NATURAL PRODUCTS AND THEIR THERAPEUTIC ADVANCEMENT IN MANAGEMENT OF CANCER

Abstract

The role of natural medicinal compounds in cancer management has gained significant attention due to their diverse therapeutic effects. Derived from plant sources, these compounds offer a potential alternative or complementary approach to conventional cancer treatments. compounds Natural medicinal possess antioxidant and anti-inflammatory properties, targeting oxidative stress and inflammation, which are key factors in cancer initiation and progression. Their multifaceted mechanisms of action, such as modulating cell signaling pathways, inducing apoptosis, and inhibiting angiogenesis, make them promising candidates for targeted cancer therapy. Additionally, these compounds may address drug resistance issues by targeting multiple pathways simultaneously. Importantly, their potential to mitigate treatment-induced side effects offers a significant advantage in enhancing patients' quality of life. However, challenges remain in terms of bioavailability, standardization, and clinical validation. Clinical trials are essential to establish their safety and efficacy, allowing these integrated compounds be into comprehensive cancer treatment strategies. The role of natural medicinal compounds in cancer management holds promise as a holistic and personalized approach, potentially reshaping the landscape of cancer therapy.

Keywords: Natural medicinal compounds, Cancer management, Therapeutic effects, Mechanisms of action, Antioxidant and anti-inflammatory, Drug resistance and Clinical validation.

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I. INTRODUCTION

Cancer, in essence, refers to a group of diseases characterized by uncontrolled and abnormal cell growth within the body. It is a complex and multifaceted condition driven by genetic mutations that disrupt the normal regulation of cell division and function. This disruption leads to the formation of a mass of tissue, known as a tumor, which can invade surrounding tissues and even spread to distant parts of the body through a process called metastasis. The pathophysiology of cancer involves a series of events that start at the genetic level. Mutations can accumulate due to various factors, including genetic predisposition, exposure to carcinogens like tobacco smoke and UV radiation, and errors in DNA replication. These mutations can activate oncogenes, which promote cell growth, or inactivate tumor suppressor genes, which normally regulate cell division and prevent unchecked growth(Dyondi et al., 2015; Moutia et al., 2018; S. and A.J., 2012).

As these genetic alterations accumulate, affected cells lose their ability to respond to the body's natural signals that control growth and death (apoptosis). Consequently, they evade programmed cell death and continue to divide uncontrollably, forming a mass of abnormal cells – the tumor. Tumors can be either benign or malignant. Benign tumors are non-invasive and usually pose minimal threats, whereas malignant tumors are invasive and have the potential to spread to other parts of the body. Metastasis is a critical phase in cancer progression. Malignant cells can invade nearby tissues and enter the bloodstream or lymphatic system, allowing them to travel to distant sites in the body. Once there, they can establish secondary tumors, further compromising organ function and overall health (Jawaid et al., 2020; Paccagnella et al., 1996).

Understanding the pathophysiology of cancer has led to the development of various treatment strategies. Traditional approaches include surgery to remove tumors, radiation therapy to target and destroy cancer cells, and chemotherapy to kill rapidly dividing cells. More recent advancements involve targeted therapies that specifically target the molecular abnormalities driving cancer growth and immunotherapies that stimulate the body's immune system to recognize and eliminate cancer cells. Moreover, cancer's pathophysiology revolves around genetic mutations that disrupt normal cell regulation, leading to uncontrolled growth, invasion, and potential metastasis. A comprehensive understanding of these processes is crucial for developing effective treatments and interventions to combat this challenging disease.

Medicinal plants and natural products have played a significant role in cancer management and treatment due to their diverse bioactive compounds and potential therapeutic properties. These resources offer a unique avenue for developing novel therapies that complement conventional treatments. The role of medicinal plants and natural products in cancer can be understood through several key aspects. Firstly, many plant-derived compounds possess potent anti-cancer properties. For instance, compounds like curcumin from turmeric, resveratrol from grapes, and epigallocatechin gallate (EGCG) from green tea have demonstrated anti-inflammatory, antioxidant, and anti-proliferative effects, inhibiting various stages of cancer development and progression(Kaneko et al., 2019; Patel et al., 2012; Zhumashova et al., 2019).

Secondly, these natural compounds often exhibit fewer side effects compared to traditional chemotherapy drugs, making them attractive candidates for supportive care during cancer treatment. They can help alleviate treatment-related symptoms like nausea, fatigue, and pain, enhancing the overall quality of life for cancer patients. Thirdly, medicinal plants and natural products have shown promise in enhancing the effectiveness of standard cancer therapies. Some compounds sensitize cancer cells to radiation or chemotherapy, making them more susceptible to treatment. Others inhibit the growth of blood vessels that supply nutrients to tumors, a process crucial for tumor survival. Furthermore, these natural products often have multi-targeted effects, impacting various signaling pathways and cellular processes involved in cancer. This can potentially address the issue of tumor heterogeneity and reduce the likelihood of developing resistance to treatment(Arcos-Martínez et al., 2016; Mishra and Kaur, 2013; S. and A.J., 2012; Tan et al., 2010).

Despite these promising attributes, it's important to note that the development of medicinal plant-derived therapies for cancer is not without challenges. Standardization of dosages, ensuring consistent quality of plant extracts, and conducting rigorous clinical trials to validate their efficacy and safety are critical steps in their integration into mainstream cancer care. Furthermore, medicinal plants and natural products offer a valuable resource in the fight against cancer. Their bioactive compounds hold potential for preventing, managing, and treating cancer by exerting anti-cancer effects, minimizing side effects, and synergizing with conventional therapies. However, further research is necessary to unlock their full potential and establish their role as effective adjuncts in cancer treatment regimens(Furman et al., 2019; Kumar et al., 2021; Sohn et al., 2010; Tan et al., 2010).

II. REVIEW FINDING

1. Role of Medicinal Plants and Their Necessity in Management of Cancer: Medicinal plants have been integral to traditional systems of medicine for centuries, and their role in the management of cancer within these systems is both significant and rooted in ancient wisdom. Traditional systems of medicine, such as Ayurveda, Traditional Chinese Medicine (TCM), and Indigenous knowledge, recognize the value of medicinal plants in the holistic approach to cancer management. In these traditional systems, medicinal plants are often prescribed based on a personalized assessment of an individual's constitution, imbalances, and the specific nature of the disease. These practices consider the interconnectedness of the body, mind, and spirit – a perspective that aligns with the modern understanding of the mind-body connection and psychosocial aspects of cancer (Mishra and Kaur, 2013; Sabir et al., 2019).

Medicinal plants used in traditional systems offer a diverse array of bioactive compounds that have shown anti-cancer properties. For instance, Ayurvedic formulations often include herbs like Ashwagandha (*Withaniasomnifera*) and Turmeric (*Curcuma longa*), which possess immunomodulatory, anti-inflammatory, and antioxidant effects, supporting the body's natural defense mechanisms against cancer(Al-Snafi, 2017; Roshan et al., 2014; Russo et al., 2001).

Additionally, traditional systems emphasize the importance of a balanced lifestyle, including diet, exercise, and stress reduction. Medicinal plants are incorporated into dietary practices to enhance overall well-being and resilience, factors crucial for cancer prevention and management. The necessity of medicinal plants in the management of cancer within traditional systems lies in their holistic approach. These systems consider not only the physical aspects of the disease but also the emotional, mental, and spiritual dimensions. This comprehensive perspective recognizes the interconnectedness of various factors contributing to cancer development and progression(Bhandari and Kamdod, 2012; Majdalawieh and Carr, 2010; Sharma et al., 2009).

Moreover, for many communities around the world, traditional systems of medicine are more accessible and culturally relevant. Medicinal plants are often an affordable and locally available resource, making them a practical option for populations with limited access to modern healthcare. While traditional systems of medicine offer valuable insights, it's important to integrate them judiciously with evidence-based modern medical approaches. Scientific research can help validate the efficacy and safety of these plants, standardize their usage, and refine their application for optimal cancer management. However, medicinal plants play a crucial role in cancer management based on traditional systems of medicine. Their incorporation is rooted in a holistic understanding of health and disease, and they offer a complementary approach to modern medical practices. Embracing the wisdom of traditional systems, while advancing their integration through research and collaboration, holds promise for a more comprehensive and effective approach to cancer care(Bhandari and Kamdod, 2012; Saini et al., 2022; Yahfoufi et al., 2018; Yue et al., 2010).

Table 1: Reported medicinal plants used as anti-cancer agents.

S.	Common	Sources	Family	Pharmacology	Mechanism of
No.	Name	<i>C</i> 1	77: '1	C : 1:1:	Action
1.	Turmeric	Curcuma longa	Zingiberacee	Curcumin exhibits	Inhibits NF-
				anti-inflammatory,	кВ and COX-
				antioxidant, and	2 pathways,
				anti-cancer	induces
				properties.	apoptosis.
2.	Green Tea	Camellia sinensis	Theaceae	EGCG possesses	Modulates
				antioxidant, anti-	multiple
				proliferative, and	signaling
				pro-apoptotic	pathways,
				effects.	including
					PI3K/Akt.
3.	Ashwaganha	Withaniasomnifea	Solanaceae	Withaferin A has	Inhibits NF-
		Ţ.		anti-inflammatory,	κB, induces
				immunomodulator	ROS-
				y, and apoptotic	mediated
				activities.	apoptosis.
4.	Garlic	Allium sativum	Amaryllidaceae	Allicin exhibits	Triggers
				antioxidant, anti-	mitochondrial
				inflammatory, and	apoptotic
				apoptotic effects.	pathway.
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5.	Ginkgo Biloba	Ginkgo biloba	Ginkgoaceae	Ginkgolides have antioxidant, anti- inflammatory, and anti-tumor activities.	Inhibits angiogenesis and promotes apoptosis.
6.	Resveratrol	Vitis vinifera	Vitaceae	Exhibits antioxidant, anti- inflammatory, and anti-tumor effects.	Activates SIRT1, inhibits NF- κB, and induces apoptosis.
7.	Curcumin	Curcuma longa	Zingiberaceae	Shows anti- inflammatory, antioxidant, and anti-proliferative effects.	Modulates Wnt/β- catenin, PI3K/Akt, and MAPK pathways.
8.	Astragalus	Astragalus membranaceus	Fabaceae	Astragalosides possess immunomodulator y and anti-tumor properties.	Enhances immune response and inhibits cell proliferation
9.	Cat's Claw	Uncariatomentosa	Rubiaceae	Contains oxindole alkaloids with anti-inflammatory and anti-cancer effects.	Suppresses NF-кB and MMPs, induces apoptosis.
10.	Reishi Mushroom	Ganoderma lucidum	Ganodermataceae	Contains polysaccharides with immunomodulator y and anti-tumor activities.	Enhances NK cell activity, inhibits angiogenesis.
11.	Artemisinin	Artemisia annua	Asteraceae	Anti-malarial, anti-cancer, anti- inflammatory	Generates oxidative stress, induces apoptosis
12.	Dandelion	Taraxacumofficinale	Asteraceae	Antioxidant, anti- inflammatory, anti-cancer	Induces apoptosis, inhibits cell proliferation

2. Reported Phytochemicals used as Anti-cancer: Natural chemical constituents have gained significant attention for their potential role in anti-cancer activity due to their diverse pharmacological properties and intricate mechanisms of action. These compounds, derived from various plants and natural sources, exhibit promising effects in inhibiting cancer cell growth, inducing apoptosis (programmed cell death), and suppressing the development of tumors. Their multifaceted pharmacology is attributed to their ability to interact with key cellular pathways and molecular targets involved in cancer progression. One prominent example is curcumin, found in turmeric, renowned for its antioxidant and anti-inflammatory properties. Curcumin's mechanism of action involves modulating nuclear factor-kappa B (NF-κB) signaling, which plays a pivotal role

in inflammation and cancer. By inhibiting NF-κB activation, curcumin disrupts the transcription of genes that promote cell survival, proliferation, and angiogenesis. Additionally, curcumin triggers apoptosis and activates tumor suppressor genes, offering a multi-pronged approach to combatting cancer.

Resveratrol, abundant in grapes, showcases antioxidant and anti-inflammatory characteristics. Its mechanism of action includes activating sirtuins (SIRT1) and inhibiting signal transducer and activator of transcription 3 (STAT3) signaling. These actions lead to cell cycle arrest and apoptosis induction, thereby impeding cancer cell proliferation. Furthermore, resveratrol's influence on multiple pathways offers potential for synergy in combination therapies.

Epigallocatechin gallate (EGCG) from green tea is recognized for its antioxidant and anti-angiogenic effects. EGCG's pharmacology involves disrupting the phosphoinositide 3-kinase (PI3K)/Akt pathway, which regulates cell survival and growth. By interfering with this pathway, EGCG suppresses cancer cell proliferation and promotes apoptosis. Its inhibition of angiogenesis further curbs tumor growth and metastasis. Quercetin, a flavonoid present in fruits and vegetables, demonstrates antioxidant and anti-inflammatory properties. Its mechanism revolves around inducing cell cycle arrest, particularly by targeting the PI3K/Akt pathway. By interfering with this pathway, quercetin halts cell cycle progression and encourages apoptosis. This dual action diminishes the survival and growth of cancer cells(Le Gall et al., 2004; Patel et al., 2012; Zhumashova et al., 2019).

Taxol, derived from the yew tree, disrupts microtubule dynamics and prevents mitosis, crucial for cell division. Taxol stabilizes microtubules, inhibiting their disassembly during cell division. This leads to cell cycle arrest and apoptosis, ultimately suppressing tumor growth(Singh et al., 2010; Tang et al., 2017). Natural compounds like vinblastine from the periwinkle plant and camptothecin from *Camptothecaacuminata* act similarly by disrupting microtubule dynamics and interfering with DNA replication, respectively. These mechanisms halt cancer cell division, underscoring their potential as anti-cancer agents(BALABHASKAR R et al., 2019; Loizzo et al., 2008).

One notable example is withaferin A, extracted from ashwagandha. Its adaptogenic properties and anti-inflammatory effects contribute to its anti-cancer potential. Withaferin A's mechanism involves disrupting microtubule dynamics, essential for cellular division, and inhibiting heat shock protein 90 (Hsp90), a molecular chaperone promoting cancer cell survival. Simultaneously, it activates apoptosis pathways and modulates NF-κB signaling, further curtailing cancer progression.Artesunate, primarily recognized as an anti-malarial agent, exhibits additional anti-cancer activity. Through its pro-oxidant effects, artesunate triggers oxidative stress in cancer cells, leading to DNA damage and apoptosis. It also interferes with angiogenesis and inhibits NF-κB, thus restraining tumor growth and metastasis. This dual action demonstrates its potential in diverse cancer contexts(Okoye et al., 2014; Verma and Kumar, 2018).

Berberine, derived from various plants, demonstrates pharmacological versatility. With its anti-inflammatory and antioxidant attributes, berberine modulates the AMP-activated protein kinase (AMPK) pathway, disrupting energy homeostasis in cancer cells.

By impeding cell proliferation and inducing apoptosis, berberine exerts potent anti-cancer effects(Gahlot and Yadav, 2021; More and Kharat, 2016; Spelman, 2001).

Lycopene, commonly found in tomatoes, offers antioxidant properties and antiinflammatory benefits. Its mechanism involves inhibiting the PI3K/Akt/mTOR pathway, responsible for cell survival and growth. Through this interference, lycopene induces apoptosis and halts cell cycle progression, limiting the expansion of cancer cells(Moody et al., 2020). Thymoquinone, a component of black seed oil, exhibits antioxidant and antiinflammatory activities. Thymoquinone's mechanism is closely linked to p53-mediated pathways, known for their role in regulating cell cycle and apoptosis. By engaging these thymoquinone triggers apoptosis and restrains pathways, cancer cell proliferation(Hameed et al., 2019; Piras et al., 2013).

Genistein, a soy-derived isoflavone, acts as a phytoestrogen and exhibits anti-cancer effects. Its inhibitory action on tyrosine kinases disrupts cell signaling pathways, particularly those driving cell survival and proliferation. Genistein's modulation of cell cycle checkpoints and induction of apoptosis further contribute to its anti-cancer potential. These natural compounds showcase the intricate synergy between their pharmacological properties and mechanisms of action. While their antioxidant and anti-inflammatory attributes provide a foundation, their targeted interactions with signaling pathways governing cell fate are crucial in thwarting cancer progression. Their multi-faceted actions, from disrupting microtubule dynamics and inhibiting key enzymes to inducing oxidative stress and apoptosis, highlight their potential to impede cancer at various stages (Chen and Chen, 2021; Dar et al., 2015; Guo et al., 2006; Hämäläinen et al., 2007; Sapozhnikova, 2014).

Nonetheless, translating these insights into effective therapies requires rigorous scientific exploration, encompassing preclinical and clinical studies. Factors such as bioavailability, dosing, and potential interactions with conventional treatments must be thoroughly understood. Collaborative efforts between researchers, clinicians, and pharmacologists are pivotal in harnessing the full potential of these natural chemical constituents for anti-cancer strategies.

It is reported that the efficacy of these natural chemical constituents varies across cancer types and individuals. Their pharmacological properties, such as antioxidant and anti-inflammatory effects, contribute to their ability to counteract carcinogenesis. However, their mechanisms extend beyond these attributes, encompassing intricate interactions with cellular pathways that regulate cell survival, growth, and death.

Table 2: Reported Phytochemicals Used for Management of Cancer.

S. No.	Natural Compound	Pharmacology	Mechanism of Action
1.	Curcumin (from turmeric)	Anti- inflammatory, antioxidant	Inhibits NF-κB signaling, induces apoptosis, inhibits COX-2, activates tumor suppressor genes
2.	Resveratrol (from grapes)	Antioxidant, anti-inflammatory	Activates SIRT1, inhibits STAT3 signaling, induces apoptosis
3. 4.	Epigallocatechin gallate (EGCG) (from green tea)	Antioxidant, anti-inflammatory	Inhibits cell cycle progression, induces apoptosis, inhibits angiogenesis
5.	Curcumin (from turmeric)	Antioxidant, anti-inflammatory	Inhibits mTOR signaling, activates apoptosis, suppresses VEGF expression
6.	Quercetin (from fruits and vegetables)	Antioxidant, anti-inflammatory	Induces cell cycle arrest, inhibits PI3K/Akt pathway, activates apoptosis
7.	Taxol (from yew tree)	Inhibits microtubule dynamics	Stabilizes microtubules, prevents mitosis
8.	Vinblastine (from periwinkle)	Inhibits microtubule dynamics	Disrupts microtubule formation, inhibits cell division
9.	Camptothecin (from Camptotheca acuminata)	Topoisomerase I inhibitor	Inhibits DNA replication and transcription
10.	Paclitaxel (from yew tree)	Enhances microtubule assembly	Stabilizes microtubules, inhibits mitosis
11.	Allicin (from garlic)	Antioxidant, anti-inflammatory	Induces apoptosis through mitochondrial pathways, inhibits angiogenesis, modulates cell cycle
12.	Silibinin (from milk thistle)	Antioxidant, anti-inflammatory	Inhibits STAT3 and NF-κB pathways, induces cell cycle arrest, apoptosis
13.	Berberine (from various plants)	Antioxidant, anti-inflammatory	Activates AMPK, inhibits cell proliferation, induces apoptosis

14.	Ellagic Acid	Antioxidant,	Inhibits DNA binding of
	(from berries and	anti-inflammatory	carcinogens,
	pomegranates)		induces apoptosis, modulates
			cell cycle
15.	Artesunate	Anti-parasitic	Induces oxidative stress,
	(from sweet	agent,	inhibits angiogenesis,
	wormwood)	anti-inflammatory	triggers apoptosis, inhibits NF-
			кВ
16.	Honokiol	Anti-anxiety,	Inhibits PI3K/Akt/mTOR
	(from magnolia)	antioxidant	pathway,
			induces apoptosis, anti-
			angiogenic effects
17.	Withaferin A	Adaptogenic,	Disrupts microtubule dynamics,
	(from ashwagandha)	anti-inflammatory	inhibits Hsp90,
			induces apoptosis, modulates
			NF-κB
18.	Lycopene	Antioxidant,	Inhibits PI3K/Akt/mTOR
	(from tomatoes)	anti-inflammatory	pathway,
			induces apoptosis, modulates
			cell cycle
19.	Thymoquinone	Antioxidant,	Induces apoptosis through p53-
	(from black seed)	anti-inflammatory	mediated pathways,
			inhibits STAT3 and NF-κB
			pathways
20.	Genistein	Isoflavone,	Inhibits tyrosine kinases,
	(from soy)	phytoestrogen	modulates cell cycle,
			induces apoptosis, anti-
			angiogenic effects

III. DISCUSSION

The role of natural medicinal compounds in the management of cancer has garnered significant attention owing to their potential therapeutic effects. These compounds, derived from various plant sources, offer a promising avenue for cancer treatment and prevention due to their diverse pharmacological properties and mechanisms of action. While conventional treatments like chemotherapy and radiation remain crucial, natural medicinal compounds provide an alternative or complementary approach, addressing the limitations and challenges associated with traditional therapies. One of the key advantages of natural medicinal compounds is their rich source of bioactive compounds with potential anti-cancer properties. These compounds often possess antioxidant and anti-inflammatory attributes that can help counteract oxidative stress and chronic inflammation, both of which contribute to cancer initiation and progression. For example, curcumin, a component of turmeric, exhibits potent antioxidant and anti-inflammatory effects. Its ability to modulate key molecular pathways involved in inflammation and cell survival makes it a promising candidate for cancer therapy(Dyondi et al., 2015; Moutia et al., 2018; Quetglas-Llabrés et al., 2022).

Furthermore, the multifaceted mechanisms of action exhibited by natural medicinal compounds make them particularly appealing. Many of these compounds target specific signaling pathways that regulate cell proliferation, apoptosis, and angiogenesis. Resveratrol, found in grapes and red wine, is known to activate sirtuins and inhibit STAT3 signaling, resulting in cell cycle arrest and apoptosis induction. This intricate modulation of cellular processes allows these compounds to selectively target cancer cells while minimizing damage to healthy cells. Natural medicinal compounds can also address the challenge of drug resistance frequently observed in conventional cancer treatments. Their diverse mechanisms of action may overcome resistance mechanisms that cancer cells develop against single-target drugs. For instance, compounds like berberine and quercetin have shown the ability to modulate multiple pathways simultaneously, potentially reducing the likelihood of resistance development(Alali et al., 2021; Kaneko et al., 2019; Rajendran et al., 2013; Wallaschek et al., 2021).

Additionally, the potential of natural medicinal compounds to mitigate side effects is a notable advantage. Traditional cancer treatments often result in adverse effects due to their cytotoxic nature. Natural compounds like curcumin and green tea polyphenols have been studied for their protective effects against these side effects. Their ability to alleviate chemotherapy-induced toxicity while enhancing treatment efficacy is a promising attribute in improving the overall quality of life for cancer patients. However, challenges persist in the translation of natural medicinal compounds into mainstream cancer management. Issues related to bioavailability, standardization, and optimal dosing need to be addressed. Clinical trials are essential to validate their safety and efficacy, providing a solid scientific foundation for their use. Moreover, while these compounds hold immense potential, they are unlikely to replace conventional treatments entirely. Instead, they can be integrated as part of treatment strategies, providing a holistic comprehensive approach management(Levi-Polyachenko et al., 2009; S. and A.J., 2012; Sabir et al., 2019; Tang et al., 2017).

Moreover, the role of natural medicinal compounds in the management of cancer is a subject of growing interest and research. Their pharmacological diversity, multifaceted mechanisms of action, and potential to address challenges associated with conventional treatments make them valuable candidates for cancer therapy. However, a balanced approach is crucial, combining rigorous scientific investigation with clinical validation to harness their full potential. As we continue to unravel the complexities of cancer biology, these compounds offer a promising avenue for innovative and personalized approaches to cancer prevention and treatment, potentially reshaping the landscape of oncology(Mathiassen et al., 2017; Mosleh-Shirazi et al., 2022).

IV. CONCLUSION

In conclusion, the role of natural medicinal compounds in cancer management holds immense promise and warrants continued exploration. These compounds, sourced from diverse plant origins, offer multifaceted therapeutic effects that target key aspects of cancer initiation, progression, and treatment challenges. By harnessing their antioxidant, anti-inflammatory, and multi-pathway modulating properties, these compounds present an innovative approach to complement traditional cancer therapies. Their potential to mitigate drug resistance and minimize treatment-induced side effects underscores their value in

enhancing overall patient well-being. However, successful integration of these compounds into mainstream cancer management requires rigorous scientific investigation, standardization, and robust clinical validation. As research advances, the synergy between natural medicinal compounds and conventional treatments may pave the way for more effective, personalized, and holistic approaches to cancer prevention and therapy, potentially reshaping the landscape of cancer care.

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