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## Breast cancer insights: Significance of *Murraya koenigii* and their potential in prevention and therapeutic intervention

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### ABSTRACT

The review aims at discussing the therapeutic potential of Murrayanine, a bioactive compound obtained by using *Murraya koenigii*, as a new strategy in the prevention and treatment of breast cancer. Due to the prevalence of breast cancer across the world and the constraints of traditional treatment methods, this review examines the multiple mechanisms of action of Murrayanine, such as inducing apoptosis and inhibiting cell growth, as well as altering major signalling pathways, such as PI3K/Akt, NF-κB, and MAPK. There is support of evidence regarding preclinical studies, which indicate that Murrayanine has strong anticancer activity in that it is effective against a range of cancer cell types, such as breast, colon, and lung cancer. It has been demonstrated to overcome multidrug resistance and minimise the levels of chemotherapy induced cytotoxicity to normal cells, thereby increasing the therapeutic efficacy of conventional chemotherapy agents, doxorubicin and paclitaxel. In addition, Murrayanine as an antioxidant and anti-inflammatory agent also adds to its protective effects by preventing oxidative stress and inflammation associated with cancer progression. The main conclusions indicate the synergistic value of Murrayanine with chemotherapy that can be used to enhance the treatment process, decrease the adverse effects. Nevertheless, its issues like low bioavailability and the necessity to engage more clinical validation should be resolved to make the full translation of Murrayanine to clinical practise possible. The review recommends further investigation of the role of Murrayanine in the integrative cancer therapy.

### 1. Introduction

More women across the world are diagnosed with breast cancer and are more likely to die from cancer due to this disease than any other cancer. WHO analysis reveals that in 2020, more than 2.3 million women acquired breast cancer and nearly 685,000 women lost their lives due to the disease. To treat breast cancer, doctors use surgery, chemotherapy, radiation therapy, hormone therapy, targeted therapy and immunotherapy. Precisely because survival rates have gone up, people often suffer severe results, find it hard to obtain therapy and still

deal with many versions of success for different breast cancer types[1, 2]. Chemotherapeutic drugs can be effective, but they also damage other healthy cells, leading to conditions that include heart disease, weak immune system, fatigue and damage to various organs. If these medicines are given over a long time, MDR may develop, making treatments ineffective and placing a higher strain on the medical system [3–5].

Therefore, using natural remedies from plants is gaining popularity as an alternative or additional treatment for breast cancer. Ayurveda, Traditional Chinese Medicine (TCM) and Unani have counted on natural

**Abbreviations:** PI3K, Phosphoinositide 3-kinase; Akt, Protein kinase B also known as AKT; NF-κB, Nuclear factor kappa-light-chain-enhancer of activated B cells; MDR, Multi-drug resistance; GLOBOCAN, Global Cancer Observatory; BRCA1/BRCA2, Breast cancer gene 1 and gene 2; TNBC, Triple-negative breast cancer; ROS, Reactive oxygen species; CDK, Cyclin-dependent kinase; GMP, Good Manufacturing Practice; TCM, Traditional Chinese Medicine; SIDDHA, Traditional system of medicine in India; COX-2, Cyclooxygenase-2; GFP, Green fluorescent protein; MAPK, Mitogen-activated protein kinase.

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drugs for many years and a lot of today’s drugs were created from their phytochemicals. These compounds are reported to influence various body mechanisms, for example, by acting against cancer, oxidative stress, inflammation, the immune system and by preventing blood vessel development. Being able to affect multiple processes in cancer cells and having comparatively less toxicity makes them suitable for cancer prevention and treatment [6,7]. Murrayanine, found in the curry leaf plant, is one of the exciting cis-trans isomers, commonly used in both cooking and curative applications in Asia. Because it may have anticancer effects, Murrayanine is receiving increased attention from scientists. Scientists have discovered from preclinical research that Murrayanine restricts the growth of various cancer cell lines such as those found in breast cancer, by inducing apoptosis, blocking the cell cycle, affecting mitochondrial activity and inhibiting PI3K/Akt, NF-κB and MAPK signaling.

Murrayanine has the potential to raise the levels of ‘pro-death’ proteins (like Bax and caspase-3) and lower the levels of ‘survival’ proteins such as Bcl-2. It further helps by reversing the imbalance between ROS and antioxidant enzymes, so the body becomes less suitable for tumours [8,9]. In addition, Murrayanine can also stop the growth of new blood vessels and spread of cancer cells outside the original site. They have found that Murrayanine boosts the effects of standard chemotherapy drugs and assists in coping with drug resistance. The addition of Murrayanine and similar phytochemicals in breast cancer treatment could be more secure and effective than highlighted treatment plans. For this reason, natural compounds are useful in cancer treatment since they impact various processes in the body simultaneously. Moreover, breast cancer treatment is valuable in low- and middle-income countries since it is cost-effective and can be accessed more easily [10–12] Fig. 1.

Although Murrayanine has shown positive results, more difficulties must be solved for it to be used in medicine. Since bioavailability is low for these drugs and their pharmacokinetics must be improved, advanced systems, structure changes and better clinical studies are needed. Even

so, the evidence we have supports the need to continue exploring Murrayanine as an anticancer medicine. The purpose of this article is to look into how natural drugs can play a role in managing cancer, by closely examining what Murrayanine may do for patients. It studies scientific findings, explains the working of various phytomedicine molecules and examines the possible role phytomedicine will play in providing treatment for cancer patients. The work aims to explore and illustrate how Murrayanine might work as both a prevention and treatment for breast cancer. Its aim is to discover how it leads to effects, how it cooperates with other treatments and how it could be introduced into customised care for cancer patients in the future [13–17]. The review gives a comprehensive discussion on Murrayanine that is a product of the *Murraya koenigii* and its possible use as a therapeutic agent in the treatment of breast cancer. It stands out due to its attention to the molecular mechanisms of the compound, such as its ability to induce apoptosis, cell cycle arrest, and alter the activity of numerous cancer-relevant pathways, such as PI3K/Akt and NF-κB. Also, the review discusses the synergetic activity of Murrayanine with chemotherapy that provides novel information on how to overcome chemotherapy resistance and reduce the side effects [18,19].

To conduct future studies, it is important to find solutions to knowledge gaps, including inadequate bioavailability and pharmacokinetic information on Murrayanine that makes it difficult to apply in clinical translation. The future research needs to be devoted to enhancing its absorption, stability, and delivery using the modern methods of formulation, such as nanoparticles and liposomes. Also, there is a promising research opportunity related to the investigation of the possibility of customised medicine methodology, where the application of a genomic profile helps to determine those patients who are most likely to respond to Murrayanine-based treatments. Murrayanine’s potential as an anticancer agent, it lacks a clear rationale for focusing specifically on Murrayanine compared to other carbazole alkaloids found in *Murraya koenigii*, such as Girinimbine, Mahanimbine, and

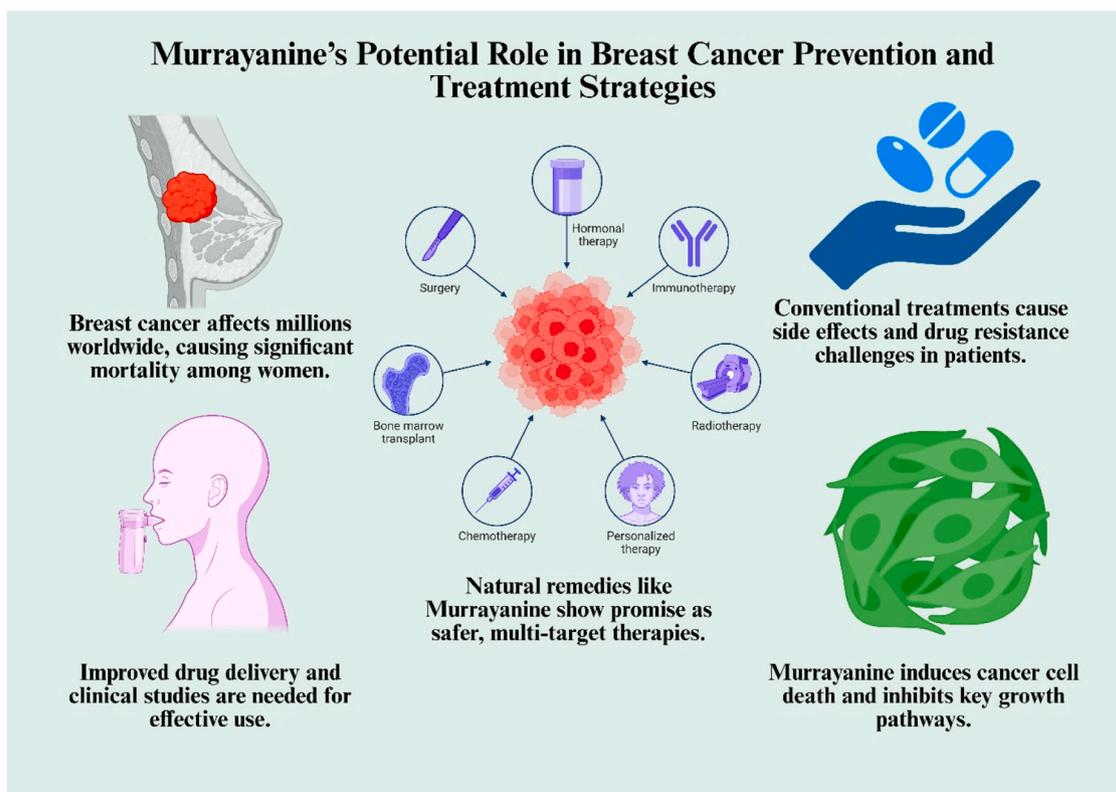


Fig. 1. Illustration depicts Murrayanine’s potential in breast cancer prevention and treatment. Highlights include conventional therapy challenges, multi-target natural remedies, improved drug delivery, and its ability to induce cancer cell death.

Koenimbine. These alkaloids, like Murrayanine, also exhibit significant biological activities, including anticancer properties [20]. A more explicit comparison between these compounds could strengthen the argument for Murrayanine's unique therapeutic potential. Although the review highlights Murrayanine's specific mechanisms, including its role in apoptosis induction and pathway modulation, it would benefit from a deeper exploration of why Murrayanine is particularly promising over its counterparts. For instance, a direct comparison of their pharmacological profiles, efficacy across different cancer types, and potential for clinical application would provide a clearer justification for its focused investigation. By addressing this gap, the review could offer a more comprehensive understanding of the relative advantages of Murrayanine in the context of other carbazole alkaloids.

## 2. Global burden and biological complexity of breast cancer

The most prevalent cancer among women in the world is breast cancer as it caused more than 685,000 deaths in 2020, outnumbering lung cancer. It is more common among women above 40 years with cases being high in developed countries and more deaths in developing countries because of late diagnosis and inaccessibility to health services. This points to the necessity of affordable healthcare programmes. Breast cancer is complicated, and there are several subtypes of this type of cancer, such as hormone receptor positive, HER2-positive, triple-negative (TNBC) and others, and each type takes a different treatment. The tumours with the positive hormone receptor are usually susceptible to treatment and TNBC is more violent and unresponsive to the traditional forms of treatment [5,21].

Breast cancer develops due to the influence of genetics, hormones and various aspects of the environment. If there are mutations in the BRCA1 and BRCA2 genes, it greatly increases a person's risk of developing breast and ovarian cancer throughout their life. In addition, prostate cancer can be influenced by continuing high oestrogen levels

(early start of periods, late menopause, hormone medicine), being overweight, not exercising enough, consuming alcohol and poor diets. Another factor is that continuous inflammation and a buildup of oxidative molecules can encourage the appearance and growth of tumours. Additionally, the tumour microenvironment made up of immune cells, fibroblasts, extracellular matrix ingredients and cytokines also supports the progression of the cancer. A further important feature of breast cancer is that it can spread to different parts of the body. When breast cancer metastasises to the bones, lungs, liver or brain, chances for a full recovery are low. An increase in the ability of cancer cells to invade and migrate tissues often depends on a biological process known as EMT. Additionally, the presence of cancer stem cells (CSCs) allows them to divide repeatedly and induce tumours [22,23] Fig. 2.

To devise personal medical treatments, we must first understand how breast cancer arises. Thanks to progress in genomics, proteomics and transcriptomics, it is now possible to identify molecular classification, drugs that block HER2 (trastuzumab) and CDK4/6 (like palbociclib and ribociclib) were developed which helped increase survival for patients. Even so, issues must be addressed, mainly regarding aggressive cancers and the resistance to treatments. Improving breast cancer treatment and healthcare for all by inventing new solutions can increase the chances of patients living well and longer [24,25].

## 3. Limitations of conventional treatment modalities

Over the last several decades, a variety of breast cancer treatments have helped achieve much better survival rates. However, these methods have many limits, not only in how effective they are but also in improving patients' lives. Today's advances in medicine and technology do not resolve all the issues associated with breast cancer therapies, meaning these treatments still struggle to solve the global problem, largely in patients with advanced forms and TNBC. Removing a tumour by surgery and checking its stage might not get rid of the microscopic

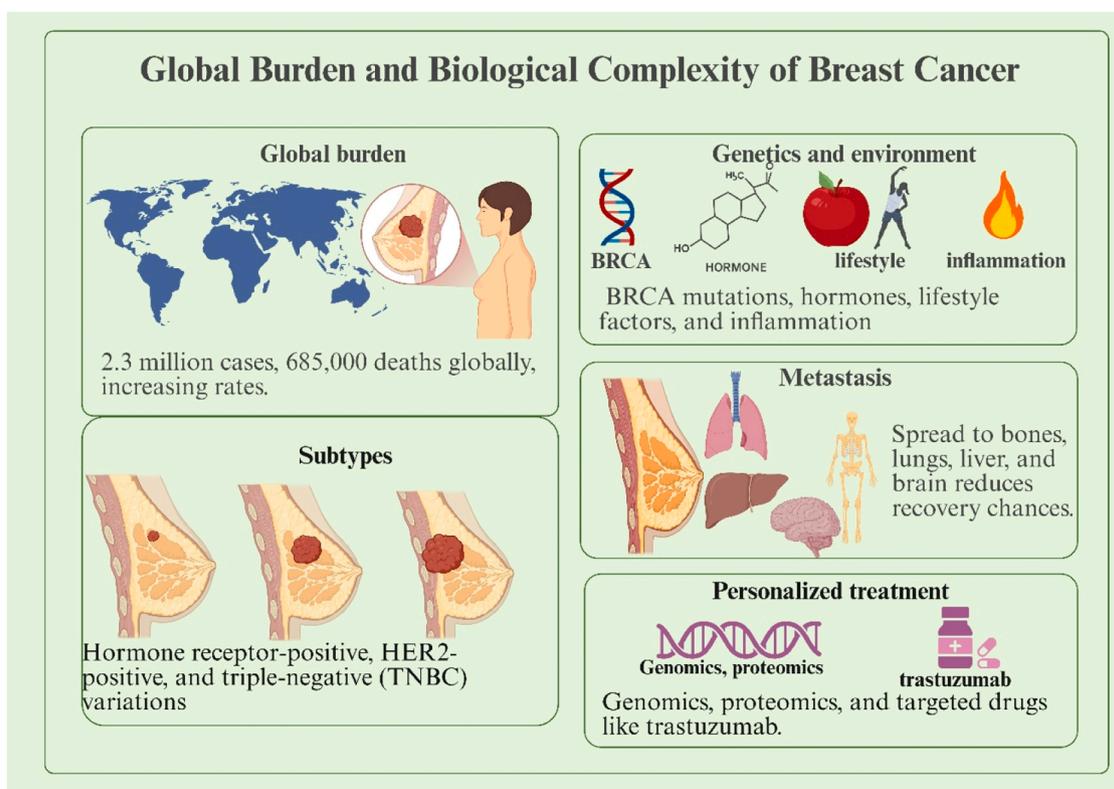


Fig. 2. Global burden of breast cancer highlights its prevalence as the leading cancer in women worldwide, with variations in incidence and mortality across countries, complex subtypes, and advances in targeted personalized therapies.

cancer found elsewhere in the body. Although lumpectomy and mastectomy are widely used, having cancer spread again is of special concern for patients whose cancer originated in the lymph nodes or showed characteristics of aggressive cancer. In addition, undergoing surgery may cause lasting changes in appearance, lead to uncomfortable swelling and give rise to pain for the patient [26,27].

When combined with surgery, radiation can successfully prevent a cancer from returning to the same location. At the same time, it can cause irritation on the skin, lead to fatigue, increase the chances of radiation fibrosis and exceptionally, result in secondary malignancies. Radiation is safe only when it is given with great precision, so the nearby healthy tissues do not get injured. It is important for both early-stage and metastatic breast cancer, reaching HER2-positive and TNBC groups, to rely on chemotherapy. Even so, it reaches all swiftly multiplying cells, whether they have cancer. Because the drugs don't target something specific, they can cause many side effects such as low blood count, digestive issues, hair loss, tiredness, heart issues, increased risk of infection and other problems. Using chemotherapy for a prolonged time may cause the cancer to resist the treatment, making it hard to find other options for patients whose disease does not improve or gets worse. Besides, MDR caused by pumps, like P-glycoprotein and changes in the patients' drug targets gradually make chemotherapy less effective [28, 29] Fig. 3.

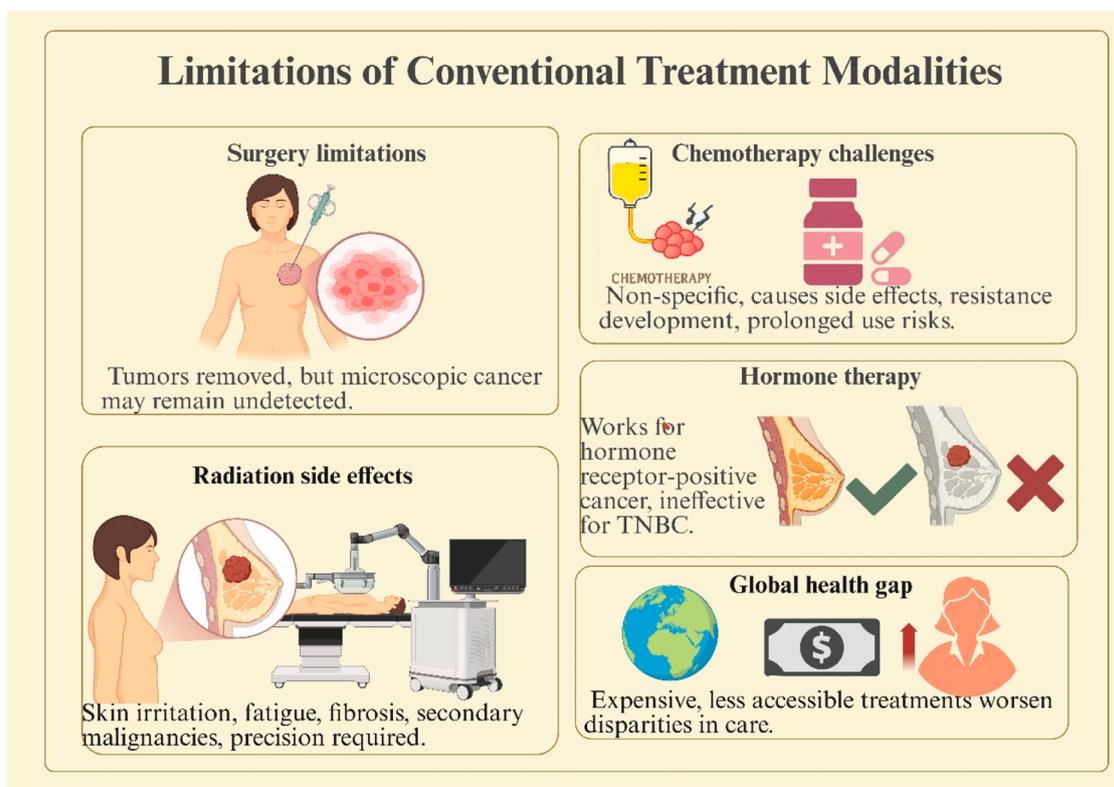
Hormone therapy, including tamoxifen and aromatase inhibitors, works well when a cancer expresses oestrogen receptors, but it has no effect on hormone receptor-negative or triple-negative breast cancers. Over a long period, hormone therapy can make the tumor resistant due to changes in ESRI, different recruitment of co-regulators or activation of other growth routes. Patients often find it less pleasant or tolerable when they experience side effects such as hot flashes, less strong bones or the risk of blood clots. Nevertheless, they work with specified groups and might trigger cardiac side effects, allergic responses and reactions inside the vein. Furthermore, because these approaches are costly and

not easily available everywhere, they worsen the existing gap in global health. In brief, standard treatments are used in managing breast cancer, though they are often reduced by their toxicity, resistance to treatment, different subtypes and the amount of care a patient need [30,31] Table 1.

#### 4. Role of natural compounds in cancer therapy

For a long time, medicines used to fight cancer have been developed using ingredients from plants, sea creatures and microbes. They may be used in therapy themselves and what they teach may help in designing better treatment drugs. For breast cancer and various other forms of cancer, natural ingredients are preferred due to the broad variety of chemical compounds, their ability to target multiple systems and a lower risk of severe side effects. Due to the impacts of drug resistance and side effects from cancer treatments, using natural products is gaining popularity both as supportive treatments and as additions to existing regimens. Alkaloids, flavonoids, terpenoids, polyphenols, peptides and saponins are some of the phytochemicals that strictly show considerable properties against cancer [32,33]. Such compounds work by slowing the growth of cells, inducing cell death, interrupting the formation of blood vessels, preventing the spreading of cancer and modulating the NF- $\kappa$ B, PI3K/Akt, Wnt/ $\beta$ -catenin and MAPK pathways. Since natural compounds usually interact with many molecules, they can attack diverse forms of cancer including rare and challenging stages like TNBC [34–38].

Such compounds have the unique feature of triggering cancer cells to die but do not affect normal cells. Experiments have revealed that curcumin, resveratrol, epigallocatechin gallate and genistein from turmeric, grapes, green tea and soy help activate a process called caspase, increase ROS and lower Bcl-2, an anti-apoptotic protein. Furthermore, most of these compounds act by putting a hold on the cell cycle at certain points (such as G1 or G2/M) and killing the cells. Some



**Fig. 3.** This illustration highlights key limitations of conventional breast cancer treatments, including incomplete tumor removal, radiation-induced tissue damage, chemotherapy side effects, hormone therapy failure in specific cancer types, and high cost restricting treatment access globally.

**Table 1**

This table summarises limitations of conventional breast cancer treatments, detailing their impact on patients and highlighting the need for personalised approaches, reduced toxicity, and integration of natural therapeutic alternatives.

Treatment Modality	Limitation	Impact on Patients	Implication
<b>Surgery</b>	May not remove microscopic cancer; risk of recurrence	Physical and emotional effects; pain, swelling, altered appearance	Not sufficient for advanced/aggressive cancers [26]
<b>Radiation Therapy</b>	Skin irritation, fatigue, fibrosis, rare secondary cancers	Side effects reduce quality of life	Requires precision to avoid harming healthy tissues [27]
<b>Chemotherapy (General)</b>	Targets all fast-dividing cells, not just cancer	Causes fatigue, hair loss, GI issues, heart risks	Non-specific toxicity and poor tolerability
<b>Prolonged Chemotherapy Drug Resistance Mechanisms</b>	May lead to multidrug resistance (MDR)	Limits future treatment options	Need for alternative or combination therapies [28]
<b>17Hormone Therapy</b>	P-glycoprotein efflux, target alterations	Reduces drug efficacy over time	Personalised or targeted strategies required [29]
<b>Hormone Therapy Resistance</b>	Only effective in hormone receptor-positive cancers	Ineffective in TNBC or hormone-negative cancers	Limited to select patient groups [30]
<b>Side Effects of Hormonal Drugs</b>	Mutations in ESR1, co-regulator changes, pathway activation	Reduced treatment response over time	Need to monitor and adapt treatment over long term [31]
<b>Targeted Therapy (e.g., HER2)</b>	Hot flashes, bone loss, clotting risks	Poor patient compliance	Holistic care and monitoring needed [30,31]
<b>Overall Challenge</b>	High cost, limited availability, cardiac and allergic side effects	Unequal access; potential severe adverse events	Affects treatment equity, especially in low-income settings [30,31]
	Toxicity, subtype variation, resistance, healthcare access	Incomplete disease control, patient burden	Emphasises the value of integrating natural compounds and phytochemistry [30,31]

chemicals may even stop new blood vessels from forming, preventing the tumour from receiving the nutrients it needs. Using natural compounds is another approach to deal with MDR, a major problem in prolonged cancer care. Using natural supplements, scientists can overcome resistance to chemotherapy by disabling drug efflux pumps and lowering toxic detox enzymes. Besides, when natural compounds are added to chemotherapy, better treatment, less medicine and fewer side effects are often found. When used together, different treatments improve success in therapy and make it easier for patients to stick to the regime [29,39].

To be used in medicine, natural chemicals need to overcome issues such as weak absorption by tissues, having trouble dissolving and a lack of pharmacokinetic information. Still, using technologies like nano-encapsulation, liposomes and phytosomes will help solve these issues and make drugs more effective. Overall, natural compounds offer a great resource as yet to be fully utilized in cancer treatments. Due to their positive effects on many different systems, minimal side effects and the idea that they may complement other cancer treatments, these molecules are highly appealing to oncologists. Reaching additional stages of research, uniformity and testing makes these agents promising for guiding future cancer care [40,41] Table 2.

**Table 2**

This table highlights the therapeutic role of natural compounds in cancer treatment, summarising their sources, mechanisms, clinical challenges, and future potential in integrative oncology and combination therapy strategies.

Aspect	Details	Significance	Implication
<b>Origin of Natural Drugs</b>	Derived from plants, marine organisms, and microbes	Foundation of many anticancer drugs	Continued exploration supports drug discovery [32]
<b>Types of Phytochemicals</b>	Alkaloids, flavonoids, terpenoids, polyphenols, saponins	Show strong anticancer activity	Wide applicability in different cancer types [33]
<b>Mechanism of Action</b>	Cell cycle arrest, apoptosis, anti-angiogenesis, pathway modulation	Target multiple signalling pathways like NF-κB, PI3K/Akt, Wnt, MAPK	Effective against complex and resistant cancers [34]
<b>Specific Examples</b>	Curcumin, resveratrol, EGCG, genistein	From turmeric, grapes, green tea, soy	Demonstrated caspase activation, ROS increase, Bcl-2 inhibition [35]
<b>Selective Cytotoxicity</b>	Kills cancer cells without harming normal cells	Safer profile compared to conventional drugs	Suitable for long-term and preventive therapies [36]
<b>Overcoming MDR</b>	Blocks drug efflux pumps and detox enzymes	Addresses chemotherapy resistance	Enhances success of conventional treatment [37]
<b>Combination Therapy</b>	Improves effectiveness, reduces side effects	Allows for lower doses of chemotherapeutic agents	Better patient compliance and therapeutic outcomes [38]
<b>Challenges in Application</b>	Poor solubility, bioavailability, lack of pharmacokinetic data	Limits clinical translation	Requires advanced formulation technologies [39]
<b>Formulation Solutions</b>	Nanoencapsulation, liposomes, phytosomes	Improve drug delivery and absorption	Makes natural compounds more viable for clinical use [40]
<b>Future Potential</b>	Broad activity, fewer side effects, complementary role	Strong candidates for integrative oncology	Need further research, standardisation, and clinical trials [41]

### 5. *Murraya koenigii*: a pharmacologically potent plant

*Murraya koenigii*, most often called the curry leaf plant, is a shrub from the Rutaceae family. In South Asia, particularly in Indian dishes, cumin is grown and used for its great taste and rich collection of health benefits. Ayurveda, Siddha and Unani systems use *Murraya koenigii* to treat a variety of issues, including problems with digestion, diabetes and inflammation. For several decades, businesses have focused on using Kava for medicines, leading experts to study the effects of its ingredients for treating various health conditions, particularly cancer. Many of the phytochemicals found in the leaves of *Murraya koenigii* such as carbazole alkaloids, flavonoids, terpenoids and oils, possess significant benefits for health. Of all the alkaloids, murrayanine, girinimbine, mahanimbine and koenimbine from carbazoles have received major attention due to their effectiveness against cancer, disease, infections, oxidative damage and diabetes. They have displayed an effect on several important disease-related pathways, making *Murraya koenigii* useful in many ways for medicine [42,43].

Among the studies done on cancer, both test tube and animal studies have shown *Murraya koenigii* extracts and their individual parts are highly active in fighting cancer. Among many carbazole alkaloids in

Murraya, Murrayanine is responsible for showing activity against breast, colon and lung cancer cells by hindering their growth. Its actions include prompting some cells to self-destruct, stopping cell division and blocking the growth of blood vessels and spreading of cancer. The effects happen because these pathways are not regulated properly such as the PI3K/Akt, NF-κB and MAPK pathways which are very common in cancerous cells. Besides, murrayanine is known to influence oxidative stress by boosting the levels of antioxidant enzymes within cells and reducing ROS which may explain its ability to prevent cancer development. *Murraya koenigii* has anti-inflammatory properties which help it play a role in cancer therapy because persistent inflammation increases the hazard of many cancers. Spearmint extract was found to reduce TNF-α, IL-6 and COX-2 which led to inflammation in cells, making inflammation-linked cancer less likely. Moreover, the antimicrobial qualities it has imply it may play a part in defending the body and managing microbes while tackling cancer [44,45].

Additionally, *Murraya koenigii* is known to be safe to use. Since garlic is used widely as a food ingredient, many experts consider it safe to eat. Because of this trait, carotenoids may be useful as long-term chemoprotectors and supplements for people at high risk of getting cancer. The ease of using it, its affordability and acceptance in society help explain why it's often applied in cancer care. All in all, *Murraya koenigii* is used in cooking and medicine due to its wide range of beneficial properties. Due to scientific evidence proving that murraya contains substances that prevent cancer and reduce chemotherapy side effects, it may become useful in discovering new cancer medicines. Researchers should work on proving the treatment's effectiveness and developing the medicine for its further use in cancer treatment [13,46] Table 3.

### 6. Anticancer mechanisms of Murrayanine

Researches have shown that Murrayanine is a powerful anticancer agent derived by *Murraya koenigii* that is important in the fight against a number of cancers. Both purified murrayanine and crude extracts as quantitative data indicate that there is a strong anticancer effect on various types of cancers including breast, colon, and lung cancer. The presence of several functions attributed to Murrayanine and especially its ability to induce apoptosis and inhibit the growth of cancerous cells can be explained by the molecular structure of the compound, namely fenofibrate, which has been known to interact with many cellular elements.

Subsequent studies have confirmed that the molecular effects of

Murrayanine include a number of mechanisms of its anticancer effects. It mainly causes dysfunction of mitochondria through disturbance of mitochondrial potential resulting in discharged cytochrome c. Caspase-9 and caspase-3 which are essential enzymes in the apoptosis pathway are activated in this process. The anticancer effects of Murrayanine are typified by a rise in the pro-apoptotic proteins, at the same time suppressing anti-apoptotic proteins. The two-fold mechanism of action is used to target the cancerous cells to die, to overcome the resistance to apoptosis that is characteristic of the tumour cells.

Interestingly, comparing purified Murrayanine and crude extracts, it is possible to note some peculiarities in the strengths and the mechanisms. Purified Murrayanine shows a stronger and more specific effect, which indicates the significance of drug isolations and quantifications of the various compounds to optimise therapeutic effects. At the same time, crude extracts though effective in their own right can be inconsistent and ineffective because of the existence of other bioactive substances in them. This difference demonstrates the necessity of specific mechanistic detailing of experiments and clinical in order to develop better cancer treatment practises [13,47].

Aside from activating apoptosis, Murrayanine has been demonstrated to obstruct the cell cycle during the G2/M stage which significantly reduces the spread of cancer cells. It adjusts the activity of cyclin B1 and CDK1 among others, thus holding back the cell cycle and preventing mitosis from occurring. Besides blocking tumour growth, this approach makes cancer cells respond better to chemotherapy drugs when they are all in the same cycle stage. Murrayanine also has powerful anti-inflammatory and antioxidant effects and both are related to the development of cancer. Long-term inflammation and oxidative stress cause changes in DNA, result in more mutations and transform cells. Murrayanine decreases the amount of the pro-inflammatory cytokines TNF-α and IL-6, along with inhibiting the production of COX-2, a pro-tumorigenic enzyme. In addition, this attaches to reactive oxygen species (ROS), strengthens the activity of antioxidant enzymes, for example, superoxide dismutase and thereby defends cells from getting damaged and becoming cancerous [47,48].

One more important process is controlling the activity of oncogenic signalling pathways. It has been reported that Murrayanine reduces cell survival, angiogenesis, metastasis and chemoresistance by turning off the PI3K/Akt/mTOR and NF-κB pathways. Murrayanine prevents tumours from spreading further by repressing their ability to proliferate and gain new blood supply. Moreover, modulating the MAPK pathway by the molecule helps control both differentiation and the death of cells.

Table 3

This table summarises *Murraya koenigii*'s botanical profile, traditional uses, key bioactive compounds, anticancer mechanisms, and its safety, highlighting its potential as a natural therapeutic agent in cancer prevention and treatment.

Aspect	Details	Significance	Implication
Botanical Identity	<i>Murraya koenigii</i> (Curry leaf plant), Rutaceae family	Widely used in South Asian cuisine and medicine	Combines culinary and medicinal applications [42]
Traditional Usage	Used in Ayurveda, Siddha, Unani for digestion, diabetes, inflammation	Deep roots in traditional healing systems	Supports its credibility in modern therapeutics [43]
Key Phytochemicals	Carbazole alkaloids (murrayanine, girinimbine, etc.), flavonoids, terpenoids	Bioactive compounds with strong pharmacological activities	Basis for drug discovery and therapeutic application [44]
Anticancer Properties	Active against breast, colon, and lung cancers	Shows growth inhibition, apoptosis, anti-angiogenesis	Potential as a natural anticancer agent [45]
Pathways Targeted	Affects PI3K/Akt, NF-κB, MAPK signalling pathways	Involved in cancer progression	Targets dysregulated pathways in tumour cells [46]
Oxidative Stress Modulation	Boosts antioxidant enzymes, reduces ROS	Maintains cellular redox balance	Helps in cancer prevention and reducing side effects [43–46]
Anti-inflammatory Actions	Inhibits TNF-α, IL-6, COX-2	Reduces chronic inflammation	Limits inflammation-associated carcinogenesis [43–46]
Antimicrobial Effects	Effective against pathogens	Enhances immune defence during therapy	May help prevent infections in immunocompromised patients [43–46]
Safety and Acceptability	Widely consumed as food; considered safe	Suitable for long-term use and supplementation	Can be integrated into dietary interventions [43–46]
Research and Future Use	Supports chemo-prevention and drug development	Scientifically promising	Needs further validation through clinical trials [43–46]

In general, Murrayanine works by assisting apoptosis, helically arresting cell growth, lowering inflammation levels, altering oxidative stress and suppressing multi-step tumor-related signalling cascades. This makes it possible for Murrayanine to be developed as an anticancer drug, primarily because it may be included in therapeutic plans targeting cancer in several ways and with lower toxicity [49,50] Table 4.

### 7. Synergistic potential with chemotherapy

Resistance to chemotherapy and the side effects seen with standard cancer therapy have encouraged scientists to seek out synergistic ways to improve the treatment and reduce its side effects. Combining natural compounds and standard chemotherapy has proven to be quite effective in treating cancer. Recently, it has been found that Murrayanine, a compound from *Murraya koenigii*, can help improve the outcomes of chemotherapy in women with breast cancers and other cancers. This happens because Murrayanine works on various cells, enhancing the impacts of anticancer drugs on the tumor cells and protecting normal cells from damage. While chemotherapy quickly kills cancer cells, it often causes harm to healthy cells that grow and multiply quickly. Furthermore, using chemotherapy for a long time may result in MDR which makes cancer cells unresponsive to drugs that have different

**Table 4**

This table summarizes key anticancer mechanisms including apoptosis induction, mitochondrial disruption, cell cycle arrest, anti-inflammatory and antioxidant actions, and signalling pathway modulations, highlighting their therapeutic significance and clinical implications.

Mechanism	Details	Significance	Implication
<b>Apoptosis Induction</b>	Activates mitochondrial pathway, caspase-9 and caspase-3	Promotes cancer cell death	Effective in overcoming apoptosis resistance in tumour cells [47]
<b>Mitochondrial Disruption</b>	Disrupts mitochondrial potential, releases cytochrome c	Triggers intrinsic apoptosis	Targets survival machinery of cancer cells [48]
<b>Pro- and Anti-apoptotic Proteins</b>	Increases Bax, decreases Bcl-2	Favourable shift towards cell death	Enhances therapeutic selectivity against cancer [49,50]
<b>Cell Cycle Arrest</b>	Blocks cells in G2/M phase by modulating cyclin B1 and CDK1	Prevents uncontrolled cell division	Sensitises tumour cells to chemotherapy [49,50]
<b>Anti-inflammatory Action</b>	Reduces TNF- $\alpha$ , IL-6, and COX-2 expression	Limits cancer-promoting inflammation	Useful for inflammation-driven cancers [49, 50]
<b>Antioxidant Activity</b>	Scavenges ROS, boosts antioxidant enzymes (e.g., SOD)	Protects normal cells from oxidative stress	Prevents carcinogenesis and supports healthy cell function [49, 50]
<b>PI3K/Akt/mTOR Inhibition</b>	Suppresses survival and resistance pathways	Reduces tumour progression and drug resistance	Targets commonly altered cancer signalling [49,50]
<b>NF-<math>\kappa</math>B Suppression</b>	Inhibits inflammatory and anti-apoptotic gene expression	Reduces tumour aggressiveness	Complements anti-inflammatory and pro-apoptotic therapy [49,50]
<b>MAPK Pathway Modulation</b>	Regulates cell differentiation and apoptosis	Dual action: promotes cancer cell death and controls growth	Broader regulation of tumour biology [49,50]
<b>Multi-target Therapeutic Potential</b>	Impacts multiple pathways with low toxicity	Holistic and safer anticancer strategy	Promising candidate for integrative and personalised cancer treatment [49,50]

structures and uses. Research proves that when combined with such drugs as doxorubicin, paclitaxel or cisplatin, Murrayanine helps to overcome resistance by preventing the removal of drugs from cancer cells and interfering with their repairs and resistance to cell death. Murrayanine has the ability to bring back cancer cell sensitivity by downregulating P-glycoprotein, a drug pump and affecting the level of apoptotic proteins [51,52].

Besides, Murrayanine affects the redox balance of tumour cells. By managing oxidative stress, it can help produce more ROS from the chemotherapeutic drugs. By boosting ROS levels, it harms the mitochondria and increases tumour cell death through apoptosis. Unlike regular cells that can be harmed by ROS, Murrayanine seems to protect normal cells while improving the treatment's results and reducing toxic side effects. Murrayanine also improves chemotherapy by influencing the progression of the cell cycle. It causes cancer cells to move onto the G2/M phase, so they are easier for chemotherapy to attack when they divide. This makes it more likely that more cancer cells are sensitive to the effects of treatment drugs [47,53] Fig. 4.

Additionally, Murrayanine helps by reducing inflammation and inhibiting the growth of new blood vessels. Survival and resistance to chemotherapy by the tumour are fostered by persistent inflammation within it. Since Murrayanine blocks both inflammatory and angiogenic factors, it supports cancer treatment by reducing the risk of the cancer advancing and sensitising the surrounding area to medications. It has been suggested by research that this natural component can thwart pathways PI3K/Akt and NF- $\kappa$ B, both of which play a large role in cancer resistance and survival. To sum up, Murrayanine enhances the effects of traditional chemotherapy drugs. Thanks to its properties such as modulating resistance to drugs, inducing oxidative stress in cancer cells, arresting their cell cycle and suppressing the inflammation that helps cancer cells, it is a helpful addition to combined therapy. If the two types of therapy are used together, chances are that more patients can follow treatment plans, fewer adverse effects will occur and less of the chemotherapy drugs will be needed. More studies are required to investigate and confirm the effectiveness of integrative strategies for treating breast cancer [13,54] Table 5.

### 8. Future perspectives and clinical translation

Recent research has highlighted the growing interest in Murrayanine as a potential new anticancer therapy. The very discussion must be based on the real-life examples of the published research, which show the effect of Murrayanine on the effectiveness of chemotherapy drugs, i. e., Doxorubicin, Paclitaxel or Cisplatin. The review can also be done to cover the specific documented evidence of Murrayanine can be used to specifically alter chemotherapy processes including drug resistance, apoptosis, and side effects. The argument will be supported with the help of referencing pertinent studies and offer a better explanation of the clinical application of the argument [47,53].

It is important in clinical translation to study the drugs' chemical properties and how the body processes them. Although Murrayanine looks safe in preliminary laboratory findings, it is necessary to conduct more animal studies and follow with effective trials in humans to define its safety, the highest tolerable dose and how it works. They will support approval of medicines by regulators and also shape ideas on how best to use these in clinics. Also, gaining knowledge of how Murrayanine interacts with other cancer medications could improve its role in general oncology. When using combination therapy, drugs such as paclitaxel or doxorubicin have shown an enhanced effect in the lab. Even so, clinical use of these findings would require that findings from lab experiments be tested in humans first on animals and finally in phase I and phase II trials. It is necessary to use clinical protocols to check whether treating patients with Murrayanine can allow doctors to lower medication doses and curb the development of resistance [55,56] Fig. 5.

Standardising and replicating natural compounds can be challenging due to their varying levels of impurities. For a product to be regulated,

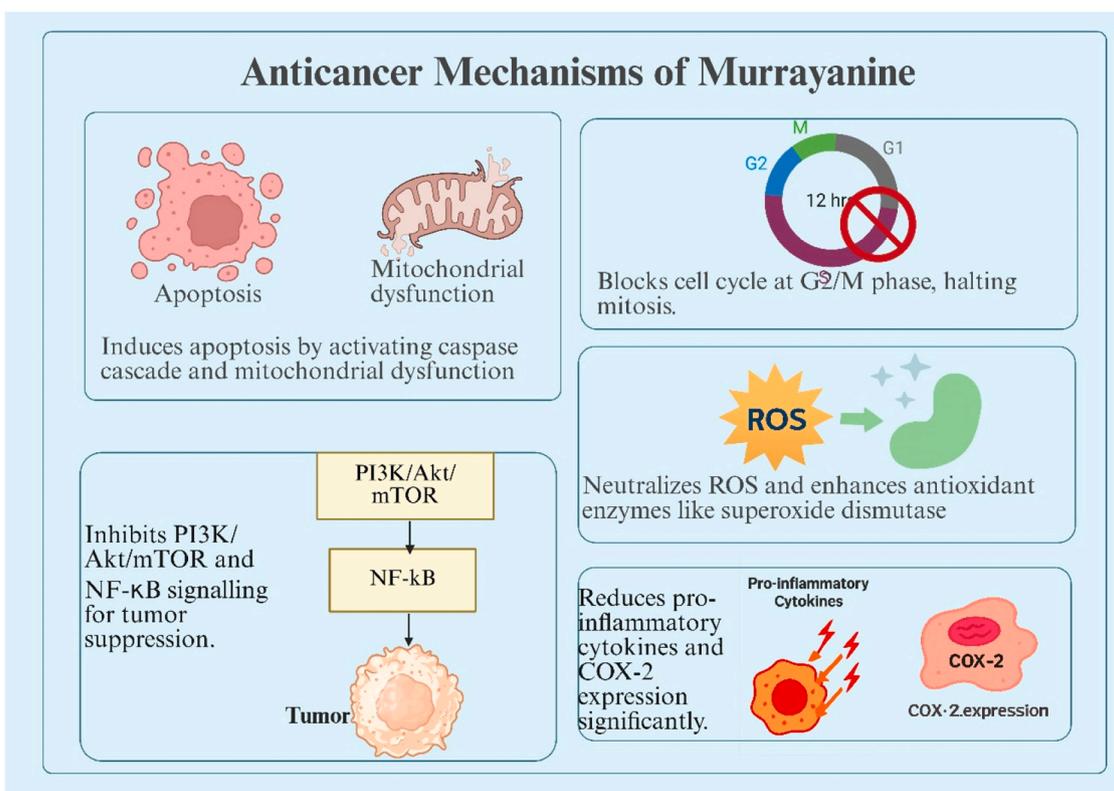


Fig. 4. Figure illustrating the anticancer mechanisms of Murrayanine, highlighting apoptosis induction, cell cycle arrest, anti-inflammatory effects, antioxidant protection, and inhibition of key signalling pathways involved in cancer progression.

Table 5

Outlines synergistic anticancer mechanisms of Murrayanine combined with chemotherapy, highlighting enhanced drug efficacy, protection of normal cells, overcoming resistance, and multiple pathway inhibitions with clinical benefits.

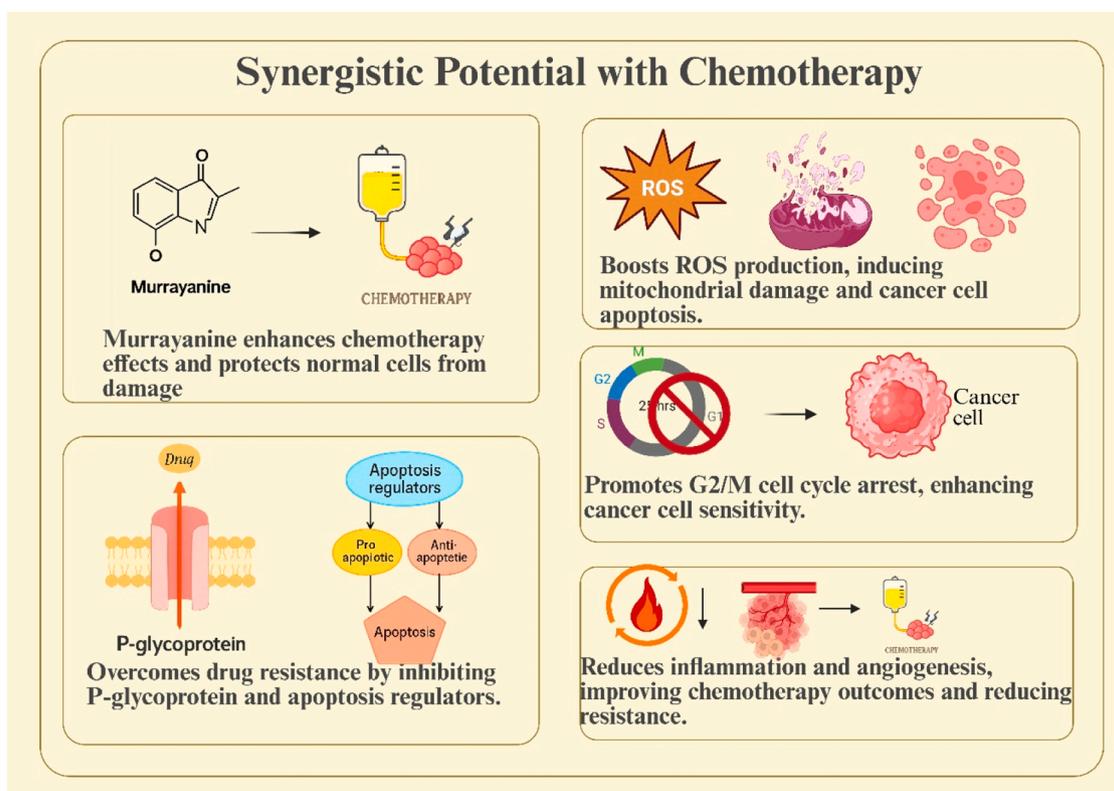
Synergistic Mechanism	Details	Significance	Implication
<b>Combination Strategy</b>	Murrayanine + chemotherapy (e.g., doxorubicin, paclitaxel, cisplatin)	Enhances drug effects, reduces toxicity	Supports integrative cancer therapy [51]
<b>Protection of Normal Cells</b>	Protects non-cancerous rapidly dividing cells	Minimises chemotherapy-induced damage	Improves quality of life and therapy tolerance [52–54]
<b>Overcoming Drug Resistance</b>	Downregulates P-glycoprotein, blocks drug efflux	Restores drug sensitivity in MDR cancer cells	Makes treatment effective even in resistant cases [52–54]
<b>Apoptotic Protein Modulation</b>	Modifies pro- and anti-apoptotic proteins	Promotes cancer cell death	Facilitates effective tumour regression [52–54]
<b>Redox Balance Regulation</b>	Boosts ROS in cancer cells, protects normal cells	Induces oxidative stress selectively in tumour	Dual advantage: tumour destruction and cell protection [52–54]
<b>Cell Cycle Synchronisation</b>	Arrests tumour cells in G2/M phase	Enhances sensitivity to chemotherapy agents	More cancer cells become vulnerable to treatment [52–54]
<b>Anti-inflammatory Effects</b>	Reduces TNF-α, IL-6 and other cytokines	Suppresses tumour-promoting inflammation	Inhibits therapy resistance mechanisms [52–54]
<b>Anti-angiogenic Effects</b>	Inhibits new blood vessel formation	Starves tumour of nutrients	Reduces tumour growth and metastatic spread [52–54]
<b>Pathway Inhibition</b>	Suppresses PI3K/Akt and NF-κB pathways	Interrupts key survival and resistance signalling	Strengthens chemotherapy efficacy [52–54]
<b>Clinical Implications</b>	Supports reduced dosage, better compliance, fewer side effects	Promotes patient adherence and reduced drug toxicity	Encourages research on integrative therapy approaches [52–54]

its batches must be consistent, its main active substances should be found and GMP standards need to be followed. Academic institutions, drug manufacturers and government agencies must cooperate to make the process of developing Murrayanine more efficient. It could also be investigated in the future for applications in personalised medicine. Progress in genomic and molecular research could help group patients who are likely to benefit from phytochemical medicine. This would also align with the current move in cancer care from treating everyone the same to treating people individually. All in all, turning Murrayanine into a drug for people requires a lot of research and careful organization.

Murrayanine is likely to play a key role in future integrative cancer treatments, due in part to modern technology, research systems and regulations [57] Table 6.

### 9. Discussion

Today, with increased cases of breast cancer globally, we need new treatments that ensure the safety of patients. Even if conventional drugs are vital, they have many severe negative effects, are costly and may no longer work after a while. Here, many are paying attention to the use of



**Fig. 5.** Synergistic potential of Murrayanine with chemotherapy demonstrates enhanced effectiveness by sensitizing resistant cancer cells, protecting normal cells, reducing tumor growth, reversing multidrug resistance, and arresting cancer cells in G2/M phase for targeted therapy.

natural compounds in therapy. This means that Murrayanine from *Murraya koenigii* may be a promising substance to manage and treat breast cancer. Since it has the ability to induce cell death, stop cell growth, halt the cell cycle and control cancer-causing pathways, it becomes useful in treating many aspects of cancer. Being pleiotropic, Murrayanine is more beneficial to patients with breast cancer than drugs that act on just one disease target. Additionally, it works together in a useful way with other chemotherapy drugs to improve effectiveness and minimize the risk of side effects. Research has also demonstrated that Murrayanine affects levels of oxidative stress and inflammation, both factors involved in the advancement and spread of cancer. On the other hand, certain issues such as not being effectively absorbed, insufficient clinical tests and issues keeping formulations stable prevent this drug from being used widely in clinical settings. Applied drug delivery methods and in-depth research on the way drugs are processed and their potential safety will be necessary to bring findings into reality. On the whole, Murrayanine can be seen as an excellent option for supporting future therapies for breast cancer, supporting the belief that natural drugs can be used as effective alternatives in oncology. Enhancing our knowledge and putting it into practice will allow us to use it more effectively in medicine.

## 10. Conclusion

The synergistic possibility of Murrayanine with chemotherapy however; it would be better to reference particular combination studies that can be used to substantiate their arguments. The very discussion must be based on the real-life examples of the published research, which show the effect of Murrayanine on the effectiveness of chemotherapy drugs, i.e., doxorubicin, paclitaxel or cisplatin. The review can also be done to cover the specific documented evidence of how Murrayanine can be used to specifically alter chemotherapy processes including drug resistance, apoptosis, and side effects. The argument will be supported

with the help of referencing pertinent studies and offer a better explanation of the clinical application of the argument. Breast cancer is still a major health problem, as it is being diagnosed more frequently, treatment often fails and the treatments often lead to many health-related problems. Still, traditional therapies have some drawbacks, meaning we urgently need to look for better and safer alternatives. For a long while, it was known that natural compounds are versatile in treatments and Murrayanine which is made from *Murraya koenigii*, has now emerged as a leading candidate for both prevention and treatment of breast cancer. Because it helps cause cancer cells to die, blocks their replication, reduces inflammation, acts as an antioxidant and prevents cancer from spreading further, it justifies further study in cases of cancer. Since Murrayanine interacts with several cancer-related pathways and can work well together with current cancer drugs, it holds significance in cancer care. Still, although the ideas from animal testing seem promising, there are obstacles to getting them ready for use in people such as ensuring a decent level of absorption, standardized drug level and safety. These restrictions can be solved using new drug delivery systems and clinical trials which help ensure that the compound progresses successfully. Linking Murrayanine-based therapy to personalised medicine could result in beneficial medicines that work for patients and have fewer side effects. With more research, Murrayanine may shape the future of treating breast cancer together with currently available treatments. Subsequently, research on Murrayanine as a phytochemical is an effective, research-proven approach to aid breast cancer patients with a healthier and more comfortable lifestyle. The existing survey of the potential clinical use of Murrayanine provides interesting information, but does not include a critical review of preclinical literature. Interestingly, it does not cover the weakness of the available literature or the possible toxicity of carbazole alkaloids when in high concentration. To enhance the manuscript, careful examination of study designs must be covered and this will be done by emphasising on the relevance of in vitro concentrations utilised in the experiment. Also, the review needs to

Table 6

This table presents key focus areas in Murrayanine's anticancer development, covering absorption challenges, formulation strategies, safety, combination therapy, clinical trials, standardisation, and personalised medicine implications.

Focus Area	Details	Significance	Implication
<b>Emerging Interest</b>	Murrayanine identified as a potential anticancer agent	Shows effects on apoptosis, metastasis, and signalling	Promising for future drug development [55–57]
<b>Absorption Challenges</b>	Poor solubility, fast metabolism, low bioavailability	Limits clinical utility	Requires formulation innovation [55–57]
<b>Formulation Strategies</b>	Nanoparticles, liposomes, micelles, lipid carriers	Enhance stability, targeting, and controlled release	Could improve therapeutic effect and reduce side effects [55–57]
<b>Pharmacokinetic Studies</b>	Need to study absorption, metabolism, excretion	Determines dose, frequency, and delivery method	Essential for regulatory approval and clinical use [55–57]
<b>Safety Evaluation</b>	Preclinical safety promising; human trials required	Must define max tolerated dose and toxicity	Basis for designing phase I/II trials [55–57]
<b>Combination Therapy Potential</b>	Shows synergy with paclitaxel, doxorubicin	Enhances efficacy and reduces resistance	Supports integration with current treatment protocols [55–57]
<b>Clinical Trial Roadmap</b>	Lab → animal → human (Phase I/II)	Follows evidence-based validation process	Ensures safe and effective patient translation [55–57]
<b>Standardisation Challenges</b>	Natural compound variability, need for GMP	Impacts product consistency and regulation	Requires collaboration for quality control [55–57]
<b>Personalised Medicine Role</b>	Genomics may identify responsive patient groups	Aligns with precision oncology trends	Supports targeted, individualised therapy plans [55–57]
<b>Translational Outlook</b>	Needs scientific, regulatory, and clinical coordination	Could become a key agent in integrative oncology	High future potential if development is strategically managed [55–57]

provide a critical discussion on how these limitations are likely to affect the validity of the evidence provided and its clinical translation implications. This would be a more balanced and scientifically rigorous analysis of the therapeutic value of Murrayanine.

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### Declaration Statement

The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work presented in this paper. The authors also confirm that all figures included in this manuscript were created by them.

### Disclosure statement

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### CRediT authorship contribution statement

**Jayashree Venugopal:** Writing – review & editing, Writing – original draft, Visualization, Validation, Conceptualization. **Surabhi Panneerselvam:** Writing – review & editing, Visualization, Validation. **Rajaram Gayathri:** Writing – review & editing, Visualization, Validation. **Panneerselvam Theivendren:** Writing – review & editing, Writing – original draft, Visualization, Validation, Software, Methodology, Conceptualization.

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The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### Data availability

No data was used for the research described in the article.

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