TRANSPUBLIKA INTERNATIONAL RESEARCH
IN EXACT SCIENCES
(TIRES)
VOLUME 1 ISSUE 4 (2022)

ANTI-CANCER PROPERTIES OF PHYTOCHEMICALS DERIVED FROM AZADIRACHTA INDICA: LITERATURE REVIEW

Alfina Aisatus Saadah
STIKES Yayasan RS Dr. Soetomo
E-mail: aisatusalfina@gmail.com

Abstract

This study aims to assess the anti-cancer properties of phytochemicals derived from Azadirachta indica (neem), given the increasing prevalence of cancer and the need for safer and more effective therapies. Phytochemicals from Azadirachta indica have been reported to have potential as anti-cancer agents, but their mechanism of action is not fully understood. Therefore, this study was conducted to explore the anti-cancer potential of various phytochemicals extracted from Azadirachta indica. This study used literature review method supported by bibliometric analysis tools such as VOSviewer and Publish or Perish. The results showed that phytochemicals from Azadirachta indica have significant cytotoxic effects on cancer cells, as well as being able to induce apoptosis through intrinsic pathways. These results suggest that Azadirachta indica has the potential to be developed as an effective and safe anti-cancer therapeutic agent. Discussion of the results of this study highlights the importance of further development and clinical trials to validate these findings.

Keywords: *Azadirachta indica, Anti-cancer Phytochemicals, VOSviewer*

1. INTRODUCTION

Cancer is one of the biggest health challenges worldwide, with high morbidity and mortality rates. Despite the development of many conventional therapies such as chemotherapy, radiation, and surgery, cancer treatment often still faces various obstacles such as significant side effects, drug resistance, and high costs. Hence, there is an urgent need to explore safer, effective and affordable therapeutic alternatives.

On the World Cancer Day on 4 February 2024, WHO through the International Agency for Research on Cancer (IARC) released the latest data revealing the increasingly alarming global cancer burden. Of the 185 countries surveyed, it was found that 10 types of cancer dominate two-thirds of new cases and are the leading cause of cancer deaths worldwide. The data recorded 20 million new cases with 9.7 million deaths, with lung cancer (12.4%) and breast cancer (11.6%) being the most common. Lung cancer mainly dominates in men, especially in Asia, while breast cancer is the biggest threat to women. WHO also highlighted that most countries are still unable to provide adequate cancer services within universal health coverage, which in turn increases the risk of death for people with cancer. In Indonesia, the dominating cancer types are breast, cervical, lung, colorectal and liver cancer, with a total of 396,914 new cases and 234,511 deaths recorded in 2020. These findings emphasise the importance of improved cancer healthcare and more effective prevention efforts at both global and national levels.

Research into the anti-cancer properties of phytochemicals derived from *Azadirachta indica*, or Neem, is a highly relevant area in the context of developing alternative and natural-based cancer therapies. *Azadirachta indica* has been widely recognised in traditional medicine in Asia and Africa for its diverse therapeutic properties, such as anti-inflammatory, anti-bacterial, and anti-oxidant (Devi and Sharma, 2023; Malakar and Mandal, 2025). In

recent decades, scientific attention to the anti-cancer potential of this plant has been increasing. Recent studies have shown that oil extracts from *Azadirachta indica* have cytotoxic effects against various cancer cell lines, especially breast cancer, by exhibiting anti-proliferative activity and minimal toxicity to vital organs. (Azam *et al.*, 2023; Lafta *et al.*, 2023).

Research by Nagesh et al. (2023) using Gas Chromatography-Mass Spectrometry to identify secondary metabolites in leaf extracts, while Singh et al. (2015) found that gallic and ferulic acids in young leaves showed significant potential anti-cancer activity. These findings provide an indication that certain phytochemical components of *Azadirachta indica* may play a key role in the observed anti-cancer effects.

Based on this background, research on the anti-cancer properties of phytochemicals derived from *Azadirachta indica* is essential. This literature review aims to investigate and summarise the existing evidence regarding the anti-cancer activities of phytochemical compounds in *Azadirachta indica*, as well as identify their potential mechanisms of action. Understanding the phytochemicals and mechanisms of action of *Azadirachta indica* may pave the way for the development of more effective, nature-based cancer therapies, as well as expanding knowledge on the use of this plant in oncology.

This study offers significant novelty by focusing on the identification and characterisation of phytochemicals from *Azadirachta indica* (Neem) in the context of its potential as an anti-cancer agent, particularly through anti-angiogenic mechanisms. Most previous studies have tended to focus on the traditional uses and anti-microbial effects of *Azadirachta indica*, whereas this study explores the specific role of bioactive compounds in inhibiting angiogenesis, the process of new blood vessel formation that is important for tumor growth.

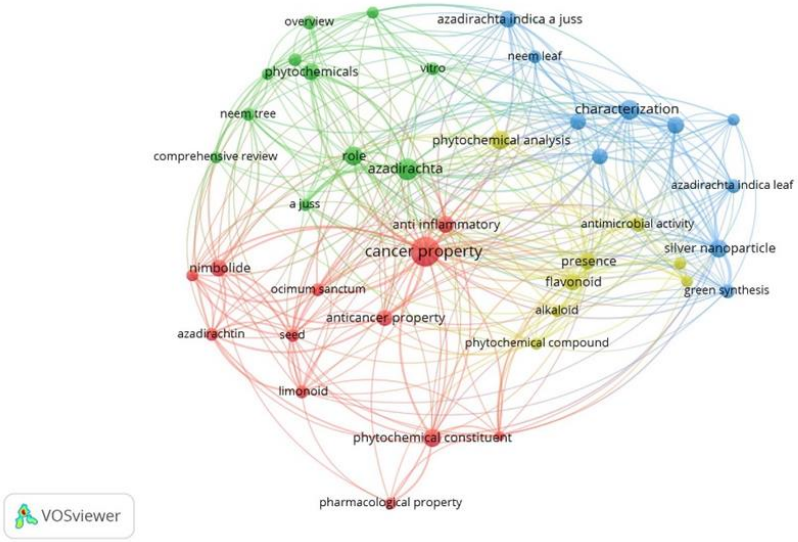
2. RESEARCH METHODS

This research uses a literature review method supported by bibliometric analysis tools such as VOSviewer and Publish or Perish. The research process began by collecting 66 articles relevant to the topic, which were selected from the time span of 2010 to 2023 to ensure up-to-date and comprehensive data coverage. The keywords used in the literature search were ‘Anti-Cancer Properties,’ ‘Phytochemicals,’ and ‘*Azadirachta indica*.’ The articles were collected using Publish or Perish, which were then further analysed using VOSviewer. This tool was used to map keyword networks, identify research trends, and explore interrelationships between articles. The data used came from recognised academic databases, such as Google Scholar, PubMed, and Scopus. Through this method, this study aims to provide a comprehensive overview of the development of studies related to the anti-cancer properties of phytochemicals contained in *Azadirachta indica*, as well as identify gaps in the existing literature.

3. RESULTS AND DISCUSSION

3.1. Research Results

This research collected English journals from Google Scholar, PubMed, and Scopus. The 66 data collected were published from 2013 to 2023. The researcher used VOSviewer.



Source: Processed by Researchers, 2024

Figure 1. Co-Occurrence of Anti-Cancer Properties of Phytochemicals derived from *Azadirachta indica*

Figure 1 shows a network visualisation that demonstrates the relationships between concepts or terms in research related to plant properties and natural compounds, especially with a focus on anti-cancer potential. In this network, nodes or points represent specific terms or concepts, while lines connecting these nodes show the relationships or associations between them.

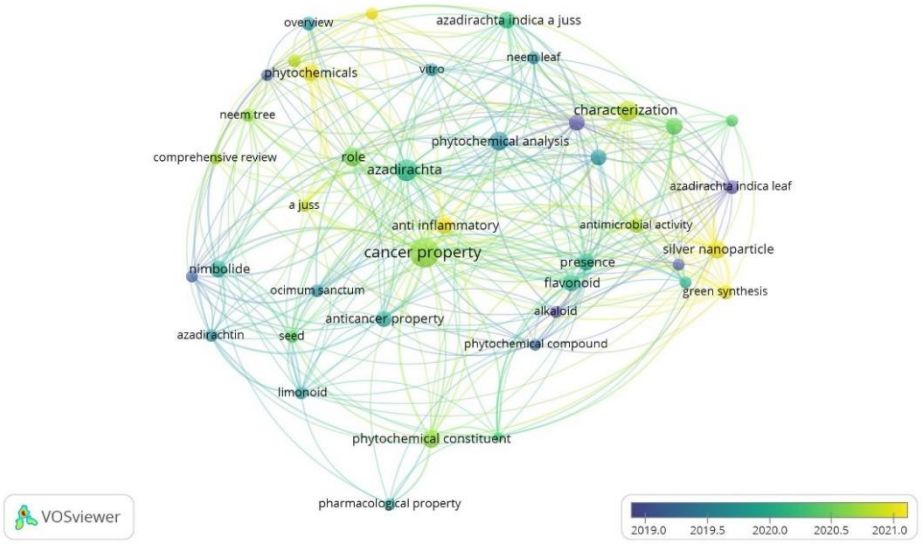
Different colours group the terms based on closely related themes or subjects. For example, the green cluster includes terms related to 'Azadirachta,' a genus of plants known for their phytochemical content, such as 'phytochemicals,' '*Azadirachta indica* tree,' and 'azadirachta.' The red clusters reflect a focus on anti-cancer properties with key terms such as 'cancer property,' 'anticancer property,' and specific compounds such as 'nimbolide,' indicating the importance of this research in identifying and understanding the potential of natural compounds for cancer treatment.

The blue clusters focus on aspects of scientific characterisation, including antioxidant and antimicrobial activity, with terms such as 'characterisation,' 'antioxidant activity' and 'silver nanoparticle.' This indicates that research is not only limited to the identification of anti-cancer potential but also involves in-depth analyses of the underlying chemical and biological properties of these compounds.

The 'cancer property' node at the centre of the network reflects the importance and interconnectedness of this theme with many other concepts in the network, suggesting that anti-cancer properties are a major focus in the literature represented by this visualisation.

The strong connections between this node and the various terms indicate the great interest in understanding the relationship between phytochemical properties and anti-cancer effects.

Overall, this image reflects a comprehensive research landscape, linking different aspects of plants and natural compounds to their therapeutic potential, particularly in the context of cancer treatment. The network illustrates the complexity and interconnectivity of these themes, indicating that research in this area is multidimensional and involves a variety of scientific approaches to understanding the potential of plants and natural compounds in medical therapy.

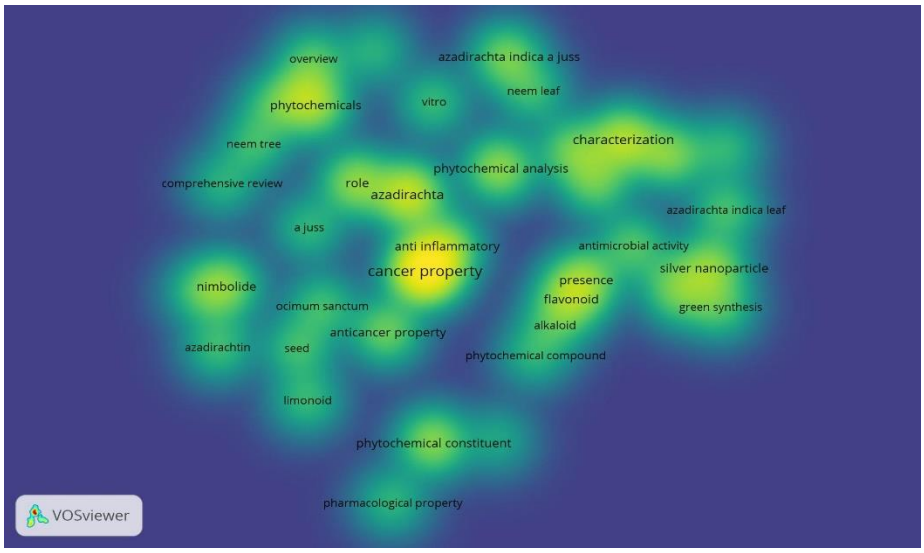


Source: Data Processed, 2024

Figure 2: Timeline Visualisation of the Anti-Cancer Properties of Phytochemicals derived from *Azadirachta indica*

Figure 2 illustrates the linkages between various research topics focusing on '*Azadirachta indica*' (commonly known as the *Azadirachta indica* tree) and its associated phytochemical compounds that have various biological activities, including anti-cancer properties. The colours of the circles and lines indicate the temporal evolution of related research, with a colour gradient from blue (earlier research, circa 2019) to yellow (more recent research, circa 2021).

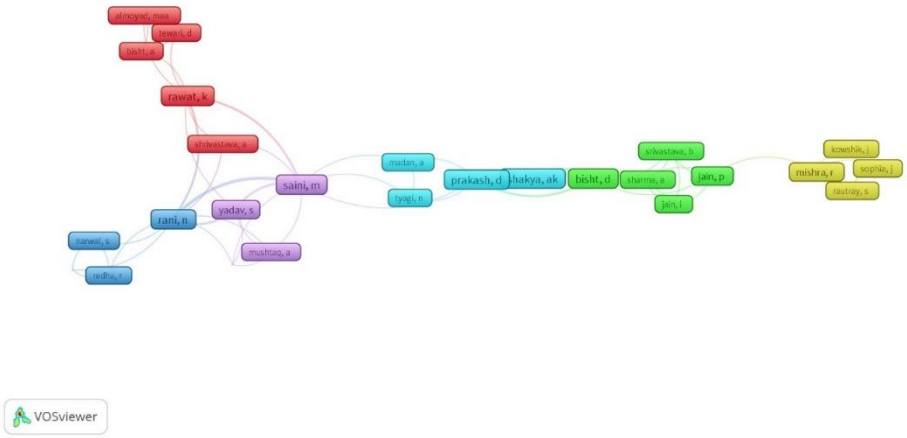
The keywords 'cancer property' and 'azadirachta' are at the centre of the map, indicating that these are the main focus of research and are often associated with various other aspects such as 'anticancer property,' 'anti-inflammatory,' and 'phytochemical analysis.' Other keywords such as 'silver nanoparticle' and 'green synthesis' appear on the right of the map, suggesting a link between green-synthesised silver nanoparticles and the antimicrobial activity that may be associated with the *Azadirachta indica* tree. Figure 2 shows that research related to '*Azadirachta indica*' has progressed significantly, with a major focus on anti-cancer properties and phytochemicals that could potentially play a role in cancer therapy. In addition, more recent research seems to be leading to the synthesis of nanoparticles and further exploration of the antimicrobial activity of these compounds.



Source: Data Processed, 2024

Figure 3. Visualisation of Topic Density Related to Anti-Cancer Properties of Phytochemicals derived from *Azadirachta indica*

Figure 3 shows that there is very limited coverage of all the topics shown, which is reflected in the faded colours in the figure. This indicates that these topics have not been widely researched or addressed in previous studies. This highlights gaps in the existing literature and suggests significant opportunities for further research. Therefore, these topics could be a key focus in future research, providing an opportunity for researchers to explore and develop a deeper understanding of this under-discussed area.



Source: Processed by Researchers, 2024

Figure 4. Co-Authorship

The VOSviewer network visualisation in Figure 4 shows the collaboration relationships between researchers in a particular academic field. The visualisation is divided

into clusters, each of which represents a group of researchers who frequently collaborate with each other. Within this network, there are several distinct clusters. The red clusters indicate groups of researchers who work very closely with each other. Other clusters that stand out are depicted in blue. In addition, there is a green cluster that indicates collaboration. This cluster also has some other researchers who are closely connected. The yellow cluster shows collaboration between several other researchers.

From this visualisation, we can see that some researchers have a central role in the collaboration network, evident from the number of connections they have with other researchers. Meanwhile, other researchers may have a more limited collaboration network, as seen from their position at the periphery of the network. This network provides a snapshot of the dynamics of academic collaboration in a particular field. To find out the articles that influence the Anti-Cancer Properties of Phytochemicals derived from *Azadirachta indica*, it is necessary to analyse the data by looking at the number of journal citations. The following are the ten most cited articles on the topic of Anti-Cancer Properties of Phytochemicals derived from *Azadirachta indica*.

Table 1. Ten most cited articles

No	Author	Title	Publisher	Citation	Citations Per Year
1	(Chaudhary *et al.*, 2017)	Progress on *Azadirachta indica* Based Biopesticides in Replacing Synthetic Toxic Pesticides	Frontiers in plant science	206	29.43
2	(Patel *et al.*, 2016)	Potential of *Azadirachta indica* (*Azadirachta indica* L.) for Prevention and Treatment of Oncologic Diseases	Seminars in Cancer Biology	131	16.38
3	(Saleem, 2018)	A comprehensive review of phytochemical profile, bioactives for pharmaceuticals, and pharmacological attributes of *Azadirachta indica*	Phytotherapy Research	92	15.33
4	(Tiwari, 2014)	*Azadirachta indica* (*Azadirachta indica*) and its potential for safeguarding health of animals and humans: A Review.	Journal of Biological Sciences	66	6.60
5	(Wang, 2016)	Anticancer properties of nimbolide and pharmacokinetic considerations to accelerate its development	*Oncotarget*	55	6.88

No	Author	Title	Publisher	Citation	Citations Per Year
6	(Subramani, 2017)	Gedunin inhibits pancreatic cancer by altering sonic hedgehog signaling pathway	*Oncotarget*	49	7.00
7	(Chaudhry *et al.*, 2022)	Cancer and apoptosis: The apoptotic activity of plant and marine natural products and their potential as targeted cancer therapeutics.	Frontiers in Pharmacology	38	3.40
8	(Nagini, 2014)	*Azadirachta indica* Limonoids as Anticancer Agents: Modulation of Cancer Hallmarks and Oncogenic Signaling.	Enzyme	34	3.40
9	(Jafari, 2013)	Cytotoxic evaluation of Melia azedarach in comparison with, *Azadirachta indica* and its phytochemical investigation. DARU	Journal of Pharmaceutical Sciences	33	3.00
10	(Gedda, 2023)	Green synthesis of multi-functional carbon dots from medicinal plant leaves for antimicrobial, antioxidant, and bioimaging applications	Scientific Reports	31	31.00

Source: Processed by Researchers, 2024

Table 1 shows that research on *Azadirachta indica* has made significant contributions in various fields, especially its medical applications. The study by Chaudhary et al. (2017) highlighted advances in the use of *Azadirachta indica*-based biopesticides as a safer alternative to synthetic pesticides, with a striking citation count of 206, reflecting its high impact in the field of plant science. Patel et al. (2016) also emphasised the potential of *Azadirachta indica* in the prevention and treatment of oncological diseases, demonstrating its relevance in cancer biology with 131 citations.

Saleem (2018) provided a comprehensive review of the phytochemical profile and pharmacological attributes of *Azadirachta indica*, which are important for pharmaceutical applications, with 92 citations. Tiwari (2014) reviewed the potential of *Azadirachta indica* in maintaining animal and human health, which is important with 66 citations. Wang (2016) and Subramani (2017) focused on the anticancer properties of *Azadirachta indica* derivatives, such as nimbolide and gedunin, highlighting their role in cancer treatment with 55 and 49 citations respectively.

Chaudhry et al. (2022) contributed to the understanding of apoptotic activity of plant and marine natural products in cancer therapy, while Nagini (2014) discussed the role of *Azadirachta indica* limonoids in modulating cancer markers, receiving 34 citations. Jafari

(2013) compared the cytotoxicity of Melia azedarach with *Azadirachta indica*, contributing to broader phytochemical research with 33 citations. Lastly, Gedda (2023) explored the green synthesis of multifunctional carbon dots from medicinal plant leaves, demonstrating novel applications with 31 citations. Taken together, these studies collectively confirm the growing interest and validation of the multifaceted therapeutic potential of *Azadirachta indica*, particularly in oncology, plant-based pesticides, and pharmaceutical applications.

3.2. Discussion

The *Azadirachta indica* plant, better known as neem, has long been used in traditional practices to treat various ailments such as inflammation, infection, fever, skin diseases, and dental disorders. Various parts of the plant, including leaves, bark, fruits, flowers, and seeds, contain bioactive compounds such as flavonoids, tannins, and glycosides. These compounds have various pharmacological activities, including anti-inflammatory, antibacterial, antiviral, antidiabetic, and antifungal. In addition to its use in traditional Indian medicine, modern research has also shown neem's potential in treating liver damage as well as its use in poultry diets for medical and nutritional benefits (Tiwari, 2014)

Devi & Sharma (2023) mentioned that there are various pharmacological activities of neem (*Azadirachta indica*) and its components. *Azadirachta indica* has many health benefits that include antioxidant activity, wound healing effects, anti-inflammatory effects, as well as the ability as an antimicrobial agent. In addition, neem also has potential antifertility, anticancer, antitumour, and antifungal effects, indicating its important role in the prevention and treatment of various diseases. Neem is also known to have hepatoprotective effects that protect the liver, neuroprotective effects that protect the nervous system, and nephroprotective effects that protect the kidneys. It is also capable of modulating the immune system, has antidiabetic properties, and plays a role in protecting the cardiovascular system. Thus, neem not only acts as a therapeutic agent for various medical conditions but also as an important preventive agent in various chronic diseases. The combination of these pharmacological effects shows how wide the medical potential of neem plants is.

Devi & Sharma (2023) in their research showed that secondary metabolites from *Azadirachta indica* leaves have various biological activities that are beneficial for human health and agriculture. *Azadirachta indica* leaves contain a number of active compounds such as azadirachtin, gedunin, and nimbidin, which have been shown to be effective as insecticides, antifungals, anti-inflammatory, and immunostimulating agents (Shrirangasami *et al.*, 2020). Research by Singh et al. (2015) showed that the concentration of phenolic acids varied between young and mature leaves, with mature leaves containing more phenolic acids. This demonstrates the importance of proper selection and preparation of plant parts to achieve optimal effectiveness in pharmacological and agricultural applications.

The chemical constituents in *Azadirachta indica* include many biologically active compounds such as alkaloids, flavonoids, triterpenoids, phenolic compounds, carotenoids, steroids, and ketones. Neem leaf extract shows therapeutic potential as an anti-hyperglycaemic agent, although its anti-inflammatory effect is less than that of dexamethasone. In addition, neem leaves have antibacterial properties that can be used to control bacterial contamination in the air, while the seeds are used in traditional medicine to treat infections especially of the eyes and ears (Prusty and Harish, 2014)

Neem is also known to have effective anticancer activity against various cancers, including oral carcinogenesis. Neem leaf extract exhibits neproprotective effects, protecting against cisplatin-induced nephrotoxicity, thanks to its antioxidant and anti-inflammatory properties. In addition, neem functions as a non-specific immunostimulant that can increase the activation of the cellular immune system and improve the response to mitogens. In terms of antimalarials, neem shows significant properties against Plasmodium falciparum, including chloroquine-resistant strains. Neem is also effective in treating skin conditions such as ringworm, scabies and eczema, with ethanol extracts showing greater anti-dermatophyte activity compared to aqueous extracts (Devi and Sharma, 2023).

Bioactive compounds such as nimbin, nimbolide, azadirachtin, gedunin and quercetin play important roles in the anticancer activity of neem. Nimbin has anti-inflammatory and anti-tumour properties, while nimbolide, the main compound in neem, has been explored for its anti-cancer effects, particularly in inducing apoptosis in various types of cancer cells. Azadirachtin, although better known as an insecticide, also shows anti-cancer potential. Gedunin has anti-proliferative activity that inhibits the growth and spread of cancer cells, while quercetin, a flavonoid, has antioxidant and anti-inflammatory properties that contribute to inhibiting cancer cell growth. The combination of these compounds works through mechanisms such as induction of apoptosis, inhibition of cell proliferation, and inhibition of angiogenesis, which are important in cancer treatment strategies (Chaudhary *et al.*, 2017).

Phytochemicals in *Azadirachta indica*, such as alkaloids, flavonoids, terpenoids, saponins, tannins, and phenolic compounds, contribute to the various pharmacological effects of this plant. Alkaloids have biological activities that include anti-arrhythmic, anti-cholinergic, anti-tumour, vasodilator, anti-hypertensive, cough expectorant, anaesthetic, analgesic, anti-pyretic, and anti-malarial effects. Flavonoids, with their anti-inflammatory and antioxidant effects, play a role in the treatment of various diseases. Terpenoids in neem extracts have antimicrobial properties, supporting the plant's ability to fight infection. The presence of these phytochemicals supports the traditional use of neem in various medical applications and emphasises the importance of further research to validate these benefits and explore its mechanism of action (Chaudhary *et al.*, 2017)

Phytochemicals in *Azadirachta indica* play a role in inhibiting cancer cell growth through several mechanisms. Nimbolide, for example, induces apoptosis in cancer cells by inducing oxidative stress and DNA damage. Nimbolide also inhibits cancer cell proliferation by arresting the cell cycle at the G2/M phase and inhibits angiogenesis by reducing the expression of pro-angiogenic factors such as VEGF. Quercetin and rutin also play a role in inhibiting cancer cell growth through antioxidant activity and inhibiting signalling pathways that favour cancer cell survival (Patel *et al.*, 2016)

Research by Ali et al. (2022) and Hussain et al. (2024) reveal that extracts from neem leaves contain a variety of bioactive compounds, including flavonoids and phenolic acids, which have antioxidant properties that can reduce oxidative stress, a contributor to cancer development. In particular, compounds such as gallic acid and myricetin have been identified as having therapeutic potential against cancer (Hussain *et al.*, 2024). Furthermore, a study focusing on non-small cell lung cancer (NSCLC) identified key target genes (EGFR, BRAF, and PIK3CA) that are affected by neem's active constituents, such as nimbolide and nimbin, suggesting a targeted approach in cancer treatment (Nath *et al.*, 2023). In addition,

the anticarcinogenic study showed a reduction in tumour incidence in the treated group, highlighting the potential of neem extract in cancer prevention (Gurav, Gade and Choudhari, 2023). Overall, the multifaceted pharmacological effects of *Azadirachta indica*, including antioxidant and targeted anticancer activities, underscore its potential as a therapeutic agent in the treatment of cancer (Atawodi and Atawodi, 2009; Gurav, Gade and Choudhari, 2023).

Nimbolide has shown positive responses in various cancers, including Waldenstrom Macroglobulinemia, colorectal cancer, breast cancer, glioblastoma, hepatocarcinoma, leukaemia and choriocarcinoma. Research by Wang (2016) and Jafari (2013) showed that nimbolide was effective in reducing tumour volume, invasion and migration of cancer cells. These findings highlight the potential of nimbolide as a versatile anticancer agent.

Several bioactive compounds in *Azadirachta indica*, such as terpenoids, limonoids, flavonoids and triterpenoids, play a role in the anticancer process. Terpenoids and limonoids, such as azadirachtin and nimbin, as well as gedunin, induce apoptosis and inhibit cancer cell proliferation. Flavonoids such as quercetin and rutin inhibit angiogenesis and induce apoptosis, while triterpenoids such as nimbolide inhibit cancer cell proliferation and metastasis by suppressing the expression of proteins associated with cancer cell migration. These compounds work synergistically by inhibiting various important signalling pathways, such as the NF-κB pathway, which is often activated in cancer (Saleem, 2018)

Azadirachta indica contains phytochemicals such as steroids, alkaloids, phenols, flavonoids, saponins, tannins, anthraquinones, and amino acids, which are associated with its antibacterial and anticancer properties. The methanol extract of this plant showed significant anticancer activity against MCF cell lines, highlighting its potential as a therapeutic agent. The study also demonstrated the cytotoxic activity and potential of neem in cancer treatment. These findings support the further use of neem's bioactive compounds in drug discovery, especially for the development of novel anticancer agents (Antonisamy *et al.*, 2015; Malar *et al.*, 2020).

Analysis provided by (Agyare *et al.*, 2018) highlights the effectiveness of phytochemicals from *Azadirachta indica*, known as neem, in fighting cancer, especially in A549 human lung cancer cells. This study reinforces previous findings showing that ethanolic extracts from neem leaves have the ability to inhibit cancer cell growth, as well as exhibit significant antioxidant activity. This antioxidant activity plays an important role in reducing oxidative stress that can trigger cancer development, thus supporting neem's potential as a promising anti-cancer therapeutic agent. Research by Madhavan (2021) strengthening these findings, suggesting that neem is not only effective in inhibiting cancer cell growth, but also has the potential to be used in cancer treatment more broadly. This potential makes neem an attractive subject for further research in the field of oncology, especially in the development of plant-based therapies that are more natural and have minimal side effects.

Research by Krishnamoorthy & Balakrishnan (2014) showed that phytochemicals in *Azadirachta indica* can modulate cancer cell behaviour through regulation of cell cycle and apoptotic pathways. Compounds from neem leaves can inhibit key regulatory proteins that facilitate cancer cell proliferation, suggesting their potential as therapeutic agents against malignancies. The biochemical interactions between these phytochemicals and specific cell cycle regulatory proteins provide hope for the identification of effective inhibitors and the development of innovative strategies in cancer prevention and treatment.

Research by Muhammad and Chandra (2022) showed that neem extracts can induce apoptosis in cancer cells and inhibit cell growth in a more effective manner and with fewer side effects compared to conventional chemotherapy. For example, in a study conducted by Patel et al. (2018), neem extract showed a significant reduction in colorectal cancer cell propagation, as well as epigenetic modifications that inhibited cancer cell growth. Furthermore, the use of nanotechnology in neem-based drug delivery also shows potential to improve therapeutic and diagnostic outcomes in cancer prevention globally (Azam *et al.*, 2023). Thus, neem serves not only as a therapeutic agent, but also as an important component in more effective cancer prevention and treatment strategies.

Research by Hussain et al. (2024) have shown that neem leaves contain important phenolic compounds, such as gallic acid and sinapic acid, which contribute significantly to their antioxidant potential. These compounds not only enhance the therapeutic value of neem leaves in the development of antioxidant drugs, but also favour its use in alternative and modern medicine. In addition, the antibacterial activity of neem leaves against various strains of microorganisms, including Escherichia coli and Staphylococcus aureus, has been attributed to the presence of phytochemicals such as flavonoids, tannins, and terpenoids. These compounds provide protection against bacterial infections and expand neem's therapeutic applications against microbial infections (Ghosh, Mahapatra and Mukhopadhyay, 2024; Hussain *et al.*, 2024).

Neem oil has also shown effective antifungal properties, particularly against pathogens such as Drechslera oryzae, which adds an important dimension to the use of neem to treat fungal infections. Beyond its medical uses, neem serves as a biopesticide, with azadirachtin acting as an insect deterrent. This not only improves pest control but also supports more environmentally friendly and sustainable farming practices (Ezin and Chabi, 2022). Overall, this combination of antioxidant, antibacterial, antifungal, and biopesticidal properties underscores neem's potential as a valuable multifaceted therapeutic agent in both traditional and modern medicine (Mudenda *et al.*, 2023).

Investigations into specific phytochemicals present in *Azadirachta indica* have revealed its potential to act as a potent anti-angiogenic agent, which may enhance its efficacy in suppressing tumour growth and metastasis through targeted intervention on angiogenic signalling pathways. Collectively, evidence suggests that the rich repertoire of phytochemicals derived from *Azadirachta indica* holds great promise as a valuable resource for the discovery of anti-cancer agents. However, although many laboratory studies have confirmed the anti-cancer potential of these phytochemicals, their clinical application still requires further research to understand their detailed mechanism of action, effectiveness and safety in humans.

4. CONCLUSION

This study concludes that phytochemicals extracted from *Azadirachta indica* show great potential as anti-cancer agents, especially through the inhibition of angiogenesis, which is a crucial step in cancer progression. These compounds not only exhibit cytotoxic activity against cancer cells, but also display a lower toxicity profile against healthy tissues, making them promising candidates for safer and more effective cancer therapies. The study also emphasises the importance of further clinical trials to confirm the effectiveness and safety of using these phytochemicals in humans. These conclusions support the idea that plant-

based therapies could be an integral part of future cancer treatment strategies, which are more personalised and focused on the overall well-being of the patient.

This study provides a solid foundation for the development of phytochemical-based anti-cancer agents from *Azadirachta indica*. The identified compounds have the potential to be developed into drugs that are not only effective against various types of cancer but also have a better safety profile compared to conventional chemotherapy therapy. In addition, the practical implications also include potential applications in combination treatment, where these phytochemicals can be used together with other chemotherapeutic agents to enhance treatment effectiveness while reducing side effects. This research also offers a more affordable and sustainable therapeutic alternative, especially in developing countries where access to expensive cancer drugs may be limited.

Theoretically, this study expands the understanding of how phytochemicals can intervene in signalling pathways involved in tumour angiogenesis. It adds to the growing body of literature in the fields of molecular oncology and cancer biology, providing empirical evidence that compounds from *Azadirachta indica* are able to inhibit the formation of new blood vessels essential for tumour growth and spread. In addition, this study also advances the theory on the use of medicinal plants in cancer therapy, supporting the idea that natural compounds can serve as effective modulators of cellular signalling. The results of this study may motivate further research to explore other plants with similar mechanisms, as well as inspire the development of new therapeutic combinations that integrate phytochemicals with modern medical approaches.

REFERENCES

Agyare, C. *et al.* (2018) 'An ethnopharmacological survey of medicinal plants traditionally used for cancer treatment in the Ashanti region, Ghana', *Journal of ethnopharmacology*, 212, pp. 137–152.

Ali, J., ur Rehman, I. and Bangash, J.A. (2022) 'Phytochemicals content and in-vitro antioxidant properties of *Azadirachta indica* seeds, leaves and twigs prepared from different extraction techniques', *International Journal of Engineering, Science and Technology*, 14(4), pp. 12–20.

Antonisamy, P. *et al.* (2015) 'Anti-diarrhoeal activity of friedelin isolated from Azima tetracantha lam. in wistar rats', *South Ind. J. Biol. Sci*, 1, pp. 34–37.

Atawodi, S.E. and Atawodi, J.C. (2009) '*Azadirachta indica* (neem): a plant of multiple biological and pharmacological activities', *Phytochemistry reviews*, 8, pp. 601–620.

Azam, H. *et al.* (2023) 'Therapeutic role of neem (*Azadirachta indica* Adr. Juss.) in different types of cancer: a systematic review', *Journal of Applied and Experimental Biology*, 2(2), pp. 97–113.

Chaudhary, S. *et al.* (2017) 'Progress on *Azadirachta indica* Based Biopesticides in Replacing Synthetic Toxic Pesticides', *Frontiers in plant science*, 8, pp. 1–13. Available at: https://doi.org/10.3389/fpls.2017.00610.

Chaudhry, G.E.S. *et al.* (2022) 'Cancer and apoptosis: The apoptotic activity of plant and marine natural products and their potential as targeted cancer therapeutics', *Frontiers in Pharmacology*, 13, p. 842376. Available at: https://doi.org/10.3389/fphar.2022.842376.

Devi, J. and Sharma, R.B. (2023) 'Medicinal Importance of *Azadirachta indica*: An Overview', *Journal of Drug Delivery and Therapeutics*, 13(6), pp. 159–165.

Ezin, V. and Chabi, I.B. (2022) '*Azadirachta indica*: Its biological, pharmacological, antidiabetic potential, and omics applications', in *Antidiabetic Plants for Drug Discovery*. Apple Academic Press, pp. 1–22.

Gedda, G. (2023) 'Green synthesis of multi-functional carbon dots from medicinal plant leaves for antimicrobial, antioxidant, and bioimaging applications', *Scientific Reports*, 13(1). Available at: https://doi.org/10.1038/s41598-023-33652-8.

Ghosh, D., Mahapatra, B. and Mukhopadhyay, R. (2024) '*Azadirachta indica*: A source of potential antibacterial activity against various bacterial strains', *International journal of advanced biochemistry research* [Preprint].

Gurav, N.V., Gade, R.M. and Choudhari, R.J. (2023) 'Bioassay of Phytochemicals Isolated from Chloroform Extracts of *Azadirachta indica* Leaves', *International Journal of Plant & Soil Science*, 35(19), pp. 994–1007.

Hussain, S. *et al.* (2024) 'Antioxidant Properties of *Azadirachta indica* Leave Extracts', *BioScientific Review*, 6(2), pp. 31–43. Available at: https://doi.org/10.32350/bsr.62.3.

Jafari, S. (2013) 'Cytotoxic evaluation of Melia azedarach in comparison with, *Azadirachta indica* and its phytochemical investigation', *DARU, Journal of Pharmaceutical Sciences*, 21(1). Available at: https://doi.org/10.1186/2008-2231-21-37.

Krishnamoorthy, M. and Balakrishnan, R. (2014) 'Docking studies for screening anticancer compounds of *Azadirachta indica* using Saccharomyces cerevisiae as model system', *Journal of natural science, biology, and medicine*, 5(1), p. 108.

Lafta, F.M. *et al.* (2023) 'Cytotoxic Potential of Neem (*Azadirachta indica* A. Juss) Oil.', *Tropical Journal of ...* [Preprint].

Madhavan, A.S. (2021) 'Phytochemical analysis and anticancer activity of *Azadirachta indica* ethanolic extract against A549 human lung cancer cell line', *J Biomed Res Environ Sci*, 2(4), pp. 280–285.

Malakar, M. and Mandal, D. (2025) 'Neem-Drug Cabinet of Mother Nature', in *Advances in Medicinal and Aromatic Plants*. Apple Academic Press, pp. vol2-55.

Malar, T. *et al.* (2020) 'In-vitro phytochemical and pharmacological bio-efficacy studies on *Azadirachta indica* A. Juss and Melia azedarach Linn for anticancer activity', *Saudi journal of biological sciences*, 27(2), pp. 682–688. Available at: https://doi.org/10.1016/j.sjbs.2019.11.024.

Mudenda, S. *et al.* (2023) 'Phytochemical composition and antibacterial activities of *Azadirachta indica* (Neem): significance of traditional medicine in combating infectious diseases and antimicrobial resistance', *Journal of Pharmacognosy and Phytochemistry*, 12(5), pp. 256–263.

Muhammad, M.B. and Chandra, R. (2022) 'Turning neem leaves anti-microbial substrate to methane-producing co-substrate for the generation of clean and affordable electricity through biogas: A case study', *Sustainable Energy Technologies and Assessments*, 52, p. 101982. Available at: https://doi.org/10.1016/j.seta.2022.101982.

Nagesh, S.V.S.D.N.A., Kannan and K, B.K. (2023) 'Pharmacophoric Evaluation of Compounds Isolated from GC-MS Analytical Method of Aqueous Extract of *Azadirachta indica* Leaves', *Biomed Pharmacol J*, 16(1).

Nagini, S. (2014) 'Neem Limonoids as Anticancer Agents: Modulation of Cancer Hallmarks

and Oncogenic Signaling', *Enzymes*, 36, pp. 131–147. Available at: https://doi.org/10.1016/B978-0-12-802215-3.00007-0.

Nath, R. *et al.* (2023) 'Identifying druggable targets from active constituents of *Azadirachta indica* A. Juss. for non-small cell lung cancer using network pharmacology and validation through molecular docking', *Phytochemical Analysis*, 34(7), pp. 855–868.

Patel, S.M. *et al.* (2016) 'Potential of Neem (*Azadirachta indica* L.) for Prevention and Treatment of Oncologic Diseases', *Seminars in cancer Biology*, pp. 100–115. Available at: https://doi.org/10.1016/j.semcancer.2016.03.002.

Prusty, A. and Harish, V. (2014) 'Phytochemical Analysis And Anti-Bacterial Effect Of Crude Extract Of *Azadirachta indica* By Using Escherichia Coli, Bacillus Subtilis And Staphylococcus Aureus', *CIBTech Journal of Pharmaceutical Sciences I*, 3(3), pp. 10–16.

Saleem, S. (2018) 'A comprehensive review of phytochemical profile, bioactives for pharmaceuticals, and pharmacological attributes of *Azadirachta indica*', *Phytotherapy Research*, 32(7), pp. 1241–1272. Available at: https://doi.org/10.1002/ptr.6076.

Shrirangasami, S.R. *et al.* (2020) 'Chemistry behind in neem (*Azadirachta indica*) as medicinal value to living forms-A review', *Journal of Pharmacognosy and Phytochemistry*, 9(6), pp. 467–469.

Singh, U.P., Maurya, S. and Singh, D.P. (2015) 'Phenolic acids in neem (*Azadirachta indica*) a major pre-existing secondary metabolites', *Journal of herbal pharmacotherapy*, 5(1), pp. 35–43.

Subramani, R. (2017) 'Gedunin inhibits pancreatic cancer by altering sonic hedgehog signaling pathway', *Oncotarget*, 8(7), pp. 10891–10904. Available at: https://doi.org/10.18632/oncotarget.8055.

Tiwari, R. (2014) 'Neem (*Azadirachta indica*) and its potential for safeguarding health of animals and humans: A Review', *Journal of Biological Sciences*, 14(2), pp. 110–123. Available at: https://doi.org/10.3923/jbs.2014.110.123.

Wang, L. (2016) 'Anticancer properties of nimbolide and pharmacokinetic considerations to accelerate its development', *Oncotarget*, 7(28), pp. 44790–44802. Available at: https://doi.org/10.18632/oncotarget.8316.