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Discovery of concealed gems: Utilizing phytochemicals from unacknowledged plants for cancer treatment

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Abstract

Cancer is considered a fatal disease across the globe, irrespective of the economic or social condition of any country. Therefore, the search for its effective cure is one of the most crucial tasks for humankind. Even after extensive research, many patients around the world still face the adversities of this incurable malady. According to ancient and modern-day innovations, all curative herbs are believed to have anti-carcinomic plant chemicals which can be used in the natural treatment of cancer. The curability of these plant chemicals was tested on a sizeable number of patients, which therefore doesn't help in gathering significant data on their proficiency. This review study was conducted on the prolonged benefits and their protective abilities to cure cancer of plant chemicals obtained from *Hibiscus rosa-sinensis* (Shoeblack plant), *Calendula officinalis* (Pot marigold), *Tabernaemontana divaricata* (crape jasmine), and *Catharanthus Roseus* (Madagascar periwinkle). These plants control the articulation of metabolism-related protein and oxidative stress thereby improving metabolism. Additionally, A handful of plant compounds are said to have a positive influence on a range of cancer-associated symptoms. Vinca alkaloids in *Catharanthus Roseus* activate apoptosis in carcinomic cells by restricting the gathering of microtubule structures and obstructing mitosis in the metaphase. Also, *C. officinalis* exhibits anti-carcinomic outcomes by complex signaling pathways, influencing cell propagation, programmed cell death, cell cycle development, and metastasis, resulting in being an important resource for carcinoma research. Likewise, *T. divaricate* shows optimistic results as an origin for a carcinoma-preventing drug. Alkaloids obtained from the shrub exhibit numerous cancer inhibitory and anti-carcinomic effects, paving the way to the cytotoxic invention. *T. divaricate* is rich in alkaloid content. Furthermore, the flavonoids in *Hibiscus rosa-sinensis* show optimistic results in combating carcinoma by aiming at fundamental cellular pathways, comprising, NF- κ B, EGFR/MAPK, PI3K/Akt, thus repressing carcinomic cell propagation. However, scant evidence shows that there is not enough resource to reinforce the efficacy of these drugs in combating cancer.

Keywords: Cancer, effective cure, drug efficacy, anti-carcinoma, plant chemicals

Introduction

According to the data published by the Global Health Organization, cancer is the predominant cause of death worldwide and is responsible for a mammoth number of deaths each year. It also contributes a considerable portion of the world's death rate [1]. The predominantly utilized methods for tumoral care are surgery, chemotherapy, and radiation therapy. Amethopterin (*Cytotoxic inhibitors*), CDDP, Adriamycin (*DNA interactive Agents*), taxanes (*anti-tubulin agents*), and Precision medicines are amongst the most overused medicaments for carcinoma cure [2].

Despite these drugs being extremely efficient in treating cancer, these drugs cause severe repercussions, such as dysfunctional red blood cell production inside the bone marrow, which leads to anemia, gastrointestinal problems, which can cause malnutrition and dehydration, hair loss, which can also result in emotional distress, body image issues, which can result in social isolation, etc. [3]. According to the following study, one out of six of all deaths in 2020 were because of malignancy, i.e., 10,000,000 deaths. The article indicates that the outbreak of the destructive coronavirus may cause a much worrisome rise in the number of people who possess neoplasms, by a rate of 57% overall [4]. Despite efforts being made to discover carcinomic therapies, there are many victims of poor prognosis. Despite such adverse conditions, efforts are still being made to discover carcinomic remedies [5]. Additionally, the seclusion of a range of botanical elements from healing herbs represented that it concludes cell death [6].

Staging of carcinoma is a process of estimating the extent to which carcinoma cells have advanced in the victim's body.

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Stage 0 embarks the first indication of the presence of carcinomic cells. The following stages report the progress of the cancer cells progressively. The letter-number combination provides more information in detail. Cancer staging aids doctors to provide the patients with the best possible prognosis [7]. Cancer can take more than 100 forms, and it is named after its origin. Carcinoma generally arises from the epithelial tissues present in our body. The most common forms of carcinoma are squamous cell carcinoma, adenocarcinoma, and basal cell carcinoma. Several other carcinomas are melanoma, leukemia, lymphoma, sarcoma, and multiple myeloma [8].

According to contemporary experts, chemicals derived from curative herbs are effective in treating cancer to some extent because they are used to treat a variety of other diseases. As per reports, it is proven that the anti-malignant consequences of organic elements with curative values may be employed to fight malignancies. Since the inception of humankind, people have believed that the usage of organic substances to treat ailments, regardless of how serious it is, is considered beneficial. The old school of thought also believed that the usage of medicinal herbs causes overall wellness to the patient [5].

The alkaloids present in *Tabernaemontana divaricata* (crape jasmine) exhibit anticarcinoma-propagation, also non-carcinomic outcomes on multiple categories of neoplasm both inside and outside the laboratory [9]. *Calendula officinalis* (Pot marigold) has abundant carotenoids and tannins where carotenoids exhibit anti-cancer outcomes by several signaling pathways of propagation, cell death, cell cycle development, formation of new blood cells, and metastasis [10]. Likewise, Tannins combat many cellular routes and molecules important in the development of cancer [11]. Flavonoids present in *Hibiscus rosa-sinensis* (Shoebblack plant) prohibit protein kinase B (Akt), phosphatidylinositide 3-kinases (PI3K), (EGFR/MAPK) epidermal growth factor receptor/mitogen-activated protein kinase also chromosomal constituent (NF- κ B) which is also known as crucial transcription factor of triggered B cells [12]. Lastly, in *Catharanthus Roseus*, Vinca Alkaloids hinder cell division in metaphase by constraining tubulin and intercepting its creation of polymers into vital elements of the cell structure [13]. Vinca alkaloids are constraints to distinctive regions on tubulin, restricting organizational elements of locomotive cell organ gathering and function. Constraining is hasty and regenerable, with higher interest at microtubule ends than along the surface [14].

The two main techniques for managing viability and cell propagation are the extracellular signal-regulated kinase and mitogen-activated protein kinase routes, [15] that may be combated by botanical-based chemicals [16]. I have especially emphasized four plants because these floras have a cultural significance in India. Apart from cultural aspects these plants have a nutritional significance and have a chance to lead the way towards the discovery of the treatment of carcinoma and plan its waste-to-wealth journey.

Evidence demonstrates that phytochemicals have a strong

antitumor potential. Discoveries indicate that these chemicals have notable anticarcinogenic features. Almost, half of all the accepted anti-carcinomic treatments from 1940 to 2014 had their inception from botanical products [17].

Priorly, several works were conducted by renowned scientists all over the world to proclaim the efficacy of phytochemicals on cancer cure, for example, a recent study conducted by Wang H [18] exhibited the emergence of natural phytochemical compounds as a promising pathway to cancer cure. It emphasizes the need for safer and more effective chemoprevention and treatment options and draws attention to the persisting difficulties in treating advanced metastasized cancer. Likewise, by illustrating the importance of the role that phytochemicals play in suppressing important signaling pathways that are responsible for promoting carcinogenesis, it was possible to depict the historical trajectory of phytochemicals in cancer research. The review henceforth contributes to a better knowledge of the potential of natural products as sources for the creation and discovery of strong anticancer medicines [19]. Meanwhile, Shu L [20] talks about recent research conducted on this topic and the difficulties and opportunities of transforming plant chemicals into real medicines shortly. A recently conducted research on this relevant topic portrayed the significant prospect of a few plant-based active compounds in inhibiting various types of cancer cells, in both (*in vitro*), and (*In vivo*) arrangements, and their roles in causing damage to cancer cells and triggering processes leading to their destruction [21].

Vinca alkaloids, derived from the periwinkle plant are natural compounds that have shown promising results in combating carcinoma treatment due to their ability to disrupt cell division and growth by affecting microtubule structures within cells. They are remarkably utilized for the treatment of certain types of leukemia, lymphomas, and solid tumors such as breast and lung cancers. Two specific vinca alkaloids are often incorporated into combination chemotherapy regimens. (*Vinblastine and Vincristine*). Though more thorough research is required before considering their broad spectrum of usage for efficient cancer treatment, new research has shown their good impacts on cancer management [22].

In recent times, various elements which are obtained from plants have been used to treat people with malignancies in the form of chemotherapy [Table 1]. The above-discussed elements include substances extracted from Madagascar periwinkle herbs such as Velban and Oncovin (both of which are vinca compounds), taxanes, etc. The usage of plant reagents as carcinoma medication has become popular in recent years. The elements extracted from plants used in chemotherapy play a crucial role in the lives of cancer patients [23].

The objective of this review is to evaluate the latest reports and cast a spotlight on the plant chemical constituents and restorative offerings of commonly utilized, yet overlooked curative botanical constituents, with a particular emphasis on their anti-cancer properties.

Table 1: Green Sources against Carcinoma

Class	Characteristics	Use	Action	References
Alkaloids	Bitter Taste, Colorless, Nitrogen-containing bases, Crystalline or liquid at room temperature	Raw material for the synthesis of useful drugs	Analgesic, Antiplasmodial, and Bactericidal effects	[24]
Phenols	Weakly acidic, the Hydroxyl group attached directly to an aromatic ring	Disinfection	Anti-septic, anti-inflammatory, Anti-microbial, Anti-tumor	[25]
Flavonoids	Water soluble, Super Antioxidant, and	In the prevention of oxidative cell damage,	Antioxidants, anticarcinogens,	[12]

	Free radical scavenger	allergies free radical microbes	antimicrobial, anti-tumor	
Saponins	Bitter taste, Foaming properties, hemolytic effect on red blood cells	Emulsifying agent	Expectorant, cough suppressant, hemolytic activity	[25]
Essential oil	Distinctive scent, aroma, and fragrance	In perfumes flavorings and medicines	Medicating soothing relief	[26]
Tannins	Unpleasant taste	In the production of leather and ink, in treating wounds, varicose ulcers, hemorrhoids, frostbite, and burns	Soothing relief regenerates skin, and anti-inflammatory, Diuretics	[25]

Plant bioactive chemicals: Phytochemicals

Chemicals derived from plants are called phytochemicals [27]. The word Phytochemicals originated from the Greek word

“*Phyto*” which means plant. These are the chemicals derived from plant sources via primary and secondary metabolites valued for their therapeutic properties [28]. [Fig 1]

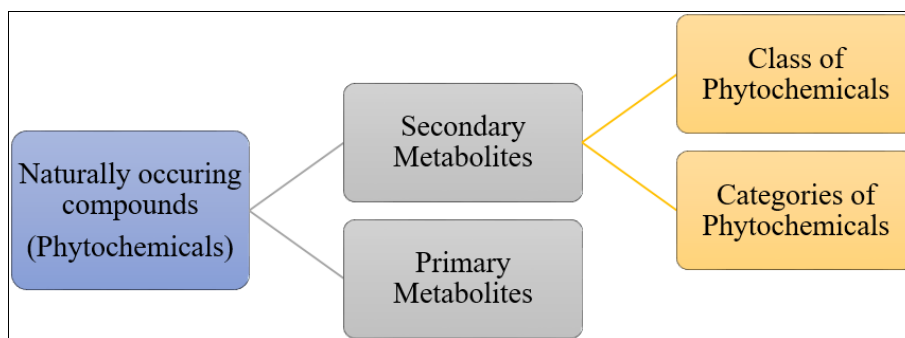


Fig 1: Classification of Phytochemicals

In the treatment of any disease, the usage of medicinal plants is divided into two phytochemical classifications which further divide the phytochemicals into two categories: nitrogen-containing phytochemicals and non-nitrogen-containing phytochemicals in which phytochemicals such as non-protein amino acids, alkaloids, amines, toxic proteins, and glycosides are nitrogen-containing phytochemicals while carbohydrates, fatty acids, organic acids, glycosides, terpenoids and phenolic compounds are termed as non-nitrogen containing phytochemicals [29]. [Fig 2]

The data on herbal-chemical evaluations were added to this review paper from the study of literature administered on Google Scholar, Research Gate, and Science Direct by

utilizing significant terms like carcinoma, plant-based compound, patients, etc. This manuscript mentions the plant-based chemical effects of wasteful herbs on anti-cancer agents and malignant victims. Plant chemicals of marigold were considered as a specimen for its beneficial reaction on cancer-related symptoms such as vomiting, pain, fatigue, etc., or on viable quality have been documented and their antineoplastic endeavors did not yield any positive consequences but it showed promising results regarding their potential usage in cancer management, can possibly be a satisfactory substitute to present curative treatments, which tries to cut down the consequences of radiation therapy [30].

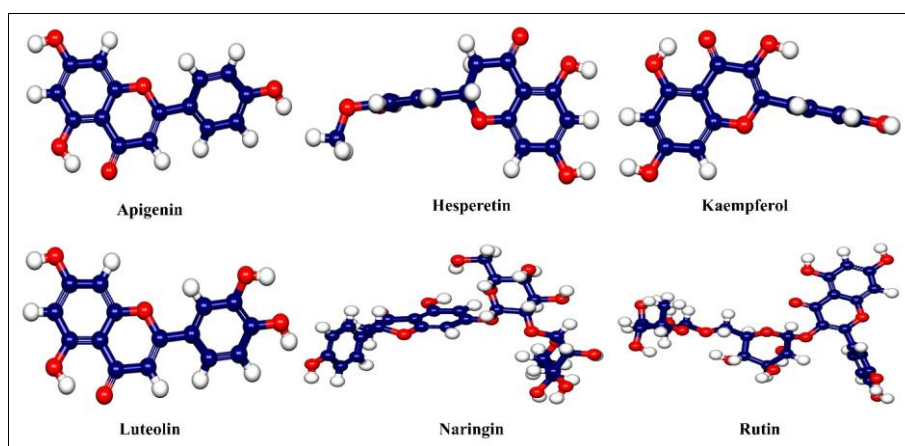


Fig 2: 3D Chemical Structures of Various Plant Phytometabolites [31]

Mechanism behind the anti-cancer therapeutics of phytochemicals

Flavonoids are reactive oxygen species that can restrain the growth of tumor cells by suppressing the nuclear feature of protein kinase B (Akt), (NF- κ B), and the (EGFR/MAPK) epidermal propagation element receptor/mitogen-activated protein kinase also phosphatidylinositide 3-kinases [31]. Similarly, in Alkaloids, the cell cycle governs cytokinesis and propagation and is controlled by various cyclin-reliant

kinases. The curative aim for cancer treatment is the restraint of cell growth by monitoring cell cycle milestones and the introduction of cell cycle arrest. Initiation of transcription factor 3 (ATF3) expression on HCT116 cells by inducing NAG1 via G1 cell cycle arrest following Berberine. By activating G2/M phase arrest in both within the living and glass studies an antiproliferative activity has been illustrated in colorectal adenocarcinoma of humans. The seizure in the G2 phase in U251 cells immensely suppressed tumor

proliferation in the glioma mouse model with the aid of Berberine treatment. Suppression of BGC-823 cell growth via S-phase seizure is achieved by activating Chelerythrine treatment. Finally the arrest of human pancreatic adenocarcinoma cell line-1 and human pancreatic cancer cell line-3 within the quiescent phase to interphase via regulation of the B-cell lymphoma 2 protein family is done by sanguinarine [32].

Polyphenols have anticancer activity over a wide range of cancers. This review shares a glimpse of the possible mechanisms of the anticancer activity of polyphenols against cancer. The regulation of various signaling pathways is mediated by the anti-cancer activity of polyphenols. Bioactive compounds such as quercetin and apigenin aid in the regulation of signaling pathways such as inflammation-related signaling pathways, intrinsic and extrinsic apoptotic pathways, estrogen-related signaling pathways, and cell cycle arrest. Components like flavonoids regulate their antioxidant activities by mediating targeted MAPK- and NFκB-equivalent networking routes. These substances can also because they exhibit symbiotic activity with other antioxidants, they function as a correspondent, such as alpha tocopherol, guiding towards the regrowth of vitamin E. Isoflavonoid such as Biochanin A is a preventive phytochemical and shows activities at odds with the occurrence of ductal carcinoma, after vulnerability to neoplastic agents in juvenile rat. It perhaps negated free radical tension via a notable rise in control of CAT GST, SOD, GPx, and DT-diaphorase (DTD), also a noteworthy deduction of lactate dehydrogenase (LDH) and lipid peroxidation (LPO) properties. Resveratrol action of protection against 17β-estradiol (E2)-induced carcinogenesis was notable in both *in vitro* and *In vivo* conditions and played a role in a notable rise in the expression of nuclear component erythroid-related factor-2 (Nrf-2), which eventually rose the remark of antioxidant genes, involving SOD3, NQO1 and 8-oxoguanine DNA glycosylase 1 (OGG1) [33].

Repressors of multiple proteins that are essential for several cell signaling pathways are termed Tannic acid. It seizes SMAD-dependent gene transcription in response to TGF-β. Aiming molecular targets of various cancers like Lung Cancer and Breast Cancer by forbidding the transcription of Transforming growth factor-β [34] effector genes. By restraining vascular endothelial growth factor and its receptor [35], tannic acids suppress an intensive vascular growth biochemical trajectory in neoplasm. Furthermore, by restraining the appearance of the Sex determining region Y-box 2 gene [36] and suppressing Epidermal growth factor and receptor biochemical trajectory and eventual propagation of cell and growth it highly marks the target of the carcinomic molecular sites of lung cancer. Also, the introduction of tumor-inhibiting proteins by tannic acid. It increases the phosphorylation of p53 responsible for Lung Cancer and gingival Cancer which increases the expression of its target genes namely p21 and BAX majorly responsible for lung and Prostate Cancer. Lastly, at a different level, Tannic acid restorative both cyclin-dependent kinase inhibitor 1 and Bcl-2-associated X protein [37] gene exhibition at once. The restorative expression of the gene of Cyclin-dependent kinase inhibitor 1B [38] and cyclin-dependent kinase inhibitor 2C (CDKN2C) majorly cover the same kind of neoplasm [39].

Native Indian Plants having potential anticancer property *Hibiscus rosa-sinensis* (Shoebblack plant)

Hibiscus is an ariel flower that marks the beginning of

summer. The plant is suitable for moist areas and has several medicinal benefits which help in the treatment of various types of cancer. According to studies *Hibiscus rosa-sinensis* is believed to have numerous health benefits as phytonutrients, antiphlogistic, and antibiotic activities [40]. The plant belongs to the genus *Hibiscus* which further belongs to the various herb species that originate from the family of *Malvaceae* and is generally grown in equatorial and sub-tropical regions [41] it also has multiple benefits for hair as it ceases hair fall, strengthens the roots, averts early graying of hair, etc. [42, 43]. The probable origination of this plant can be traced back to tropical regions. Cultivated all over the Pacific islands, China, and Japan parallelly for many years, it was a general thought that it was originally from South China. *Hibiscus* is acknowledged as a versatile plant because of its curative abilities across various traditions. The herbs' varied range of parts, containing its roots, foliole, fruits, and seeds, contains a diverse array of chemical compounds that contribute to its wide-ranging uses. Only compounds such as Alkaloids, Phenols, Flavonoids, Saponins, Essential oils, and Tannins have the prospective potential for anticancer and antiphlogistic effects. Compounds that have been identified as a key constituent responsible for their therapeutic values, and anti-cancer properties are Vitamin C, Beta-carotene, flavylum (2-phenylchromenylium) ion, and polyphenols [41].

Research also indicates that consumption of *H. rosa sinensis* eliminates the chances of Type-I collagen and α-SMA in perisinusoidal lipocyte growth by preserving internal ROS and GSH content [44]. It is also said that the consumption of the flowers of *H. rosa sinensis* has a preventative impact on skin and breast cancer [45, 46].

Also, a study conducted recently stated that extracts of *H. rosa sinensis* are competent in ductal carcinoma and can protect triple receptor-negative (TRN) lobular carcinoma while maintaining its acuteness for active robust units this plant also reinforces chemo-preventive processes as a contributive which leads to an additional precise diagnostic method to lessen chemotherapy-related harm [46]. *H. rosa sinensis* may also have the capability to minimize severe malignancies resulting in demises by aiding in the establishment of malignancies by halting the progression of carcinomic units [45].

Since ages, *Hibiscus* has been regarded as a very useful plant for its medicinal utility across cultures. In Indian and Chinese cultures, it has been traditionally employed to alleviate cancer-related issues [47].

***Calendula officinalis* (Pot marigold)**

The medicinal plant known as "pot marigold" is a member of the *Daisy family* [48] The plant shows a significant potential to be used as a medicinal herb, turning it into a value rather than just waste. They are regarded as the Asteraceae family's most prolific bloomers [48]. The plant's wide chemical composition contributes to its broad application. Many substances, including tannin, cardiac glycosides, flavonoids, phenolics, quinones, alkaloids, etc., have the potential to have anti-inflammatory and anti-cancer properties [49]. The botanical chemicals obtained from *Calendula officinalis* (Pot marigold) are considered of great use for carcinoma treatment. Pot Marigolds contain large amounts of gallic acid, carotenoids, quercetin, and phenolics, which are credited as the main components responsible for their medicinal effects, specifically their anti-inflammatory and anti-cancer characteristics [50].

Even though there are very few evaluations of autonomous

reports which claim to reinforce carcino-preventive results, contemporary researchers suggest that efflorescence extracts of pot marigolds hinder the evolution of human hepatic malignant cells, the ethanol, and aqueous flower extracts impede the human hepatocellular carcinoma (HepG2) cell line, and obstruct unit expansion in the human fetal renal cells (HEK 293T). Therefore more scientific evidence is required to validate their curative efficacy in the regimen of carcinoma [51].

Since ancient times, pot marigolds have been prized for their

therapeutic benefits by many cultures. They are regarded as a revitalizing agent that uses the advantages of the entire plant to reduce the formation of cancer cells and inflammatory cells that resist treatment. This idea has already been used in South Asian tradition to treat cancer [52]. As mentioned earlier, this herb demonstrates encouraging outcomes regarding its prospective employment in precautionary, and in comfort care. This herb may be used as a relevant asset to carcinoma supervision and control [53].



Fig 3: Some Native Indian Plants Having Anti-Cancer Property

***Tabernaemontana divaricata* (Crape jasmine)**

Tabernaemontana divaricata, sometimes referred to as the pinwheel flower, is a perennial bulbous plant revered in Chinese cultures for its striking, dramatic colors as well as its healing properties. In Southeast Asia, it is frequently accessible in every home [54]. The plant belongs to the *Tabernaemontana* subfamily, which contains the *T. divaricata* species, which is a native member of the *Apocynaceae* family [55]. Typically thrives in sparsely forested areas and small branches of mountains, [55]. Its bitter flavor has several potential healing effects and aids in the treatment of various intestinal disorders [56]. This plant is a native of Southeast Asia, particularly India [57]. A wide range of beneficial properties, including anti-rheumatic, carminative, phytonutritive, pain-relieving, anti-bacterial and fungal, glucose-lowering, anti-cancer, and hepatoprotective effects, are present in this plant. The study claims that the shrub includes a range of plant-based substances, including bioflavonoids, enzymes, corticosteroids, alkaloids, and phenolic acids [58]. According to recent studies, the alkaloids 2,2'-[4-(Dimethylamino) butane-1 and 6,7-epoxy-8-oxo-vincadifformine are key elements responsible for this shrub's full therapeutic potential [59].

As per the latest research-based report, Crepe jasmine was found to have anti-tumor properties in the case of MCF-7 (breast), 502713 (colon), HCT-15 (colon), PC-3 (prostate), and HT-29 (colon) cell lines, according to the most recent research-based report. It showed that topoisomerase inhibitory and hydroxyl radical scavenging properties are included in the

leaf extracts used in immunosuppressive procedures (ethyl acetate, hexane, methanol, and chloroform). While the other three colon carcinoma unit lines were shown to be effective with the Trichloromethane extract, only one colorectal carcinoma unit line (502713) was found to be effective with the ethyl ethanoate extract. Furthermore, in the DNA gyrase tranquil analysis, the 1-acetoxy ethane extracts carefully inhibited topo-II. As one of the most researched plants, the pinwheel flower is the subject of numerous AgNps research studies [60]. Similarly, the anti-tumor characteristics against MCF-7 cell lines. The conclusion demonstrates that anabolized AgNps obtained from *T. divaricata* extracts might decrease calcite-influenced cataractogenesis in a living system while preserving convex calcium equilibrium by ignoring modification in vital bulging macronutrients [61]. Also, the following study states that pinwheel flowers are safe and efficacious for treating abdominal neoplasm and alveolus cancer on the other hand it is difficult to talk about the least effect of pinwheel flower chemicals as it is too early and more thorough research should be conducted to understand its anti-cancer properties [58, 62].

Overall, based on the studies conducted by Ghosh, [58] pinwheel flowers may aid in the healing management for cancer patients, therefore, more thorough research should be conducted.

***Catharanthus Roseus* (Madagascar periwinkle)**

Madagascar periwinkle is native to the Red Island and is also grown in Tanzania, Ukiriguru, and other parts of the world

[63]. This shrub is used both for adornment and medical purposes. Its scientific name is *Catharanthus Roseus*. This plant provides us with carcinoma combating compounds such as oncovin and Velban. With a focus on its anti-cancer characteristics, it possesses a wide range of biological properties, including anti-diabetic, antispasmodic, antioxidant, hypotensive, and anti-microbial properties [64]. Preliminary research states that plant-based compounds in this shrub have curative benefits for numerous tumor unit lines comprising neoplasm of the lymph nodes, neck malignancies, modifying liver tissue, and ductal malignancies [65]. According to the reports, institutionalized antineoplastic biotic chemicals i.e., Lemblastine and Leurocristine are extracted from the stalk and leaflet of this medicinal shrub which impedes the increase of metastatic lumps. It is responsible for the comprehensive viability in the victims with improved or transmutation skin carcinoma in children and cases with metastatic lymphatic node carcinoma. Many prospects of the Methyl Alcohol basic extracts of *C. roseus* were established to demonstrate the notable antitumor action opposed to many cell varieties in the artificial environment, and note-worthy significant action was discovered against antibiotic-resistant lump types [66]. There is a probability that this shrub has synergistic effects with concurrent therapy agents and is also appropriate for patients in chemotherapy.

C. roseus is one of a kind out of twenty-one thousand vital

curative botanicals discovered yet. It is used for treating many ailments such as leukemia, mouth ulcers, sore mouth, and diabetes. It fabricates approximately one hundred and thirty phytochemicals i.e., alkaloids such as Sandril, Ajmalicine, and Raubasine. Anti-skin cancer properties are demonstrated by Vincalcucoblastin and Leurocristine. Distinct phytochemicals i.e., alkaloids are manufactured by distinct parts of this shrub, from which rhizome husk rind cortex manufactures the largest amount i.e., approximately 1.79% of the plant's alkaloids.

Few research supports the shrub's anti-infectious properties in opposition to enterobacteria, *Pseudomonas aeruginosa*, etc. Its plant-based nutrients and anti-malignant activities were reported but intensive research is required to inspect its anti-metastatic properties [66]. The results obtained from contemporary studies suggest that the effective use of *C. roseus* basic aqueous isolations to distinctive properties of hindering the propagation of preserved lines of human T lymph cells and encouraging standard incidental blood-resistant cell procreation. This shrub's curative properties ought to be constructive in victims of this sort of malignancy [67].

Table 2 shows a brief knowledge of other plant derived phytochemicals and their mode of anti-cancer actions in a tabulated way.

Table 1: Comprehensive Index of organic chemicals with their associated anti-carcinomic activities

Natural compound	Source	Type of cancer	Outcome	Reference (s)
Curcumin	Turmeric	Head and neck cancer, Lung neoplasm, AML, Ductal carcinoma, Colon neoplasm, Gastric neoplasm	Lower vulnerability of CD44 and CD166 in colon neoplasm that is resistant to chemotherapy Inhibition of ALDH+ /CD133 + cell tumor propagation Gli-1, Notch-1, and cyclin D, Downregulation Cyclin D1's mRNA and protein expression are downregulated	[19]
Proanthocyanidins	Grape seeds	Pancreatic adenocarcinoma	Reversal of the epithelial-mesenchymal transition process and Reduction of NF- κ B expression	[67]
Tannins/ Tannic acid	<i>Syzygium guineense</i> , Gall nuts	Lung cancer, Prostate cancer, Pancreatic cancer, Colon neoplasm, Liver carcinoma, Triple-negative Breast neoplasm, Ovarian neoplasm, Embryonic neoplasm	By inhibiting cellular propagation through β -catenin produced by Wnt3a Diminish the JAK/STAT pathway. Stop the cell cycle by arresting the G1/S phase. Reduce the EMT and NF- κ B activation generated by TGF- β . Work in concert with oxaliplatin and cisplatin Encourages extrinsic apoptosis triggered by TRAIL.	[67]
Quercetin	Nuts, tea, onions, apple and in plant sources	Triple-negative Breast cancer, Colorectal cancer	TRAIL-induced extrinsic apoptosis is encouraged.	[67]

Safety and Toxicity of Plant-based Chemicals in Cancer Patients

The following article emphasizes the utilization of herbal medicines for treating carcinoma, showcasing positive outcomes in both *in vitro* and *In vivo* settings. Multiple compounds, that are extracted from plants, such as vinblastine, vincristine, dihydroartemisinin, artesunate, and berberine, show characteristics such as impeding tumor growth and inducing apoptosis. Meanwhile, these finding shows positive results in managing cancer, extensive Phase III clinical trials with regulatory approval are necessary for drug development, as some pharmaceutical companies rush human

testing, possibly leading to inadequate safety and efficacy data due to investor pressures. The usage of plant-based compounds for managing cancer is beneficiary as these are often less toxic, however, it may pose unknown risks when used without any regulation. Regulatory harmonization and standardized production are vital for ensuring the quality, safety, and efficacy of herbal drugs. Moreover, operations of information technology and bioinformatics amplify drug discovery through databases and *in silico* methods, even though threats remain in predicting the roles of several phytochemicals within complex formulations.

Developmental Challenges of Phytochemicals on various level

The developmental obstructions and limitations of phytochemicals encompass various aspects. This comprises the requirement of comprehensive characterization of their physical and chemical properties, challenges in enhancing their potency and bioavailability, addressing issues related to crystal structures and formulation, ensuring appropriate regulatory compliance, and navigating potential toxicity concerns. Furthermore, the debate surrounding the effects of natural compounds, differences between dietary supplements and prescription drug regulations, and the complexity of their interactions additionally adds to the challenges in developing phytochemicals as effective drugs.

Conclusion

The ever-growing number of fatalities caused by carcinoma has caused an overriding urgency to discover advanced cures for the same. Plant-based chemicals have always been a reliable source of novel cures for societal ailments. Therefore, plant-based chemicals can be a prospective source for the development of carcano-preventive medications. Only a few plants that have undergone research for carcinoma have successfully passed in a fabricated condition and tests on Animals and are currently undergoing medicinal evaluations to evaluate their efficacy. The curative quality of the wasteful plants such as *Hibiscus rosa-sinensis* (Shoebblack plant), *Calendula officinalis* (Pot marigold), *T. divaricata* (crape jasmine), and *Catharanthus Roseus* (Madagascar periwinkle) was effectively established by their phytochemical analysis and their functions on cancer patients. Therefore, these plants can also probably be used as complementary drugs for treatment along with modern carcano-preventive remedies, which are presently being used. Although some other plant-based chemicals could have also been added to this list, due to the lack of curative evidence of these chemicals on carcinoma prevention is available, they are not mentioned in the review article. Additionally, there is still more to be discovered concerning the medicinal absorption pharmacological responses, optimal doses, overtime assurance, and negative consequences of botanical chemicals that have been suggested as remedies for malignancies. Henceforth, it is too early to conclude the carcinoma-preventive capabilities of some plant-based chemicals. They involve Cellular senescence, stimulation of programmed cell death, combating ROS and RNS, mutagen deactivation, proliferation resistant, and prevention of vascular development, or an amalgamation of these pathways. According to studies, multiple plant-based chemicals are believed to have a much greater impact and produce superior treatment entities on ailment prevention and treatment the advanced results seem encouraging, and additional study designs on this subject are especially necessary.

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Conflict of interest

The author hereby declares, regarding the publishing of this paper, that there is no conflict of interest.

References

1. Youness R, Kamel R, Elkasabgy NA, Shao P, Farag MA. Recent Advances in Tannic Acid (Gallotannin)

Anticancer Activities and Drug Delivery Systems for Efficacy Improvement: A Comprehensive Review. *Molecules* (Basel, Switzerland). 2021;26(5):1486. Available from:

<https://doi.org/10.3390/molecules26051486>

2. Abdal Dayem, A Choi, HY Yang, GM Kim, KS Saha SK, Cho SG. The Anti-Cancer Effect of Polyphenols against Breast Cancer and Cancer Stem Cells: Molecular Mechanisms. *Nutrients*. 2016;8(9):581. Available from: <https://doi.org/10.3390/nu809058>
3. Adhirajan N, Ravi Kumar T, Shanmugasundaram N, Babu M. *In vivo* and *in vitro* evaluation of hair growth potential of *Hibiscus rosa-sinensis* Linn. *Journal of Ethnopharmacology*. 2003;88(2-3):235-239. Available from: [https://doi.org/10.1016/S0378-8741\(03\)00231-9](https://doi.org/10.1016/S0378-8741(03)00231-9)
4. Agnantis NJ, Goussia A, Zagorianakou P, Bai M. Alterations of the Cell Cycle Regulating Proteins in Invasive Breast Cancer. In: *Handbook of Immunohistochemistry and In situ Hybridization of Human Carcinomas*. 2002;1:425-438. Elsevier. Available from: [https://doi.org/10.1016/S1874-5784\(04\)80053-9](https://doi.org/10.1016/S1874-5784(04)80053-9)
5. Lusweti A, Wabuyele E, Ssegawa P, Mauremootoo J. *Catharanthus Roseus* (Madagascar Periwinkle). *Bionet-International Secretariat-UK*. (n.d.).
6. Ahmad NH, Rahim RA, Mat I. *Catharanthus Roseus* Aqueous Extract is Cytotoxic to Jurkat Leukaemic T-cells but Induces the Proliferation of Normal Peripheral Blood Mononuclear Cells. *Tropical Life Sciences Research*. 2010;21(2):101-113.
7. Ahmed MB, Islam SU, Alghamdi AAA, Kamran M, Ahsan H, Lee YS. Phytochemicals as Chemo-Preventive Agents and Signaling Molecule Modulators: Current Role in Cancer Therapeutics and Inflammation. *International Journal of Molecular Sciences*. 2022;23(24):15765. Available from: <https://doi.org/10.3390/ijms232415765>
8. Awosika AO, Below J, Das JM. *Vincristine*. *Treasure Island (FL): StatPearls Publishing; Bookshelf ID: NBK537122. PMID: 30725807*. (n.d.).
9. *Ayurveda Kerala. Hibiscus for Hair: Benefits, Uses & More! India; c2022, October 28.*
10. Bayala B, Bassole IH, Scifo R, Gnoula C, Morel L, Lobaccaro JMA, *et al.* Anticancer activity of essential oils and their chemical components: A review. *American Journal of Cancer Research*. 2014;4(6):591-607. Available from: <https://doi.org/10.1016/j.jtcm.2016.01.005/>
11. Breslin A. *The Chemical Composition of Green Plants*. *Sciencing; c2017*. (n.d.).
12. Chahar MK, Sharma N, Dobhal MP, Joshi YC. Flavonoids: A versatile source of anticancer drugs. *Pharmacognosy Reviews*. 2011;5(9):1-12. Available from: <https://doi.org/10.4103/0973-7847.79093>
13. Cruceriu D, Balacescu O, Rakosy E. *Calendula officinalis*: Potential Roles in Cancer Treatment and Palliative Care. *Integrative Cancer Therapies*. 2018a;17(4):1068-1078. Available from: <https://doi.org/10.1177/1534735418803766/>
14. Cruceriu D, Balacescu O, Rakosy E. *Calendula officinalis*: Potential Roles in Cancer Treatment and Palliative Care. *Integrative Cancer Therapies*. 2018b;17(4):1068-1078. Available from: <https://doi.org/10.1177/1534735418803766/>
15. De La Taille, Hayek Buttyan, Bagiella, Burchardt, Katz. Effects of a phytotherapeutic agent, PC-SPES, on

- prostate cancer: A preliminary investigation on human cell lines and patients: Effects of pc-spes on prostate cancer. *BJU International*. 2001;84(7):845–850. Available from: <https://doi.org/10.1046/j.1464-410x.1999.00285.x>
16. Rowinsky E. The Vinca Alkaloids. In: Kufe DW, Pollock RE, Weichselbaum RR, *et al.*, editors. *Holland-Frei Cancer Medicine*. 2003; 6th edition. Hamilton (ON): BC Decker.
 17. Ferlay J, Colombet M, Soerjomataram I, Parkin DM, Piñeros M, Znaor A, Bray F. Cancer statistics for the year 2020: An overview. *International Journal of Cancer*. 2021;149(4):778–789. Available from: <https://doi.org/10.1002/ijc.33588>
 18. Flanders KC, Burmester JK. Medical applications of transforming growth factor-beta. *Clinical Medicine & Research*. 2003;1(1):13-20. Available from: <https://doi.org/10.3121/cmr.1.1.13/>
 19. Ghosh P, Poddar S, Chatterjee S. Morphological features, phytochemical and ethnopharmacological attributes of *Tabernaemontana divaricata* Linn.: A comprehensive review. *Journal of Pharmacognosy and Phytochemistry*. 2021;10(6):31–36. Available from: <https://doi.org/10.22271/phyto.2021.v10.i6a.14253/>
 20. Goldberg KH, Yin AC, Mupparapu A, Retzbach EP, Goldberg GS, Yang CF. Components in aqueous *Hibiscus rosa-sinensis* flower extract inhibit *in vitro* melanoma cell growth. *Journal of Traditional and Complementary Medicine*. 2017;7(1):45-49. Available from: <https://doi.org/10.1016/j.jtcme.2017.01.001>
 21. Hashem S, Ali TA, Akhtar S, Nisar S, Sageena G, Ali S, *et al.* Targeting cancer signaling pathways by natural products: Exploring promising anti-cancer agents. *Biomed Pharmacother*. 2022;150:113054. <https://doi.org/10.1016/j.biopha.2022.113054/>
 22. Hosseini A, Ghorbani A. Cancer therapy with phytochemicals: Evidence from clinical studies. *Avicenna J Phytomed*. 2015;5(2):84-97.
 23. Housing News Desk. Chandni flower: How to grow and care for Togor flower? *Housing.com*. 2023 Oct 6.
 24. Conservatory of Flowers. *Tabernaemontana divaricata*. San Francisco Recreation and Park Department; c2019.
 25. Naidu RT. *Hibiscus (Hibiscus rosa-sinensis)*. *Infopedia.gov.singapore*, I. 2020 Dec.
 26. Mishra JN, Verma NK. A brief study on *Catharanthus Roseus*: A review. 2017, 2(2).
 27. Ifemeje JC. Biological Functions and Anti-nutritional Effects of Phytochemicals in Living System. *IOSR J Pharm Biol Sci.*; c2015. <https://doi.org/10.9790/3008-10231019/>
 28. Kawale DK. An Overview of Major Classes of Phytochemicals: Their Types and Role in Disease Prevention. *Hislopia J*. 2016, 9(1-2).
 29. Khan T, Ali M, Khan A, Nisar P, Jan SA, Afridi S, Shinwari ZK. Anticancer Plants: A Review of the Active Phytochemicals, Applications in Animal Models, and Regulatory Aspects. *Biomolecules*. 2019;10(1):47. <https://doi.org/10.3390/biom10010047/>
 30. Khristi V, Patel VH. Therapeutic Potential of *Hibiscus rosa sinensis*: A Review. *Int J Nutr Diet*. 2017;4(2):105-123. <https://doi.org/10.17654/ND004020105/>
 31. Kleszcz R, Majchrzak-Celińska A, Baer-Dubowska W. Tannins in cancer prevention and therapy. *Br J Pharmacol*; c2023. <https://doi.org/10.1111/bph.16224/>
 32. Koklesova L, Liskova A, Samec M, Zhai K, Abotaleb M, Ashrafizadeh M, *et al.* Carotenoids in Cancer Metastasis-Status Quo and Outlook. *Biomolecules*. 2020;10(12):1653. <https://doi.org/10.3390/biom10121653/>
 33. Kopustinskiene DM, Jakstas V, Savickas A, Bernatoniene J. Flavonoids as Anticancer Agents. *Nutrients*. 2020;12(2):457. <https://doi.org/10.3390/nu12020457/>
 34. Kumari P, Ujala, Bhargava B. Phytochemicals from edible flowers: Opening a new arena for healthy lifestyle. *J Funct Foods*. 2021;78:104375. <https://doi.org/10.1016/j.jff.2021.104375/>
 35. Liu X, Wang N, Fan S, Zheng X, Yang Y, Zhu Y, *et al.* The citrus flavonoid naringenin confers protection in a murine endotoxaemia model through AMPK-ATF3-dependent negative regulation of the TLR4 signaling pathway. *Sci. Rep*. 2016;6(1):39735. <https://doi.org/10.1038/srep39735/>
 36. Lu JJ, Bao JL, Chen XP, Huang M, Wang YT. Alkaloids Isolated from Natural Herbs as the Anticancer Agents. *Evid Based Complement Alternat Med.*; c2012. p. 1-12. <https://doi.org/10.1155/2012/485042/>
 37. Mir RA, Ahanger MA, Agarwal RM. Marigold: From Mandap to Medicine and from Ornamentation to Remediation. *Am J Plant Sci*. 2019;10(02):309-338. <https://doi.org/10.4236/ajps.2019.102024/>
 38. Molyneux RJ, Lee ST, Gardner DR, Panter KE, James LF. Phytochemicals: The good, the bad and the ugly? *Phytochemistry*. 2007;68(22-24):2973-2985. <https://doi.org/10.1016/j.phytochem.2007.09.004/>
 39. Moudi M, Go R, Yien CYS, Nazre M. Vinca alkaloids. *Int J Prev Med*. 2013;4(11):1231-1235.
 40. Janel N, Noll C. Polyphenols in Chronic Diseases and their Mechanisms of Action. *Polyphenols in Human Health and Disease*, source; c2014.
 41. Newman DJ, Cragg GM. Natural Products as Sources of New Drugs from 1981 to 2014. *J Nat Prod*. 2016;79(3):629-661. [<https://doi.org/10.1021/>]
 42. Nguyen C, Baskaran K, Pupulin A, Ruvinov I, Zaitoon O, Grewal S, Scaria B, Mehaidli A, Vegh C, Pandey S. *Hibiscus* flower extract selectively induces apoptosis in breast cancer cells and positively interacts with common chemotherapeutics. *BMC Complementary and Alternative Medicine*. 2019;19(1):98. <https://doi.org/10.1186/s12906-019-2505-9/>
 43. Types of Cancer, NIH: National Institute of, N. N. I. of. (n.d.).
 44. Cancer Staging. NIH: National Institute of, N. I. of. (n.d.).
 45. Nussbaumer S, Bonnabry P, Veuthey JL, Fleury-Souverain S. Analysis of anticancer drugs: A review. *Talanta*. 2011;85(5):2265-2289. <https://doi.org/10.1016/j.talanta.2011.08.034/>
 46. Pradeep Parihar HS, Leena Parihar. (n.d.). Review on cancer and anticancerous properties of some medicinal plants. *Journal of Medical Plants Research*. 2011, 5(10). <https://doi.org/10.5897/JMPR/>
 47. Preetha Devaraj, Renganathan Arun, Chirom Aarti, Prachi Kumari. (n.d.). Synthesis and characterization of silver nanoparticles using *Tabernaemontana divaricata* and its cytotoxic activity against MCF-7 cell line. *Int. J Pharm Pharm Sci*. 2013;6(8):86-90.
 48. Prof Dr Ali Esmail Al-Snafi. Chemical constituents, pharmacological effects, and therapeutic importance of *Hibiscus rosa-sinensis*: A review. July 2018;8(7):101-

119. ISSN: 2319-4219.
49. Renjini KR, Gopakumar G, Latha MS. The Medicinal Properties of Phytochemicals in *Catharanthus Roseus*: A Review. *European Journal of Pharmaceutical and Medical Research*. 2017;4(11):545-551. ISSN 2394-3211.
 50. Riaz M, Khalid R, Afzal M, Anjum F, Fatima H, Zia S, *et al*. Phyto-bioactive compounds as therapeutic agents for human diseases: A review. *Food Science & Nutrition*. 2023;11(6):2500-2529. <https://doi.org/10.1002/fsn3.3308/>
 51. Roberts RE. The extracellular signal-regulated kinase (ERK) pathway: A potential therapeutic target in hypertension. *Journal of Experimental Pharmacology*. 2012;4:77-83. <https://doi.org/10.2147/JEP.S28907/>
 52. Sadhana Raut, Poonam Shende, Nupur Gargate, Harshad Kapare. Pharmacognostic and Pharmacological Aspects on *Tabernaemontana divaricata* Plant. *Acta Scientific Pharmacology*. 2020, 3(10). Available at: <https://actascientific.com/ASPC/pdf/ASPC-03-0207.pdf/>
 53. Saklani A, Kutty S. Plant-derived compounds in clinical trials. *Drug Discovery Today*. 2008;13(3-4):161-171. <https://doi.org/10.1016/j.drudis.2007.10.010/>
 54. Sathishkumar K, Chaturvedi M, Das P, Stephen S, Mathur P. Cancer incidence estimates for 2022 & projection for 2025: Result from National Cancer Registry Programme, India. *Indian Journal of Medical Research*. 2022 Oct-Nov;156(4&5):598-607. DOI: 10.4103/ijmr.ijmr_1821_22.
 55. Sharif moghaddasi Mohammad, Hamed Haddad Kashani. Pot marigold (*Calendula officinalis*) medicinal usage and cultivation. *Scientific Research and Essays*. 2012;7(14):1468-1472. Available online at <http://www.academicjournals.org/SRE> DOI: 10.5897/SRE11.630 ISSN 1992-2248 ©2012.
 56. Shibuya M. Vascular Endothelial Growth Factor (VEGF) and Its Receptor (VEGFR) Signaling in Angiogenesis: A Crucial Target for Anti- and Pro-Angiogenic Therapies. *Genes & Cancer*. 2011;2(12):1097-1105. <https://doi.org/10.1177/1947601911423031/>
 57. Stevens GHJ, Robles L. Neuromuscular complications. In *Supportive Oncology*. 2011;283-291. Elsevier.
 58. Szopa A, Klimek-Szczykutowicz M. Pot Marigold (*Calendula officinalis* L.): A Position in class phytotherapy and newly documented activities. *Acta Scientiarum Polonorum Hortorum Cultus*. 2020;19(3):47-61. <https://doi.org/10.24326/asphc.2020.3.5/>
 59. Taouji S, Wolf S, Chevet E. Oligomerization in Endoplasmic Reticulum Stress Signaling. In *Progress in Molecular Biology and Translational Science*. 2013;117:465-484. <https://doi.org/10.1016/B978-0-12-386931-9.00017-9/>
 60. Thenaruvi Herbal Village. Crape Jasmine (Nandyarvattam). Retrieved from T. herbal; c2020.
 61. Thind TS, Agrawal SK, Saxena AK, Arora S. Studies on cytotoxic, hydroxyl radical scavenging, and topoisomerase inhibitory activities of extracts of *Tabernaemontana divaricata* (L.) R.Br. *Ex Roem. And Schult. Food and Chemical Toxicology*. 2008;46(8):2922-2927. <https://doi.org/10.1016/j.fct.2008.05.036/>
 62. Wang H, Khor TO, Shu L, Su ZY, Fuentes F, Lee JH, Kong ANT. Plants vs. cancer: A review on natural phytochemicals in preventing and treating cancers and their druggability. *Anti-Cancer Agents in Medicinal Chemistry*. 2012;12(10):1281-1305. <https://doi.org/10.2174/1871520128038330263/>
 63. Wikipedia. *Calendula officinalis*. Wikipedia. (n.d.-a).
 64. Wikipedia. *Tabernaemontana divaricata*. Wikipedia. (n.d).
 65. Yun D, Yoon SY, Park SJ, Park YJ. The Anticancer Effect of Natural Plant Alkaloid Isoquinolines. *International Journal of Molecular Sciences*. 2021;22(4):1653. <https://doi.org/10.3390/ijms22041653/>
 66. Zhang S, Cui W. Sox2, a key factor in the regulation of pluripotency and neural differentiation. *World Journal of Stem Cells*. 2014;6(3):305-311. <https://doi.org/10.4252/wjsc.v6.i3.305/>
 67. Zhuang SR, Chen SL, Tsai JH, Huang CC, Wu TC, Liu WS, *et al*. Effect of citronellol and the Chinese medical herb complex on cellular immunity of cancer patients receiving chemotherapy / radiotherapy. *Phytotherapy Research*. 2009;23(6):785-790. <https://doi.org/10.1002/ptr.2623/>