



NATURAL PRODUCTS AS SOURCES OF ANTICANCER AGENTS: MOLECULAR TARGETS AND THERAPEUTIC POTENTIAL

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ABSTRACT

Natural products represent an important source of structurally diverse bioactive compounds with significant potential in cancer prevention, drug discovery, and therapy. This review synthesizes current evidence on natural products with anticancer activity, focusing on their biological sources, molecular targets, mechanisms of action, therapeutic potential, and challenges related to clinical translation. Relevant scholarly literature was identified from peer-reviewed sources and organized thematically according to natural-product sources, molecular pathways, anticancer mechanisms, therapeutic applications, translational barriers, and emerging research trends. The findings indicate that medicinal plants are the most extensively investigated sources, while marine organisms, microalgae, microorganisms, and other biological materials also contribute promising anticancer compounds. Major classes include polyphenols, flavonoids, alkaloids, terpenoids, phenolic acids, quinones, and sesquiterpenes. These compounds influence important cancer-related pathways such as PI3K/Akt/mTOR, MAPK/ERK, NF- κ B, JAK/STAT, Wnt/ β -catenin, p53, apoptosis-related proteins, angiogenic regulators, and telomerase. Their major biological effects include induction of apoptosis, cell-cycle arrest, modulation of oxidative stress, inhibition of angiogenesis, and suppression of invasion and metastasis. Natural products also show potential as adjuncts to conventional cancer therapies. However, poor solubility, low bioavailability, rapid metabolism, source variability, safety concerns, and limited clinical evidence continue to restrict translation into routine treatment. Overall, natural products remain promising candidates for the development of more effective and mechanistically informed anticancer therapies.

Keywords: Natural products, Anticancer agents, Molecular targets, Cancer therapy, Therapeutic potential



1. Introduction

Cancer continues to be one of the most complex diseases, with uncontrolled growth of cells, genetic instability, abnormal cell signaling, resistance to cell death and the ability to spread to other tissues. Chemotherapy, radiotherapy and targeted therapy have revolutionised cancer management; however, these agents are often limited by toxicity, resistance of the cancer to therapy, recurrence and variable response. These restrictions have spurred interest in the use of natural products as alternative or additional sources of anticancer drugs. Natural products from plants and marine sources have demonstrated the capacity to act as inhibitors of key pathways in cancer cells and are thus considered important candidates in the search for new anticancer drugs (Lichota & Gwozdziński, 2018). Natural products have played an important role in the development of pharmaceuticals and continue to serve as valuable chemical scaffolds in modern anticancer therapy. They can interact with several targets in biology, which can be helpful in direct drug use or in creating modified drug candidates. The medicinal plants are among the most widely examined ones as they are rich in a variety of secondary metabolites that exhibit cytotoxic, antiproliferative, antioxidant, anti-inflammatory and apoptosis-inducing activity (Gezici & Şekeroğlu, 2019). Due to their wide biological activities and pharmacological significance, natural bioactive compounds have also played a significant role in the discovery of anticancer drugs (Asma et al., 2022).

Terrestrial plants are not the only sources of natural anticancer compounds. Marine organisms offer structurally unique metabolites that may be available as new opportunities in cancer. For instance, marine sponges are a source of secondary metabolites that have significant anticancer activity and are hence important sources of novel therapeutic candidates (Calcabrini et al., 2017). Microalgae also generate biologically active metabolites, which could have pharmaceutical applications, thus increasing the diversity of natural compounds available for drug research (Khavari et al., 2021). Other molecules encountered in the natural world, like lectins, have also been studied for their anticancer activity, based on their effects on cancer-cell survival and molecular signaling (Huldani et al., 2022). Among the important classes of chemical compounds with anticancer activity are polyphenols, flavonoids, alkaloids, terpenoids, phenolic acids, quinones and sesquiterpenes. Phenolic acids have shown promise in cancer therapy, affecting mechanisms such as proliferation, apoptosis, oxidative stress, and others (Abotaleb et al., 2020). Other phenolic compounds from medicinal plants have been linked with therapeutic and health-promoting properties as well (Sun & Shahrajabian, 2023). Another large group of compounds with reported anticancer activity are terpenoids, which exhibit growth inhibition, apoptosis induction, and intracellular signalling pathway modulation (Kamran et al., 2022).

A key property of natural anticancer compounds is their activity against several molecular targets. There are a multitude of interconnected signaling systems which regulate cancer progression. Natural compounds can affect PI3K/Akt/mTOR, MAPK, NF- κ B, JAK/STAT, Wnt/ β -catenin, p53, Bcl-2 family proteins, caspases, cyclins and other regulatory mechanisms. Such interactions may have an impact on proliferation, survival, apoptosis, angiogenesis, inflammation and metastasis. Thus, the knowledge of these molecular targets is crucial to provide an explanation of the anticancer activity of natural compounds and to identify those with the highest therapeutic potential (Kubczak et al., 2021). Natural products can also augment traditional cancer treatments. Enhancing treatment sensitivity and mechanisms involved in therapeutic resistance have been demonstrated with some compounds, thus potentially using them as adjuvants (Lin et al., 2020). Some of the plant-based products could also have antiproliferative, antioxidant and anti-inflammatory properties that play a role in cancer prevention and chemoprevention, as has been reported for bioactive constituents of *Mangifera indica* (Mirza et al., 2021).

Clinical translation is still difficult, even though they show promise. Limits are related to poor bioavailability, low solubility, rapid metabolism, variable pharmacokinetics, lack of standardization, potential toxicity and insufficient clinical evidence. These barriers necessitate careful pharmacological, toxicological and clinical evaluation. The aim of this review is to consolidate



current evidence regarding natural products with anticancer activity and to discuss their biological sources, molecular targets, modes of action, therapeutic potential, and difficulties related to clinical translation.

2. Methodology

This study is designed as a comprehensive review that can be used to gain an overall understanding of the findings from various scientific studies regarding natural products used as sources of anticancer agents, with special focus on the molecular targets and therapeutic potential of such products. The literature was identified from peer-reviewed journals, academic books and reputable peer-reviewed sources from the Google Scholar, DOAJ, Web of Science and ScienceDirect databases. The review only included empirical research and relevant review articles pertaining to natural anticancer compounds, and did not include non-scientific publications or those not related to cancer therapy. A structured keyword strategy was used with various combinations of the following terms: natural products, anticancer agents, plant-derived compounds, marine natural products, molecular targets, apoptosis, cancer signaling pathways, therapeutic potential and drug resistance. The retrieved records were screened according to title and abstract, and then the full text was assessed for relevance. Eligible studies were subsequently grouped into themes based on natural-product sources, molecular targets, anticancer mechanisms, therapeutic applications, clinical translation challenges, and trends. The chosen evidence was compared and combined to look for trends, therapeutic possibilities and research gaps. The literature review process, from identifying the literature to screening and thematic classification to synthesis of the literature, is shown in Figure 1.

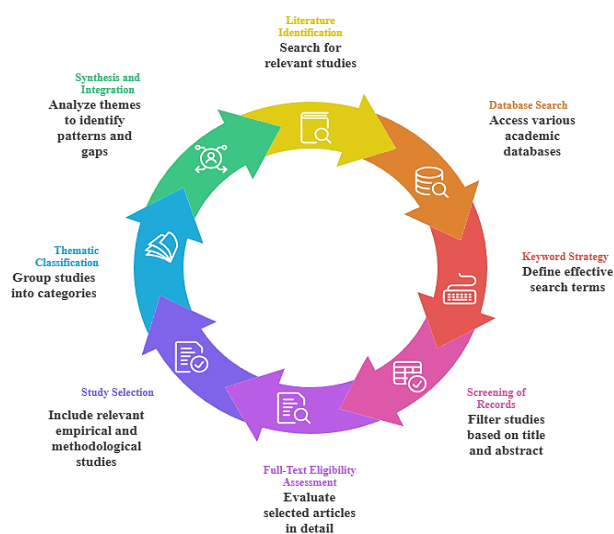


Figure 1. Overview of the Comprehensive Review Process

3. Results

3.1 Major Sources and Classes of Natural Anticancer Agents

Natural anticancer agents are derived from a variety of sources including medicinal plants, marine organisms, microorganisms and algae. The most studied ones are those derived from plants, such as polyphenols, flavonoids, alkaloids, terpenoids, phenolic acids, quinones and sesquiterpenes. Marine organisms yield structurally unique metabolites having potential for anticancer drug discovery, and microalgae and microbial sources contribute to the diversity of chemicals that can form therapeutic candidates. Some of the natural compounds that are often studied are resveratrol, apigenin, thymoquinone, zerumbone, costunolide, and Vinca alkaloids. Although chemically very different and of very different biological origin, all these compounds provide excellent examples of the importance of natural sources as repositories of molecules useful for cancer prevention, pharmacological study and drug development. Some representative examples are listed in Table 1.

**Table 1. Major Natural Products and Their Reported Anticancer Potential**

Natural product/group	Main source	Chemical class	Major anticancer relevance	Reference
Resveratrol	Grapes and berries	Polyphenol/stilbene	Antiproliferative and chemopreventive potential	Berman et al. (2017)
Apigenin	Fruits, vegetables, medicinal plants	Flavonoid	Modulates proliferation, apoptosis, and signaling	Salehi et al. (2019)
Thymoquinone	Nigella sativa	Quinone	Multitarget anticancer activity	Goyal et al. (2017)
Zerumbone	Zingiber zerumbet	Sesquiterpene	Antiproliferative and pro-apoptotic effects	Girisa et al. (2019)
Costunolide	Medicinal plants	Sesquiterpene lactone	Associated with apoptosis and cell-cycle regulation	Kim & Choi (2019)
Vinca alkaloids	Catharanthus roseus	Alkaloids	Established natural-product-derived anticancer drugs	Martino et al. (2018)
Marine natural products	Marine organisms	Diverse metabolites	Source of structurally novel anticancer compounds	Khalifa et al. (2019)

3.2 Molecular Targets and Signaling Pathways of Natural Anticancer Compounds

Natural anticancer compounds engage with various molecular pathways that are implicated in cancer-cell proliferation, survival, inflammation and progression. Commonly reported pathways are PI3K/Akt/mTOR, MAPK/ERK and NF- κ B, JAK/STAT and Wnt/ β -catenin pathways. Natural compounds can also affect other proteins involved in tumour suppression, e.g., p53, and/or proteins involved in apoptosis, e.g., the Bcl-2 family and caspases. In this way, they can suppress signals that support survival, inhibit abnormal growth and enhance the sensitivity to programmed cell death. In the case of cancer, which is a disease of the malfunctioning of multiple molecular networks, the ability to manipulate several pathways is of crucial importance (Kubczak et al., 2021; Papadopoulou et al., 2026).

Other targets of interest are cyclins, cyclin-dependent kinases, angiogenic regulators, telomerase and oxidative-stress-associated proteins. Modulation of cyclins and CDKs could disrupt uncontrolled cell-cycle progression, while inhibition of signaling through VEGF could inhibit tumor vascularization. Another important target is Telomerase, which is a constantly active enzyme that helps malignant cells proliferate for longer periods of time; there are several naturally occurring molecules that have been examined as possible inhibitors of Telomerase (Ganesan & Xu, 2017). In addition, natural polyphenols and other bioactive compounds could also affect cellular redox balance and inflammatory responses. Overall, it can be deduced that the therapeutic potential of natural products is closely related to their wide spectrum and multitarget activity on cancer-related molecular pathways (Naeem et al., 2022). Figure 2. Major Signaling Pathways Targeted by Natural Anticancer Compounds.

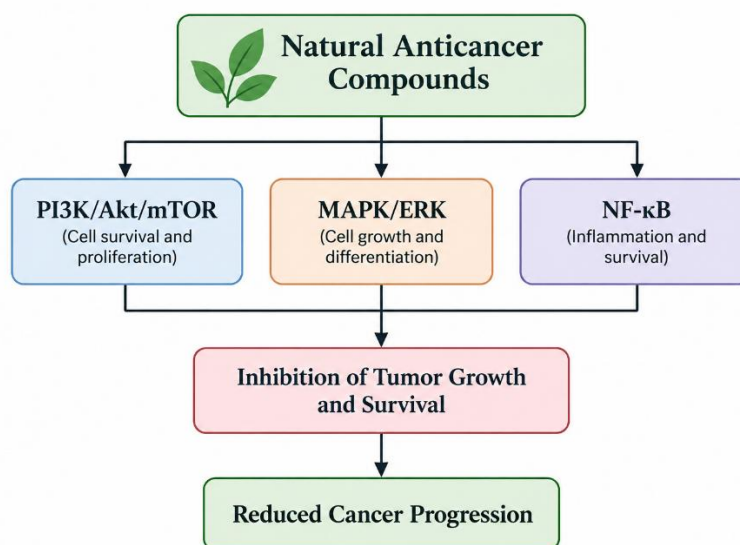


Figure 2. Molecular Targets of Natural Anticancer Compounds

This figure illustrates how natural anticancer agents can affect several important signaling pathways that play a role in the survival of cancer cells, their proliferation and inflammation. PI3K/Akt/mTOR, MAPK/ERK and NF-κB signaling are all modulation targets that can help to decrease growth promoting and survival-related processes in the tumor cell. Together, control of these pathways can help inhibit tumor growth and survival, and, consequently, decrease the progression of cancer. The activity is also pathway-based, thereby showing the multitarget aspect that is observed for many of the naturally occurring compounds and their importance in anticancer drug discovery.

3.3 Major Anticancer Mechanisms of Natural Products

The anticancer activity of natural products is achieved by a number of interrelated cellular mechanisms. Mitochondrial dysfunction, altered Bcl-2/Bax balance, and caspase activation are among the most frequently reported effects, which include the induction of apoptosis. Natural compounds can also inhibit uncontrolled proliferation by arresting the cell cycle, as well as the regulation of the cyclins and cyclin-dependent kinases. Other mechanisms involve modulation of oxidative stress, inhibition of tumor angiogenesis, suppression of invasion and metastasis, interference with telomerase activity and regulation of autophagy. The activity of some naturally derived compounds also inhibits microtubule dynamics and mitotic division. Many of the naturally occurring anti-cancer agents can have multiple complementary biological pathways, as these processes may occur simultaneously. The main mechanisms found in the literature are summarized in Table 2.

Table 2. Major Anticancer Mechanisms of Natural Products

Anticancer mechanism	Main molecular process	Major biological effect	Representative evidence	Reference
Apoptosis induction	Bcl-2/Bax, caspases	Promotes programmed cancer-cell death	Plant and marine natural products	Chaudhry et al. (2022)
Cell-cycle arrest	Cyclins and CDKs	Restricts uncontrolled proliferation	Multiple natural compounds	Kubczak et al. (2021)
Oxidative-stress modulation	ROS and antioxidant systems	Alters cancer-cell redox balance	Plant polyphenols	Liu et al. (2023)



Anti-angiogenic activity	VEGF-related pathways	Limits tumor vascular development	Natural anticancer compounds	Papadopoulou et al. (2026)
Anti-metastatic activity	EMT and migration pathways	Reduces invasion and metastatic spread	Multitarget natural products	Naeem et al. (2022)
Telomerase inhibition	Telomere-maintenance mechanisms	Limits prolonged cancer-cell proliferation	Natural telomerase inhibitors	Ganesan & Xu (2017)
Microtubule disruption	Tubulin and mitotic spindle	Prevents mitotic division	Vinca alkaloids	Martino et al. (2018)

3.4 Therapeutic Potential of Natural Products in Cancer Treatment

Natural products are proving to be therapeutic candidates as direct anticancer agents, as new compounds for the pharmaceutical industry, and as supportive agents for conventional cancer treatments. They have not only cytotoxic and antiproliferative properties, but also pro-apoptotic and cell-cycle-regulating, that render them as important starting points for anti-cancer drug discovery. Some of the natural-product derived agents that have already been used are already in well-defined clinical roles in cancer treatment, proof that naturally sourced molecules can be successfully translated to clinical therapeutics. Other plant- and marine-derived compounds are also in the preclinical stage of investigation but continue to be excellent chemical scaffolds for drug development. Natural products are also being investigated for chemoprevention due to their potential to impact oxidative stress, inflammation, and early stages of the carcinogenic process (Aldrich et al., 2022; Dehelean et al., 2021).

A further key therapeutic approach is that of natural compounds to be used as supporting agents to conventional cancer therapy. Selected natural products have been shown in preclinical studies to affect pathways of resistance, sensitise treatment and complement conventional chemotherapy or other treatment modalities (Lin et al., 2020). The multitarget activity could be beneficial if resistance is occurring via multiple mechanisms. But the data is still inconsistent between compounds, and a lot of candidates are based on cell and animal studies. Resveratrol is one of the more extensively studied and investigated examples; however, the therapeutic efficacy of resveratrol is not consistently confirmed in all cancer types (Berman et al., 2017). Thus, further translational and well-designed clinical studies are still required (Chunarkar-Patil et al., 2024). The major therapeutic applications of natural products in cancer treatment are summarized in Figure 3.

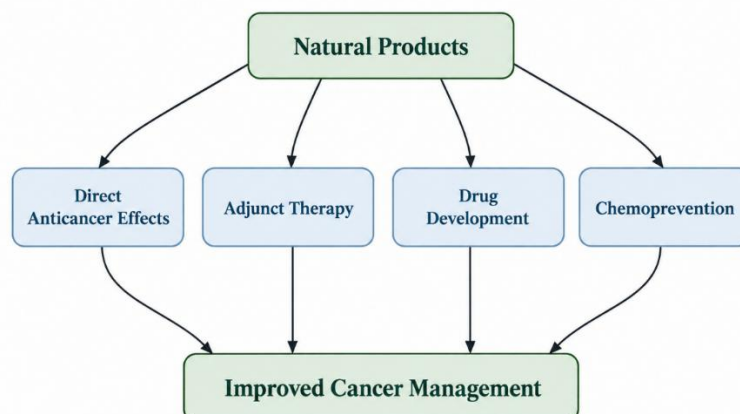


Figure 3. Therapeutic Potential of Natural Products in Cancer Treatment

The figure shows that natural products have four key therapeutic functions in the treatment of cancer,



which are direct anticancer activity, adjunctive therapy, drug development, and chemoprevention. The pathways provide examples of natural compounds that can be active therapeutic agents or supportive components for current treatment strategies. Their wide range of biological activity makes them valuable chemical scaffolds for future development of anticancer drugs and as potential agents for the reduction of cancer initiation and progression.

3.5 Challenges in the Therapeutic Development of Natural Anticancer Agents

Though some experimental results are promising, clinical translation of natural anticancer agents is hindered by several limitations. Low bioavailability and poor aqueous solubility can hinder the absorption, and limit the effective exposure at tumor sites, while rapid metabolism can lead to a short therapeutic activity. Natural variability may also lead to differences in chemistry, which can make standardization and reproducibility difficult. Other issues involve the inconsistencies of dosage, lack of tumor specificity, possible toxicity and interactions with standard anti-cancer drugs. One of the significant problems is that a therapeutic effect seen in cell lines or in animal studies may not be the same in humans. Table 3 provides a list of the barriers to and possible solutions for the translation process found in the literature.

Table 3. Major Challenges and Strategies for Clinical Translation

Major challenge	Effect on therapeutic development	Potential strategy	Reference
Poor solubility	Limits dissolution and absorption	Improved formulations and delivery systems	Tauro et al. (2024)
Low bioavailability	Reduces systemic exposure	Bioavailability-enhancing formulations	Najmi et al. (2022)
Rapid metabolism	Shortens therapeutic activity	Pharmacokinetic optimization	Tauro et al. (2024)
Source variability	Causes inconsistent composition	Standardized extraction and characterization	Najmi et al. (2022)
Potential drug interactions	May alter efficacy or safety	Interaction and pharmacokinetic studies	Tauro et al. (2024)
Limited clinical evidence	Makes patient benefit uncertain	Controlled clinical trials	Berman et al. (2017)
Preclinical–clinical gap	Laboratory efficacy may not translate clinically	Stepwise translational evaluation	Chunarkar-Patil et al. (2024)

3.6 Emerging Trends and Patterns in Natural-Product-Based Cancer Research

The literature examined shows that the screening of natural compounds has shifted to mechanism-based and translational research in the field of cancer. Multitarget activity has emerged as an area of research due to the fact that many natural products simultaneously target multiple pathways that are associated with growth and survival of tumors. The use of combination therapies with natural compounds and conventional therapies also is gaining in interest, especially in the context of treatment resistance. A new trend is towards pharmaceutical strategies to enhance solubility, bioavailability and delivery. Marine derived compounds are now attracting interest due to their structural novelty and emphasis is now placed on the link between molecular mechanisms and clinical relevance. The trends indicate that in the future, research will focus more on combining natural-product discovery, molecular pharmacology, formulation development, and translational evaluation. The major emerging patterns are summarized in Table 4.

**Table 4. Emerging Trends in Natural-Product-Based Anticancer Research**

Emerging trend	Main focus	Potential significance	Reference
Multitarget anticancer activity	Regulation of multiple signaling pathways	May address complex tumor biology	Naeem et al. (2022)
Combination therapy	Natural compounds with conventional treatment	May improve therapeutic response	Lin et al. (2020)
Improved drug delivery	Enhancement of solubility and bioavailability	May increase therapeutic exposure	Tauro et al. (2024)
Marine natural-product discovery	Identification of novel marine metabolites	Expands structural diversity of drug candidates	Khalifa et al. (2019)
Mechanism-based investigation	Linking compounds with molecular targets	Supports rational anticancer drug development	Kubczak et al. (2021)
Clinical translation	Progression from experimental to human studies	Strengthens therapeutic evidence	Chunarkar-Patil et al. (2024)
Natural-product-derived drug development	Optimization of bioactive natural scaffolds	Supports discovery of new anticancer agents	Aldrich et al. (2022)

4. Discussion

Based on the results of this review, it can be concluded that natural products are still relevant in the field of anticancer drug discovery due to their wide variety of chemicals, their multitarget nature and their capacity to impact multiple biological processes related to tumor development. The overwhelming majority of the literature analyzed reveals that the source of bioactive compounds is plant-based, however promising bioactive compounds are also derived from marine organisms, microalgae and other natural sources. One thing that reflected throughout the results was that very rarely do natural anticancer agents work on just one mechanism. Rather, many affect multiple apoptosis, cell-cycle, oxidative stress, angiogenesis, invasion, metastasis and resistance pathway. This multitarget behavior is especially relevant in the field of cancer, where the spread of the disease is propelled by the interdependent and intricate molecular abnormalities.

These observations are corroborated by comparison with previous ones. Medicinal plants continue to be an important source of bioactive anticancer molecules and plant-derived compounds like *Mangifera indica* are reported to possess cancer-preventive and therapeutic properties (Mirza et al., 2021). The same evidence has been reported for naringenin which exhibits several biological activities related to cancer such as antioxidant, anti-inflammatory, and signaling related mechanism (Arafah et al., 2020). The significance of the regulation of oxidative stress as identified by the present review is also consistent with the previous study, which highlights that plant polyphenols can modulate oxidative stress, inflammation, cellular senescence and cancer associated processes (Liu et al., 2023). The role of the tumour microenvironment and extracellular matrix in cancer progression also reinforces the notion of anticancer activity beyond just direct cytotoxicity – broadly controlling invasion, signalling and treatment response (Huang et al., 2021). Moreover, other reports on functionalized quinoline derivatives and pyrrole or pyrrolidine analogues have also highlighted the therapeutic potential of structurally diverse chemical scaffolds for drug discovery (Ajani et al., 2022; Jeelan Basha et al., 2022). The wider therapeutic potential of natural products in other complex diseases further supports their pharmacological versatility (Rahman et al., 2021), and advanced bioengineered systems presents an opportunity to further optimize natural and biologically compatible platforms for therapeutic use (Eda et al., 2019).

The results of these studies have consequences for cancer pharmacology and drug development.



Natural products cannot only be considered as traditional medicine, but also as excellent source of pharmacologically active molecules and lead compounds. Their omniregulatory properties might be beneficial for multi-targeted strategy used in the treatment of heterogeneous tumors. They also might be used as complementary treatment in the existing therapeutic methods, especially in cases of treatment resistance, which result in poor clinical responses. Simultaneously, it seems that the focus for therapeutic development should be on compounds with well-defined mechanisms, reproducible composition and acceptable safety.

A number of gaps are still apparent in the existing evidence. A lot of literature remains in vitro experiments and animal models so that there is not yet an immediate transfer of the literature to the clinic. Natural extracts are not necessarily consistent in composition and can be very different depending on the source, extraction techniques and formulations. Poor solubility and bioavailability, rapid metabolism and uncertain dosing, further diminishes the translational potential. Besides that, mechanistic studies are mostly focussed on isolated pathways whereas natural compounds often have more general biological effects.

Future studies should thus concentrate on standardized preparations of natural products, in-depth pharmacokinetics and toxicology, and better correlation of molecular effects and clinical outcomes. Increased focus on combination therapy, better drug delivery systems, biomarker guided selection and well-designed clinical trials should also be given. The combination of natural-product chemistry and molecular oncology and translational pharmacology could lead to the discovery of compounds that have the potential to be safe and effective drugs in the treatment of cancer.

5. Conclusion

This review concludes that natural products represent a significant and chemically diverse source of anticancer agents with great potential for cancer prevention, drug discovery and therapeutic development. The results highlight that, despite the extensive studies conducted, medicinal plants are still the most investigated sources of bioactive compounds, but also marine organisms, microalgae, microorganisms, and other biological materials are informative. Major bioactive compounds including polyphenols, flavonoids, alkaloids, terpenoids, phenolic acids, quinones and sesquiterpenes exhibit wide-ranging anticancer actions and have varied modes of action. The analyzed evidence showed that natural compounds can modulate vital pathways in situations of cancer such as PI3K/Akt/mTOR, MAPK/ERK, NF- κ B, Jak/Stat, Wnt/ β -catenin, proteins associated with p53, proteins involved with apoptosis, cyclins, proteins related to angiogenic regulation and proteins related to the telomere. These include induction of apoptosis, cell-cycle arrest, modulation of oxidative stress, inhibition of angiogenesis, suppression of invasion and metastasis and interference with treatment-resistance mechanisms. These multitarget properties hold promise for them both as anticancer agents on their own and as complementary agents in conventional therapy. However, the clinical translation has been hampered by limited solubility, bioavailability, rapid metabolism, source variability, uncertainty of dosing, potential toxicity, and lack of human evidence. Advances in formulation, standardization, pharmacokinetic and toxicological assessment and good clinical trial design will therefore be necessary. In general, natural products are a good starting point for the design of more effective, safer, and rationally designed anticancer drugs.

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