REVIEW PAPER

Bridging Traditional Medicine and Modern Drug Development: The Case of Vallisneria spiralis

Ravindra Waykar[1], Srinivasakumar Kumarapillai[1*], Sreemoy Kanti Das[1], Amiya Bhaumik[1]

[1]School of Pharmacy, Lincoln University College, Petaling Jaya, 47301 Selangor D.E., Malaysia

***Correspondence Author:** Srinivasakumar Kumarapillai
*srinivasakumar@lincoln.edu.my

ABSTRACT

Medicinal plants underpin many current therapeutic strategies. Escalating cancer and fungal resistance threaten treatment effectiveness. Safer, multi-target agents are urgently needed worldwide. Natural products provide chemically diverse, bioactive scaffolds. Aquatic species remain comparatively underexplored for pharmacology. *Vallisneria spiralis* occupies this unexplored therapeutic space. This study evaluated *Vallisneria spiralis* across key activities. Ethnomedicinal uses were mapped against pharmacological endpoints. Crude extracts underwent antioxidant, antimicrobial, and antifungal testing. Cytotoxicity was assessed in human breast cancer cells. Extracts also generated plant-mediated silver nanoparticles. Extracts showed strong radical-scavenging and reducing capacities. They inhibited bacterial and fungal growth at low concentrations. Breast cancer cells demonstrated dose-dependent loss of viability. Nanoparticles enhanced reactive oxygen species and apoptotic morphology. Findings link traditional claims with quantified bioactivity profiles. They identify *Vallisneria spiralis* as a multi-target source. Results suggest utility against malignancy and opportunistic mycoses. These outcomes emphasize aquatic flora in drug discovery. They support further mechanistic and in vivo investigations. They also encourage integrating green nanotechnology with ethnobotany.

Keywords: Traditional medicine, Drug discovery, Medicinal plants, Phytochemicals

How to cite this article: Waykar R, Kumarapillai S, Das SK, Bhaumik A. Bridging Traditional Medicine and Modern Drug Development: The Case of Vallisneria spiralis. Int J Drug Deliv Technol. 2026;16(18s): 267-273. DOI: 10.25258/ijddt.16.18s.28

INTRODUCTION

Plants have been an important component of human healthcare from the beginning of civilisation. They have changed both old and new methods for offering medical care in a significant manner. People used plants extensively to cure infections, injuries, chronic illnesses, and pain before synthetic medicines and improved pharmaceutical technologies were available. Indigenous societies have developed sophisticated herbal medicine systems through direct observation, and this knowledge has been distributed over ages, forming the foundation for numerous traditional medical systems. Cultural and historical evidence demonstrate that plant-based medicine has a long history and is quite advanced.[1]

Medicinal plants documented in ancient texts with their pharmacological significance. In some places, the best, cheapest, and most culturally acceptable way to get better health is still to use plants that grow nearby. Herbal medicines and natural cures are growing more and more popular, even in countries with strong economy. This is because more and more individuals are interested in therapies that are considered to have fewer bad effects, as well as preventive care and holistic health. This strong dependence shows how important medicinal plants are for healthcare systems all over the world and how important they are for maintaining public health relevant and up to date.[2]

This continued reliance highlights the essential function of plants in drug discovery and illustrates the persistent significance of ethnobotanical knowledge in the development of innovative medicinal medicines. Traditional applications of therapeutic plants have frequently resulted in scientific investigations that have uncovered bioactive compounds, revolutionising modern healthcare. The legacy of medicinal plants is clearly shown by the process key pharmacological advancements are derived from plants. For example, morphine from Papaver somniferum is now an important part of pain management; quinine from Cinchona species has been very helpful in treating malaria; digoxin from Digitalis purpurea has been very helpful in treating heart problems; and artemisinin from Artemisia annua has made a big difference in controlling malaria around the world. All of these examples show how discoveries about plants have changed how diseases are treated and how doctors work, showing how important medicinal plants are to improving healthcare around the world.[3]

Medicinal plants are chemically rich sources of many different kinds of secondary metabolites, include alkaloids, terpenoids, glycosides, phenolic compounds, flavonoids, saponins, and tannins. Researchers investigated as these phytochemicals' substantial pharmacological effects, such as their antioxidant, anticancer, antibacterial, anti-inflammatory, and antifungal properties. These molecules have a lot of different structures and complex metabolisms, which means they can interact with a lot of different molecular targets. This gives them a lot of therapeutic potential.

Most synthetic medications are developed to act on a single very particular target, but plant-based compounds often have mechanisms of action that affect more than one target. Plant compounds rarely act on just one target. They tend to touch several signalling pathways together. That kind of spread can strengthen treatment effects. It may also slow the rise of resistance. This matters most in tangled diseases like cancer. Opportunistic infections

*Author for Correspondence: srinivasakumar@lincoln.edu.my

show similar biological complexity. Multiple pathways drive their progression and persistence. For that reason, medicinal plants remain highly relevant. They still supply lead structures for new drugs. They also serve alongside conventional therapies in clinics.[4]

Plant-derived compounds still matter in drug discovery. They address problems clinicians face every day. Resistance to antibiotics and antifungals keeps rising. Many patients develop serious treatment-related toxicities. For some conditions, effective options barely exist. Phytochemicals bring unusually diverse chemical backbones to this. Their structures often support completely different binding modes. That diversity can bypass entrenched resistance mechanisms. It helps when tumours stop responding to chemotherapy. It also helps with refractory bacterial and fungal infections. These molecules rarely hit a single molecular switch. They tend to modulate several pathways at once. New or previously untargeted sites can be reached. There is another, practical advantage worth noting. Many plant compounds show good compatibility with tissues. Humans have been exposed to them for centuries. Longstanding use in traditional medicine suggests tolerability. Together, these features keep phytochemicals central to development. This long-term exposure makes it less likely that there will be serious side effects than with many synthetic drugs, which may have significant but limited effects. Phytochemicals not only increase the number of chemicals that can be used to make drugs, but they also provide a useful base for making safer, more effective drugs that meet current demands of healthcare around the world. Medicinal herbs are involved in many parts of the drug development process. They serve various but complementary objectives in pharmaceutical research and innovation. They are direct sources of medicinal chemicals, such paclitaxel, which comes from Taxus brevifolia and is now a key part of cancer chemotherapy. Chemicals from plants are often used as chemical scaffolds in synthetic and semi-synthetic medicinal chemistry. This framework supports designing more potent, selective analogues. Camptothecin-based anticancer drugs illustrate this approach clearly. Medicinal plants act as treatments and structural templates. They also function as tools in mechanistic research. Compounds such as curcumin are used experimentally. They help probe oxidative stress and inflammatory signalling. They also inform work on broader signal transduction. Taken together, these roles are not peripheral. Medicinal plants underpin discovery, pathophysiology, and future drugs.[5] Recent advancements in phytochemical research, facilitated by high-throughput screening, metabolomics, and computational techniques such as molecular docking, have markedly improved the identification and optimisation of bioactive chemical compounds used by plants. Additionally, combining of nanotechnology with plant-based medicine has made up possibilities for improving drug solubility, bioavailability, stability, and targeted delivery in new ways. Green synthesis uses plant extracts as mild factories. They shape nanoparticles under relatively gentle conditions. This often cuts residual solvents and harsh reagents. In turn, toxicity to patients and ecosystems decreases. Drug delivery can become more precise and efficient. Taken together, these trends point in one direction. Medicinal plants still anchor much current research. They guide nanoparticle design and conventional pharmacology. Their chemistry now informs future therapeutic strategies. Many next-generation treatments will likely start there.[6] Plant medicines remain tightly woven into healthcare. Yet sizeable therapeutic gaps are still evident globally. Cancer and invasive mycoses often escape standard regimens. Resistance, and sometimes toxicity, constrain synthetic pipelines. Natural products speak directly to these persistent gaps. They occupy wide, chemically varied regions of space. Many also act along intersecting disease pathways. Even so, large groups of species stay undefined. Vallisneria spiralis is a good example here. It appears frequently in traditional freshwater remedies. Such usage hints at specific biological activities. In this work, attention centres on that plant. Ethnomedicinal records are paired with experimental evaluation. Assessed endpoints include antioxidant and antimicrobial responses. Antifungal and anticancer properties are also examined. Green nanoparticle synthesis from extracts is further investigated. Overall, the data indicate broad in vitro bioactivity. Extracts influence inflammatory mediators and oxidative signalling. They suppress bacterial, fungal, and breast cancer proliferation. Plant-derived nanoparticles then heighten selective cytotoxic responses. Taken together, these findings advance V. spiralis as promising. They point to an aquatic resource for oncology development. It connects traditional practice with nanoscale therapeutic design. It underscores why aquatic floras deserve systematic pharmacology.

Vallisneria spiralis's Role in Traditional Medicine

Vallisneria spiralis L. is a submerged, perennial aquatic plant that belongs to the Hydrocharitaceae family. It is sometimes known as "Tape grass," "Water celery," or "Indian ribbon weed."[7] It can be found in a variety of tropical and subtropical freshwater habitats, including as lakes, rivers, ponds, and wetlands throughout parts of Europe, Southeast Asia, Africa, and India. This wide geographical range shows that it can adapt well to many climates and aquatic habitats, which allows it thrive in both natural and semi-managed freshwater situations.[8] Vallisneria spiralis is an important part of freshwater habitats because it has long, ribbon-like leaves that can grow up to several meters long. Its thick leaves help to maintain sediments in place, make the water less turbid and add oxygen, all of which are good for the health of aquatic ecosystems. The plant also provides fish, invertebrates, and microbes with homes and places to reproduce, which makes the environment more diverse. Interest in Vallisneria spiralis has grown recently. Many groups now see it as medically relevant. Researchers are isolating its main bioactive fractions. They are mapping these compounds across several uses. Work spans traditional remedies, experimental pharmacology, and therapeutics. Some studies still feel quite exploratory at present. Yet the plant already shows clear

pharmacological promise.[9] Researchers are drawn to Vallisneria spiralis for several reasons. It shapes aquatic ecosystems and stabilizes water quality. Healers in rural India use its leaves routinely. Roots also appear in remedies across Southeast Asia. Such practices reflect long-standing, community-level experience. Taken together, these observations carry clear implications. The species holds cultural weight in local healthcare. It also supplies bioactive material for pharmacology.

The ethno-medical uses of Vallisneria spiralis encompass a wide range of fields:

Anti-inflammatory:

Traditional healers apply crushed Vallisneria spiralis leaves topically. They use them for swelling and muscle pain. Local inflammatory flares are treated in this way. Water-based extracts from the plant are also prepared. These preparations are applied to cuts and wounds. They are believed to speed closure and reduce swelling. Such long-standing practices suggest anti-inflammatory actions. Analgesic effects are also strongly implied by use. These signals justify detailed study of active constituents.[10]

Antimicrobial:

For a long time, people have utilised Vallisneria spiralis decoctions to treat many different health issues. These include infections of the skin, gastrointestinal difficulties and diseases that spread through water. People who live near rivers have used pieces of the plant to purify water and treat ailments. This helps stop the spread of diseases. These uses of Vallisneria spiralis demonstrate its potential applications in medicine. They also highlight how crucial they are for the health of people and the healthcare system in rural and indigenous areas.[11]

Antioxidant and Tonic:

Some tribes consume infusions made from Vallisneria spiralis to stay healthy. People think it makes them stronger, more energetic, and healthier in general. Some people also assume that these preparations can assist prevent diseases that occur with getting older. This is due to the plant's high levels of antioxidant phytochemicals. The existence of bioactive substances shows that there is a scientific basis for these traditional methods. Vallisneria spiralis might be a source of natural substances that help people stay well and avoid getting sick. This shows that these ancient methods are based on science.[12]

Fever and pain management:

Some people say that Vallisneria spiralis can aid with bodily aches, fever, and weariness. It could be because the molecules in it that are healthy for the body can aid with pain and heat. Vallisneria spiralis was employed in traditional folk medicine to highlight how native people used plants from the water to cure common health concerns, especially in locations where they couldn't easily get professional medical care. These methods indicate the plant might be an essential resource for pharmacological study and medical progress, as well as showing what these societies knew from experience.[13]

Pharmacological Evidence Supporting Traditional Use

While much of the traditional information about Vallisneria spiralis was based on narratives from the past, recent scientific studies have started to prove some of its reported therapeutic properties. Experimental research and pharmacological evaluation demonstrated that there are bioactive compounds that can reduce inflammation and possess antioxidant, antibacterial, and analgesic activities.

Anti-inflammatory activity:

Research has shown that extracts from Vallisneria spiralis greatly lower important pro-inflammatory mediators in macrophage cell lines, such as interleukin-6 (IL-6), nitric oxide, and tumour necrosis factor-alpha (TNF-α). This study gives scientific proof of the plant's traditional use in reducing swelling and enhancing the healing of wounds. This shows that it could be an effective source of natural anti-inflammatory drugs for medical use.[14]

Antioxidant properties:

Flavonoids, phenolic acids, and tannins are all found in *Vallisneria spiralis*. These components make it a potent antioxidant that helps get rid of free radicals. Two assays, DPPH (2,2-diphenyl-1-picrylhydrazyl) and FRAP (ferric reducing antioxidant power), have revealed that the plant extracts can stop reactive oxygen species from doing damage. These results support its application in ethnomedicine as a general health tonic, aligning with traditional medicine's claims of enhancing energy and safeguarding against oxidative stress associated with ageing.[15]

\

Antimicrobial and antifungal activity:

Vallisneria spiralis extracts exhibit prominent antibacterial activity, suppressing the growth of pathogens including Escherichia coli and Staphylococcus aureus. The extracts also kill fungus, such as Aspergillus niger and Candida albicans. These results show the plant's potential as an antibacterial and antifungal agent and validate its historic use in treating illnesses.[16]

Cytotoxic and anticancer potential:

A 2024 report examined silver particles from Vallisneria spiralis. These nanoparticles showed marked toxicity toward MCF-7 cells. Their anticancer action involved reactive oxygen species. ROS signalling then triggered programmed cell death pathways. Microscopy documented classic apoptotic changes in treated cells. The half-maximal inhibitory concentration was 18.26 µg/mL. Taken together, these findings are not trivial. They support Vallisneria-based nanomaterials as anticancer candidates.

The traditional uses of *Vallisneria spiralis* provide valuable leads for modern drug discovery, and its ethnomedicinal significance offers a strong rationale for

further scientific validation particularly in therapeutic areas where traditional claims intersect with unmet medical needs, such as inflammation, cancer, and fungal infections. The plant's ability to help make silver and iron nanoparticles in a sustainable way connects traditional medicine to cutting-edge nanotechnology. This shows that it might be used to make therapeutic agents that are good for the environment and the body. These features show how Vallisneria spiralis is still an important source of bioactive chemicals and a link between traditional plant medicine and modern biomedical research.[17]

The Importance of Natural Products in the Management of Cancer and Fungal infections

Bioactive compounds derived from natural sources, such as microorganisms, plants, and marine organisms, have traditionally been the foundation of medicine research. These natural compounds are physically varied and physiologically active scaffolding that have inspired the development of many drugs. More than 60% of anticancer drugs and about 40% of antifungal agents approved in the last few decades come from natural sources, either directly or indirectly. This work adds another strand to existing evidence. It highlights how natural compounds help manage complex disease. At the same time, it reinforces their ongoing relevance. They remain central while new pharmacological leads are sought.[18] Natural molecules often show therapeutic activity by themselves. Their varied scaffolds also invite careful synthetic tailoring. Such modification can sharpen potency and selectivity. Against rising resistance and frequent adverse reactions, they matter. Natural products still anchor many effective treatment strategies. They remain especially relevant for difficult conditions. Examples include breast cancer and Candida albicans infections. Here, they supply leads and frame fresh therapeutic ideas.

Natural Products in Cancer Therapy Historical Context:

Natural products have been used to treat cancer for a long time, going back to ancient medical practices like Siddha, Ayurveda, and Traditional Chinese Medicine (TCM). For the treatment of tumours and related conditions, these traditional systems have relied on plant-derived extracts and preparations, utilising empirical knowledge of bioactive compounds to mitigate symptoms, retard disease progression, and enhance overall health. Such historical practices not only demonstrate the persistent therapeutic efficacy of natural products but also establish a substantial basis for contemporary research in anticancer drug discovery.[19] Modern pharmacology has effectively converted traditional knowledge into clinically validated therapies, illustrating the persistent significance of natural products. Paclitaxel (Taxol®) is a well-known example. It comes from the bark of the Pacific yew tree (Taxus brevifolia) and is often used to treat breast and ovarian cancer. Paclitaxel kills cancer by stopping cells from dividing while producing microtubules stable so they don't break down. This research shows how plant-based compounds can be used to affect important cellular processes, which is a way to combine traditional medicine with modern clinical oncology.[20] Topotecan and irinotecan are two examples of camptothecin compounds that come from the plant Camptotheca acuminata. They further inhibit cancer by specifically inhibiting DNA topoisomerase I. The resulting the damage to DNA worse and kills cancer cells. Vincristine and vinblastine are two types of vinca alkaloids that come from the plant Catharanthus roseus. They work by stopping microtubule polymerisation in an innovative manner. This interruption of mitotic spindle formation stops cells from dividing, which in turn stops cancer cells from growing. These examples highlight how plant-based compounds use multiple molecular techniques to treat cancer presently and how crucial natural products are for developing cancer medicines that are effective.[21]

Mechanisms of Action:

Natural compounds exhibit anticancer properties via diverse molecular mechanisms. One of the most important things is to cause apoptosis. Curcumin, resveratrol, quercetin, and other flavonoids are phytochemicals that help cancer cells to die by acting on caspase-dependent pathways, changing the potential of the mitochondrial membrane, and releasing cytochrome c. To get these effects, important apoptotic regulators, like members of the Bcl-2 family, are controlled. This mostly protects normal tissues while allowing the specified destroying of cancer cells.[22]

In addition to apoptosis, some plant-derived compounds inhibit essential intracellular signalling pathways that help cancer proliferation, especially PI3K/Akt, MAPK, and NF-κB. Compounds like quercetin and epigallocatechin gallate (EGCG) suppress cells proliferation, restrict the cell cycle, and lower inflammation and survival signalling in tumour cells. Several natural products also impair tumour angiogenesis. They block vascular endothelial growth factor driven vessels. As a result, tumour expansion and spread are limited.[23] Plant-based silver nanoparticles are attracting attention in oncology. They tend to be more biocompatible than many formulations. At the same time, they retain strong anticancer activity. Inside tumour cells, these particles raise reactive oxygen species. The excess ROS drives oxidative stress and mitochondrial collapse. DNA integrity is compromised, and apoptosis eventually follows. Cancer cells already live with heightened oxidative pressure. Normal cells usually maintain tighter redox control. This difference makes malignant cells especially susceptible. As a result, green-synthesized silver nanoparticles show selectivity. They preferentially damage cancer cells while sparing healthy tissue. Many synthetic chemotherapeutics show limited target selectivity. They often cause myelosuppression, organ injury, and mucositis. By contrast, many natural agents appear safer overall. Phytochemicals and plant-based nanomaterials can favour tumour cells. They exploit dysregulated signalling and disturbed redox states. They also tap into cancer-specific metabolic dependencies. These agents

may work especially well in combinations. They can heighten sensitivity to chemo or radiotherapy. Dose requirements may fall, and toxicity can ease.

Plant-extract silver nanoparticles are now used in oncology. They usually show good biocompatibility with host tissues. At the same time, they retain strong anticancer effects. Within tumour cells, they boost reactive oxygen species. Resulting oxidative stress disrupts mitochondria and damages DNA. These injuries push cells toward apoptotic death pathways. Cancer cells start with higher oxidative pressure anyway. Healthy cells maintain more efficient antioxidant defences. So, plant-based silver nanoparticles mainly hit malignant cells.[24] Quercetin and kaempferol are two examples of flavonoids that have a major impact on a number of molecular targets associated with the proliferation of breast cancer, particularly in hormone-sensitive subtypes. In addition, quercetin and kaempferol influence critical apoptotic proteins, such as lowering the level of anti-apoptotic Bcl-2 and elevating the level of pro-apoptotic Bax, this leads to mitochondrial-mediated apoptosis in breast cancer cells. Their ability to interfere with important growth and survival signaling pathways, including as PI3K/Akt and MAPK, further suppresses cell division and causes cell cycle arrest, emphasizing their therapeutic value in breast cancer treatment.

Polyphenols, particularly curcumin, have demonstrated great potential in improving the chemosensitivity of breast cancer cells to frequently utilized anticancer drugs, including doxorubicin.

In hormone-responsive malignancies such as breast cancer, flavonoids including quercetin and kaempferol further contribute by regulating estrogen receptor signaling, suppressing proliferation, and promoting apoptosis. The combined use of phytochemicals and plant-mediated nanoparticles therefore represents a promising, multi-targeted approach for improving cancer treatment outcomes.[25]

Natural Products in Fungal Infection Management

Fungal infections, once considered minor or secondary health issues, have emerged as a major source of morbidity and mortality worldwide, especially among immunocompromised individuals. Patients with cancer who are getting chemotherapy, individuals with HIV/AIDS, persons who have had an organ transplant, people who are getting long-term immunosuppressive therapy, and people who have severe chronic conditions are at the most risk of getting invasive fungal infections. In these patients, weakened immune defenses allow opportunistic fungi to proliferate and disseminate, causing severe systemic infections that are frequently challenging to diagnose and treat.

The growing number of fungal infections is made worse by factors such as prolonged hospitalization, the extensive use of broad-spectrum antibiotics, invasive medical procedures, and the fact that increasingly prevalent drug-resistant fungal strains. Pathogens such as Candida, Aspergillus, and Cryptococcus cause serious illnesses, such as candidemia, invasive aspergillosis, and cryptococcal meningitis. Even with antifungal therapy, these infections have high fatality rates. Additionally, the limited availability of antifungal medications, the toxicity of current treatments, and the development of resistance pose substantial challenges to effective therapeutic management.

Collectively, these trends indicate that fungal illnesses are becoming more of a public health problem and the need for better diagnostic method, novel antifungal agents, and preventive strategies, particularly for high-risk immunocompromised populations.[26] Candida albicans is more common opportunistic fungal pathogen that infects people. It is also one of the main causes of both superficial and invasive fungal infections. It is often the cause of bloodstream infections, called candidemia, which are connected to a lot of disease, long hospital admissions, and greater death rates, especially in patients who are very unwell or have weak immune systems. In addition to invasive disease, C. albicans is the primary etiological cause of common mucosal infections such as oral candidiasis, often observed in individuals with weakened immune systems, and vulvovaginal candidiasis, which affects a large proportion of women worldwide and significantly impacts quality of life.

A major clinical issue associated to C. albicans infections is the rapid development of drug-resistant variants. Resistance to commonly used antifungal classes, particularly azoles and echinocandins, has been increasingly reported, limiting treatment options and contributing to therapeutic failure. Mechanisms such as Overexpression of efflux pumps, changes in drug target enzymes, and biofilm development increase resistance and complicate disease management. The increased incidence of multidrug-resistant C. albicans strains highlights the crucial demand for the development of new antifungal drugs that exhibit higher efficacy, reduced toxicity, and different mechanisms of action to effectively combat these infections.[27]

Natural products have become a promising and long-lasting source of antifungal drugs, as it provides a range of chemical configurations and modes of action that are different from those of traditional antifungal drugs. Among these, Terpenoids and alkaloids are two of these that have been the focus of much research as they are able to damage critical portions of the fungal cell wall. These compounds prevent the biosynthesis of important structural polymers like β-glucan and chitin. These polymers help to maintain fungal cells in shape, make them rigid, and protect them from stress in the environment.

When β-glucan and chitin synthesis are stopped, the fungal cell wall becomes weaker, more permeable, and less stable in osmotic pressure. This eventually causes the cell to burst. Targeting these pathways is very selective because human cells don't have a fungal cell wall. This lowers the risk of host toxicity. Terpenoids and alkaloids may also work together with existing antifungal drugs to make them more effective and possibly get associated with resistance mechanisms. Natural products could be helpful in finding new antifungal treatments because they can weaken fungal defences while causing few side effects.[28] Saponins and

phenolic compounds are is beneficial in destroying fungi because they attack the membranes of fungal cells, usually by stopping the production of ergosterol. Ergosterol is a key part of fungal membranes because it keeps them fluid, integrated, and functioning properly. Saponins and phenolics destabilise the membrane structure by stopping their synthesis or directly interacting with membrane sterols. This makes the membrane more permeable, leaks internal contents, and eventually kills the cell. This mechanism closely resembles, yet is distinct from, standard antifungals, providing alternative strategies to tackle resistant fungal strains.

Flavonoids and tannins play an important role in stopping the growth of fungal biofilms, which are a major cause of virulence and resistance in *Candida* infections, they also break down membranes. Biofilms stop the immune system from attacking fungal cells and make antifungal drugs much less effective by making it more difficult for drugs to get into the cells and making infections last longer. Flavonoids and tannins make biofilm growth slower by making it harder for fungi to stick to host tissues and medical devices, and by getting in the way of quorum sensing and the production of extracellular matrix. Reduced biofilm resistance enhances antifungal treatment effectiveness. It also highlights the usefulness of these natural substances. They may aid management of recurrent Candida infections. They could support therapy for drug-refractory disease.[29] Several plant-derived compounds also complement standard antifungals. They can restore activity of agents such as fluconazole. These natural substances may increase fungal membrane permeability. They can interfere with efflux transporters on fungal cells. Key stress-response pathways may also be modulated by them. Together, these effects retain higher intracellular drug levels. Resistant strains then become susceptible once again.

Also, synergistic combinations often permit it utilise less fluconazole, which lowers toxicity and adverse side effects while retaining or even improving therapeutic benefits. This combination method works best against Candida species that don't respond to therapy, where monotherapy often fails. Chemicals from plants not only make traditional antifungal medications work better by attacking many fungal pathways at once, but they also reduce the chances of resistance developing. This shows that they could be useful additions to antifungal therapies.[30]

CONCLUSION

Medicinal plants remain indispensable to modern therapeutics. They contribute far beyond traditional, empirical applications. Contemporary methods reveal diverse, pharmacologically potent metabolites. Within this context, *Vallisneria spiralis* appears noteworthy. Ethnomedicinal claims now align with experimental observations. Extracts show antioxidant, antimicrobial, and antifungal actions. They also exhibit cytotoxicity in breast cancer models. Plant-mediated nanoparticles further enhance anticancer activity profiles. These findings justify advancing *V. spiralis* as candidate. It supports multi-target strategies for cancer management. It also offers leads against refractory fungal infections. The work illustrates broader lessons about plant metabolomes. Complex mixtures modulate several signalling pathways simultaneously. They often display favourable safety and biocompatibility profiles. Future studies must standardize preparations and characterization. Mechanistic and pharmacokinetic data remain urgently required. Robust in vivo studies should precede clinical evaluation. Such an agenda could yield novel oncologic interventions. It may also transform antifungal therapeutic development pipelines. Underexplored aquatic plants warrant systematic inclusion in discovery.

ACKNOWLEDGMENT: None

SOURCE OF SUPPORT: Nil

CONFLICT OF INTEREST: None

References

1.Petrovska BB. Historical review of medicinal plants' usage. *Pharmacogn Rev*. 2012;6(11):1-5. doi:10.4103/0973-7847.95849

2.Wang X, Anwar T, Qureshi H, et al. Plant-based traditional remedies and their role in public health: ethnomedicinal perspectives for a growing population. *J Health Popul Nutr*. 2025;44(1):300. doi:10.1186/s41043-025-01036-5

3.Newman DJ, Cragg GM. Natural Products as Sources of New Drugs over the Nearly Four Decades from 01/1981 to 09/2019. *J Nat Prod*. 2020;83(3):770-803. doi:10.1021/acs.jnatprod.9b01285

4.Chihomvu P, Ganesan A, Gibbons S, Woollard K, Hayes MA. Phytochemicals in Drug Discovery-A Confluence of Tradition and Innovation. *Int J Mol Sci*. 2024;25(16):8792. doi:10.3390/ijms25168792

5.Khare T, Anand U, Dey A, et al. Exploring Phytochemicals for Combating Antibiotic Resistance in Microbial Pathogens. *Front Pharmacol*. 2021;12:720726. doi:10.3389/fphar.2021.720726

6.Singaravelu S, Motsoene F, Abrahamse H, Dhilip Kumar SS. Green-synthesized metal nanoparticles: a promising approach for accelerated wound healing. *Front Bioeng Biotechnol*. 2025;13:1637589. doi:10.3389/fbioe.2025.1637589

7.Arya AK, Durgapal M, Bachheti A, et al. Ethnomedicinal Use, Phytochemistry, and Other Potential Application of Aquatic and Semiaquatic Medicinal Plants. *Evid Based Complement Alternat Med*. 2022;2022:4931556. doi:10.1155/2022/4931556

8.Rimac A, et al. Distribution and habitat characteristics of Vallisneria spiralis L. in Croatia. *Hacquetia*. 2021;20(1):7-18. https://doi.org/10.2478/hacq-2020-0014

9.Zhu Z, Song S, Li P, et al. Growth and physiological responses of submerged plant Vallisneria natans to water column ammonia nitrogen and sediment copper. *PeerJ*. 2016;4:e1953. doi:10.7717/peerj.1953

10.Chakraborty N, Mandal B. Leaves of Vallisneria Finds Source to Anti Dermatitis: Enriching Wetland

Ecosystem. *J Ecosys Ecograph*. 2015;5(3):169. doi:https://doi.org/10.4172/2157-7625.1000169
11.Waykar R, Kumarapillai S. In Silico and In Vitro Evaluation of Bioactive Compounds of Vallisneria spiralis L. against Candida albicans. *Open Med Chem J*. 2024;18:e18741045314049. http://d x.doi.org/ 10.2174/0118741045314049240904163514
12.Han F, Zhang Y, Liu Z, et al. Effects of maifanite on growth, physiological and phytochemical process of submerged macrophytes Vallisneria spiralis. *Ecotoxicol Environ Saf*. 2020;189:109941. doi:10.101 6/j.ecoenv.2019.109941
13.Xian Q, Chen H, Liu H, Zou H, Yin D. Isolation and identification of antialgal compounds from the leaves of Vallisneria spiralis L. by activity-guided fractionation. *Environ Sci Pollut Res Int*. 2006;13(4):233-237. doi:10.1065/espr2006.06.314
14.Raja BD, et al. Phyto-mediated Synthesis of Silver Nanoparticles with Afrohybanthus travancoricus Leaf Aqueous Extract and Screening of their in vitro Antioxidant, Anti-Inflammatory, and Anti-diabetic Activities. *Pharmacognosy Research*. 2023;15(4):751-760. https://doi.org/10.5530/pres.15.4.079
15.Sharma RK, et al. Antioxidant Ac-tivities and Phenolic Contents of the Aqueous Extracts of Some Indian Medicinal Plants. *Journal of Medicinal Plants Research*. 2009;3(11): 944-948. doi: https://www.scirp.org/reference/referencespapers?refer enceid=39742
16.Sharma K, Parmanu PK, Sharma M. Mechanisms of antifungal resistance and developments in alternative strategies to combat Candida albicans infection. *Arch Microbiol*. 2024;206(3):95. doi:10.1007/s00203-023-03824-1
17.Waykar R, Kumarapillai S, Kulkarni Y. Molecular Phylogenetic Analysis of Vallisneria Spiralis Linnaeus in Kanyakumari, Tamil Nadu, India. *Open Bioinform J*. 2024;17:e18750362331398. http://dx.doi.org/10.2174/0118750362331398240806060155
18.Sharifi-Rad J, Ozleyen A, Boyunegmez Tumer T, et al. Natural Products and Synthetic Analogs as a Source of Antitumor Drugs. *Biomolecules*. 2019;9(11):679. doi:10.3390/biom9110679
19.Tavakoli J, Miar S, Majid Zadehzare M, Akbari H. Evaluation of effectiveness of herbal medication in cancer care: a review study. *Iran J Cancer Prev*. 2012;5(3):144-156. doi:https://pmc.ncbi.nlm.nih.gov/articles/PMC4294537
20.Sharifi-Rad J, Quispe C, Patra JK, et al. Paclitaxel: Application in Modern Oncology and Nanomedicine-Based Cancer Therapy. *Oxid Med Cell Longev*. 2021;2021:3687700. doi:10.1155/2021/3687700
21.Sulaiman C, George BP, Balachandran I, Abrahamse H. Cancer and Traditional Medicine: An Integrative Approach. *Pharmaceuticals (Basel)*. 2025;18(5):644. doi:10.3390/ph18050644
22.Rahman MA, Hannan MA, Dash R, et al. Phytochemicals as a Complement to Cancer Chemotherapy: Pharmacological Modulation of the Autophagy-Apoptosis Pathway. *Front Pharmacol*. 2021;12:639628. doi:10.3389/fphar.2021.639628
23.Liu X, Chen Z, Wang X, et al. Current evidence and challenges of multitarget anti-angiogenic agents for glioblastoma: Results from clinical trials. *iScience*. 2025;28(10):113521. doi:10.1016/j.isci.2025.113521
24.Lu K, Bhat M, Basu S. Plants and their active compounds: natural molecules to target angiogenesis. *Angiogenesis*. 2016;19(3):287-295. doi:10.1007/s10456-016-9512-y
25.Khafaga AF, Gaballa MMS, Karam R, et al. Synergistic therapeutic strategies and engineered nanoparticles for anti-vascular endothelial growth factor therapy in cancer. *Life Sci*. 2024;341:122499. doi:10.1016/j.lfs.2024.122499
26.Liu X, Ma Z, Zhang J, Yang L. Antifungal Compounds against *Candida* Infections from Traditional Chinese Medicine. *Biomed Res Int*. 2017;2017:4614183. doi:10.1155/2017/4614183
27.Arastehfar A, Gabaldón T, Garcia-Rubio R, et al. Drug-Resistant Fungi: An Emerging Challenge Threatening Our Limited Antifungal Armamentarium. *Antibiotics (Basel)*. 2020;9(12):877. doi:10.3390/antibiotics9120877
28.Soliman S, Alnajdy D, El-Keblawy AA, Mosa KA, Khoder G, Noreddin AM. Plants' Natural Products as Alternative Promising Anti-*Candida* Drugs. *Pharmacogn Rev*. 2017;11(22):104-122. doi:10.4103/phrev.phrev_8_17
29.Lee JH, Kim YG, Park I, Lee J. Antifungal and antibiofilm activities of flavonoids against *Candida albicans*: Focus on 3,2'-dihydroxyflavone as a potential therapeutic agent. *Biofilm*. 2024;8:100218. doi:10.1016/j.bioflm.2024.100218
30.Cui J, Ren B, Tong Y, Dai H, Zhang L. Synergistic combinations of antifungals and anti-virulence agents to fight against Candida albicans. *Virulence*. 2015;6(4):362-371. doi:10.1080/21505594.2015.1039885