most widely discussed compounds include epigallocatechin gallate (EGCG), berberine, curcumin, and cardiotonic steroids (CTS). EGCG is known to trigger ferroptosis by increasing oxidative stress in cancer cells. Berberine works by inducing apoptosis and autophagy (Amin, Amelia, et al., 2025), and inhibiting the metastasis process through various molecular pathways. Curcumin has broad activities, such as antiproliferative, anti-inflammatory, and antioxidant, while CTS exhibits anticancer effects through inhibition of the Na^+/K^+-ATPase enzyme and regulation of signaling pathways that play a role in cancer cell growth. However, the utilization of these compounds still faces various obstacles, such as low bioavailability, less than optimal stability, and potential toxicity in some types of compounds.

To overcome these limitations, medicinal chemistry approaches are crucial. Possible efforts include modifying chemical structures, synthesizing new derivatives, and developing modern drug delivery systems such as nanoparticles, liposomes, and conjugation with targeting molecules. This approach aims to increase the effectiveness and selectivity of compounds, while simultaneously reducing side effects and improving safety in clinical use. Thus, combining the potential of natural products with innovations in medicinal chemistry offers the potential for the development of selective and safe anticancer agents in the future (Amin, Amelia, et al., 2025).

Natural Products as Anticancer Agents: Current Status and Future Perspectives

Research shows that cancer is a complex disease characterized by uncontrolled abnormal cell growth and the ability to spread to other tissues (metastasis). The process of cancer development (carcinogenesis) occurs through several stages: initiation, promotion, and progression, which involve the gradual accumulation of genetic mutations. Although various therapeutic methods such as surgery, radiotherapy, chemotherapy, and targeted therapy have been implemented, their effectiveness remains limited due to high side effects and the emergence of drug resistance. For example, conventional chemotherapy targets not only cancer cells but also normal cells, thus causing toxic effects such as nausea, hair loss, and hematological disorders (Naeem et al., 2022).

In this regard, natural products offer a promising alternative due to their diverse chemical structures and broad biological activities. Compounds from natural sources can act through various molecular mechanisms, such as inhibiting cell proliferation, inducing apoptosis, and suppressing angiogenesis and metastasis. Furthermore, many currently used anticancer drugs are derived from or inspired by natural products, demonstrating their crucial role in the development of modern therapies. Other advantages include their relatively low toxicity and their ability to increase cancer cell sensitivity to conventional therapies (Naeem et al., 2022).

However, the use of natural products still faces several challenges, such as low bioavailability, suboptimal stability, and variations in biological effectiveness. Therefore, further development strategies are needed, for example through combination therapies and the use of modern drug delivery systems to enhance their effectiveness. Furthermore, natural products also have the potential to act as chemosensitizers, capable of overcoming drug resistance by simultaneously targeting multiple molecular pathways. Therefore, the integration of conventional therapies and natural products opens up significant opportunities for the development of more effective, safe, and sustainable cancer therapies in the future (Naeem et al., 2022).

Enhanced anticancer potential of Punica granatum fruit extract in combination with Pheophorbide-a mediated photodynamic therapy on MCF-7 breast cancer cells

According to research, cancer is a complex disease with a steadily increasing incidence globally and a significant physical, emotional, and economic burden. Conventional therapies such as chemotherapy, radiotherapy, and surgery still have various limitations, particularly high side effects and the emergence of drug resistance. Therefore, more effective and safe therapeutic approaches are needed. One emerging approach is the use of combination therapy, which combines several agents with different mechanisms of action to increase treatment effectiveness while reducing toxicity.

In this study, Punica granatum fruit extract combined with photodynamic therapy using pheophorbide-a showed a significant increase in anticancer activity compared to single therapy. The test results showed that the combination therapy was able to reduce the viability of MCF-7 breast cancer cells more effectively, with a lower IC50 value than the extract alone. In addition, changes in cell morphology such as cell shrinkage, loss of adhesion, and an increase in the number of dead cells indicated greater cell damage in the combination therapy. The main mechanism involved is the induction of apoptosis as indicated by increased caspase-8 and caspase-9 activity, as well as an increase in the Bax/Bcl-2 ratio and cytochrome-c release.

The effectiveness of this combination therapy can be explained by the synergistic effect between the phytochemical compounds in Punica granatum extract and the production of reactive oxygen species (ROS) from photodynamic therapy. Phytochemical compounds act as chemotoxic agents that modulate cancer cell signaling pathways, while pheophorbide-a produces ROS that directly damage cell components. The combination of these two mechanisms produces a stronger cytotoxic effect than either alone. Thus, a combination approach based on natural ingredients and modern technologies such as photodynamic therapy

has great potential as a more effective cancer treatment strategy, with the possibility of reducing the dosage and side effects of conventional therapies (Fakudze et al., 2026).

Antioxidant and anticancer properties of citrus-mediated nanoformulations revealed by meta-analysis

Significant antioxidant and anticancer activity, although results vary depending on the testing method and parameters used. In general, the antioxidant activity of CMNs does not always show significant results, except for the IC50 parameter which indicates a strong effect (Budiarto et al., 2025).

This indicates that antioxidant effectiveness is significantly influenced by the type of test, nanoparticle composition, and the plant part used. For example, peel extract and the use of coating materials such as polyvinyl alcohol yielded more significant results than other variables (Budiarto et al., 2025).

In terms of anticancer activity, CMNs exhibit a much more consistent and significant effect. Meta-analysis results indicate that CMNs are capable of significantly reducing cancer cell viability, with strong effect values on various parameters such as IC50 and cell viability percentage. This effectiveness is influenced by several factors, such as the type of citrus species, nanoparticle size (Budiarto et al., 2025), and the type of nanoparticle used. Nanoparticles with a size of 101–500 nm, for example, show a more optimal anticancer effect compared to other sizes. In addition, various types of nanoparticles such as Ag-NPs, Au-NPs, and CeO_2-NPs have been shown to be effective in inhibiting cancer cell growth in various cell lines such as HeLa, A-549, and MCF-7.

The effectiveness of CMNs in inhibiting cancer cells is thought to stem from a combination of citrus phytochemicals and the unique properties of nanoparticles that enhance penetration and specific targeting of cancer cells. Furthermore, the use of citrus extract as a coating also enhances the stability and biological activity of the nanoparticles. However, variations in results between studies indicate the need for method standardization and formulation optimization. Thus, CMNs hold great potential as a more effective nanotechnology-based anticancer therapy, but further research is needed to ensure their safety and clinical effectiveness.(Fakudze et al., 2026)

Green synthesis, characterization, evaluation of anticancer and antioxidant potentials of gold and copper oxide nanoparticles using jujube fruit extract

Based on research results, jujube fruit (Ziziphus jujuba Mill.) has the potential as a reducing agent and natural stabilizer in the green synthesis of gold nanoparticles (AuNPs) and copper oxide (CuO NPs) (Reports, 2026). This approach is considered more environmentally friendly, cost-effective, and safe because it does not involve toxic chemicals as in conventional methods. The phytochemical content in jujube extract, such as phenolic compounds, flavonoids, and polysaccharides, plays an important role in reducing metal ions into nanoparticles and maintaining their stability. This shows that natural materials can be optimally utilized in the development of green synthesis-based nanotechnology.

The results of the physicochemical characterization showed a clear difference between the AuNPs and CuO NPs produced. JFE-AuNPs are generally spherical with an average size of about 78.74 ± 6.40 nm and have a characteristic absorbance peak at a wavelength of about 650 nm. Meanwhile, JFE-CuO NPs have a larger size, which is about 159.14 ± 22.53 nm, with an irregular morphology and two main absorption peaks at 265 nm and 360 nm. XRD analysis showed that AuNPs have a face-centered cubic crystal structure, while CuO NPs are in the monoclinic phase. In addition, the zeta potential value of both nanoparticles indicates good colloidal stability, which means the presence of electrostatic repulsion that is able to prevent particle aggregation.

In biological activity testing, both types of nanoparticles showed potential as antioxidant and anticancer agents. In the antioxidant test using the ABTS method, AuNPs showed higher activity than CuO NPs with an IC_{50} value of 70.32 ± 2.73 µg/mL. In anticancer testing on several cell lines, such as A549, MDA-MB-231, and SH-SY5Y, both nanoparticles were able to reduce the viability of cancer cells in a concentration-

dependent manner. Although CuO NPs showed a stronger cytotoxic effect, AuNPs were considered superior due to their better biocompatibility and lower toxicity to normal cells. Overall, these findings indicate that jujube-based green synthesis has great potential for development in nanotechnology therapy, although further research, especially in vivo testing, is still needed to ensure its safety and effectiveness (Reports, 2026).

Enhanced antibacterial and anticancer activities of plant extract mediated green synthesized zinc oxide-silver nanoparticles

Based on the research results, the green synthesis of zinc oxide–silver nanocomposites (ZnO–Ag NPs) using pomegranate (Punica granatum) peel extract has been proven to be an effective, environmentally friendly, and sustainable method. In this process, the plant extract functions as a reducing agent and a natural stabilizer, thus replacing the use of hazardous chemicals in conventional methods. Characterization shows that increasing the pH during synthesis contributes to increasing the crystallinity of the nanoparticles. In addition, the formed silver particles have a spherical morphology with an average size of around 14–16 nm and are evenly distributed in the ZnO matrix, which supports their stability and biological activity (Nur et al., 2023).

ZnO-Ag NPs nanocomposites exhibit higher biological activity than pure ZnO. In antibacterial testing, these nanoparticles have a broad spectrum of activity, both against Gram-positive bacteria such as Staphylococcus aureus and Bacillus subtilis, and Gram-negative bacteria such as Escherichia coli and Salmonella enterica. This antibacterial activity is influenced by the synergistic effect between Zn^{2+} and Ag ions, which can damage the structure of bacterial cell walls and trigger oxidative stress. Therefore, the combination of the two metals in the form of nanoparticles provides more optimal effectiveness in inhibiting the growth of pathogenic microorganisms.

In addition, the anticancer activity of ZnO-Ag NPs also shows promising potential. This nanocomposite is able to inhibit cancer cell proliferation in a dose-dependent manner, especially in colorectal (HCT116), lung (A549), and cervical (HeLa) cancer cells. A significant inhibitory effect has been seen at a relatively low concentration of around 31.25 µg/mL, indicating higher efficacy compared to pure ZnO which requires higher concentrations. Overall, the integration of silver into the ZnO structure through a green synthesis approach has been proven to increase the therapeutic potential of nanoparticles, thus having great potential for development as an anticancer agent as well as a solution to overcome antimicrobial resistance in the future (Nur et al., 2023).

Table 1. Comparison of 15 Journals on the Potential of Phytochemical Compounds as Anticancer Agents

No.	Method	Source Material	Compound / Material	Target / Model	Parameter	Source
1	Literature study	Natural materials	Flavonoids, alkaloids, taxanes	Multi-target	Not specific	Elrayess & El-Hak, 2025
2	Molecular docking	Mangosteen skin	Xanthone	ER-α	Affinity is not detailed	Amin et al., 2023
3	Molecular docking	Apple	Quercetin, catechin	Brain protein	No data	Hançer et al., 2026
4	Review	Tropical plants	Flavonoid	PI3K/Akt, MAPK	There isn't any	Ramdhiani & Amin, 2025

5	In vitro + nano	Pomegranate peel	ZnO–Ag NP	Cancer cells	IC50 ±31.25 µg/mL	Mohamad Sukri et al., 2023
6	Review	Medicinal plants	EGCG, curcumin	PI3K/Akt	Apoptosis	Amin et al., 2025
7	Review	Natural products	Flavonoid	Multi-target	±50% of nature	Naeem et al., 2022
8	In vitro	Pomegranate	Phytochemicals	MCF-7	IC50 ±129 µg/mL	Fakudze et al., 2025
9	Meta-analysis	Citrus	Nano-flavonoid	Cancer cells	High effect	Budiarto et al., 2025
10	Docking	Green tea	EGCG	Cancer protein	Low energy	Zhang et al., 2021
11	Docking	Turmeric	Curcumin	Cancer protein	Strong affinity	Praditya et al., 2020
12	In silico	Garlic	Allicin	Cancer protein	Stable	Rahman et al., 2019
13	In vitro	Soursop	Acetogenin	Cancer cells	Cytotoxic	Moghadamtousi et al., 2015
14	Review	Asian Herbs	Bioactive	Apoptosis	Induction	Chen et al., 2018
15	Docking	Ginger	Gingerol	Cancer enzymes	Low energy	Dugasani et al., 2010

CONCLUSION

Based on various studies that have been conducted, it can be concluded that bioactive compounds derived from natural materials, such as flavonoids, alkaloids, terpenoids, and phenolic compounds, show great potential as anticancer agents through multitarget mechanisms of action, which include inhibiting cancer cell proliferation, triggering apoptosis, suppressing angiogenesis processes, and reducing oxidative stress levels. Computational medicinal chemistry approaches, especially molecular docking techniques, have proven effective in the early stages of identifying candidate compounds with high affinity for cancer protein targets, thereby accelerating the process of drug discovery and development. This potential is further enhanced by the integration of modern technologies, such as nanotechnology and combination therapy, which can improve the stability, bioavailability, and selectivity of compounds, as demonstrated by stronger cytotoxic activity and reduced cancer cell viability with lower IC_{50} values and more stable molecular bonds. However, several limitations remain, including low bioavailability, compound instability, variations in the composition of natural materials, and the need for further validation through in vitro, in vivo, and clinical trials to ensure their safety and effectiveness. Therefore, further research needs to be directed at optimizing compound structures, developing drug delivery systems such as nanoparticles or liposomes, and exploring synergistic effects in combination therapy, by integrating computational, experimental, and clinical approaches as a strategic step in developing more effective, selective, and sustainable natural-based anticancer agents.

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