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Review Article

Significant Role of Medicinal Botanicals Hostile to Cancer

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Abstract: In medical systems, medicinal plants have always held an important place. Plant phytochemicals with known biological activity, such as antiviral, antibacterial, and anticancer properties, are crucial in treatment. It has demonstrated little to no negative effects in recent years and is regarded as safe to use. The use of medicinal plants is essential for preventing illnesses, especially cancer, which is the second leading cause of death worldwide. It was discovered that scientists had been effective in finding anti-cancer compounds up to this point such as eugenol, allicin, catechins, curcumin ursolic acid, anethol, lycopene, resveratrol, 6-gingerol from ginger, tomato, garlic, turmeric, blueberries, milk thistle, cranberries, walnuts which can assist in blocking or activating cancer cell activation signalling pathways cycloxigenase, matrix metalloproteinases MMP, COX-2, topoisomerase enzyme, Bax, Bak proteins and accelerating enzymes (antioxidant potential) that protect the body. Cancer is now treated with a few plant-based products and their phytoconstituents. Even though the management and control of cancer progression have advanced significantly, there are still many gaps and untapped prospects. As a result, this review article emphasizes the value of medicinal plants in maintaining human health as well as lists the phytochemicals from medicinal plants that can be used to cure cancer.

Keywords: Medicinal plants, Cancer, Phytochemicals, Secondary metabolites, Therapeutics.

1. INTRODUCTION

Ancient therapeutic knowledge has been pioneered ever since the beginning of the historic era, which has been saved as well as transferred to every single corner of the globe. All the ancient discoveries regarding drug detection come in nature along with the herbal side. Countless crucial drugs are obtained through organic products or natural means. Plants are one of the extremely significant means of novel pharmacologically effective elements which enter the medicine production sector for the formation of drugs, having a sustained record in the therapy of numerous disorders. To date, there are plant species (35,000-70,000) that have already been analyzed for medicinal purposes [1]. Countless individuals have relied on medicinal plants for basic healthcare since prehistoric times. The traditional knowledge of local communities and indigenous peoples is closely related to this type of traditional medicine. Due to the fact that many traditional herbal practices have contributed to the discovery of medications, interest in traditional knowledge has increased. Ethnobotany is the name of the scientific field that investigates how local groups and indigenous peoples use plants. In reality, there are various approaches that can be used to choose plants for pharmacological studies, and the ethnobotanical paradigm is just one of them. Drugs found via ethnobotanical leads include aspirin, codeine, ipecac, reserpine, and others. In fact, it gives the scientist quick hints for choosing the candidate species for more research [2, 3]. Paul Alan Cox and Michael L. J. Balick deserve credit for exploring and emphasizing the role that conventional knowledge plays in contemporary drug development in the early 1990s [3]. The discovery of quinine is regarded as the greatest medical advance of the seventeenth century. Since the 1600s, quinine, a substance found in the bark of the cinchona (*Cinchona pubescens*) tree, has been used to alleviate malaria. Indigenous consumption is also the source of the discovery of artemisinin, another antimalarial medication. Since the

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discovery of artemisinin, the Artemisia annua plant has been used in China to cure fevers for at least two millennia. The value of documenting conventional understanding scientifically is clearly demonstrated by these examples. Despite the development of new chemical, biological, and screening methods, conventional knowledge persists to be extremely applicable as natural product research progresses [3]. Plants possessing ethnopharmacological ability are principal resources of medication intended for initial drug detection concerning their novel ethnopharmacological uses. In the current era, the exploration of drugs originates from plants depending on their bioactivity. About 1/3 (39.1 %) of each of the authorized drugs by the FDA are of natural source. Natural compounds are considered one of the most valuable bases in the procedure of drug detection. In the practice of drug finding, the incidence of more than 200,000 natural metabolites represents the diverse bioactive properties giving immense importance to natural products. However, therapeutic (medicinal) plants happen to be the most prominent sources of natural products [1]. Between 350,000 and almost half a million species of vascular plants, or 10 % of all plants, are thought to be utilized as medicines. Initially, the trial-and-error approach was employed to treat illnesses or even just to feel better, and in this way, valuable plants with positive properties were identified [4]. The major goal of this review is to highlight the usefulness and significance of medicinal plants for maintaining human health, as well as their phytochemicals for oncogenic treatment, which represents a novel strategy that may contribute to the advancement of the pharmaceutical industry.

2. MEDICINAL PLANTS

Medicinal plants can be described as plants that hold healing attributes otherwise, they employ positive pharmacologic outcomes over an animal or human health [5]. Medicinal Plants are currently in need, also their acknowledgment is gradually rising. Unquestionably, plants possess a significant position in offering important services in bio-networks. However, devoid of plants individuals as well as other living organisms are unable to thrive in the manner living beings would. Nonetheless, herbals, particularly medicinal herbs have continuously operated as a general indicator of the health of bionetwork. Also, medicinal plants have undeniably been reflected by individuals ever since the prehistoric era. It can be supposed that previously as well as early human beings acknowledged as well as manipulated plants surrounding them for shelter, clothes nutrition, along with fuel because they turn out to have awareness of their properties. Medicinal plants have been transmuted in some of the earliest disciplines in nations like Greece, Egypt, India as well as in China. Plants were frequently utilized as medicine as well as a disinfectant in ancient Persia (currently named Iran). Meanwhile, above a tenth of the plant varieties (greater than 50,000 species) are employed in cosmetics along with therapeutic products. Though the distribution of medicinal plants is not the same across the globe, in addition, those medicinal herbs are assembled largely through the natural world. Certainly, the need for natural resources has been boosted by dint of 8 % to 15 % in Asia, Europe along with North America annually in current years. The phrase medicinal plant describes a range of vegetation that holds therapeutic features. Such plants are a valuable resource of components that can be utilized for drug-making (Figure 1). The portion of medicinal plants which might be consumed is distinct kinds of skin, seeds, flowers, fruit, leaf, root, or even entire plant. Dynamic components inside major portions of such plants pose explicit or else implicit healing results thus being employed as medicinal agents. The parts of such plants carry a variety of substances that are being formed and then accumulated which are described as active substances, exerting physiological impacts on living organisms. Human beings are dependent upon natural plant substances to be acquainted with therapeutic requirements for sustaining health as well as disease treatment. Medicinal plants are utilized for medication since they have specific properties, which include interactive activities. The components of plants might act together then such an interface would be advantageous or unfavorable to any of them or else reduce the toxic consequences of both [6].

The most primitive data being acknowledged is the utilization of 1000 plants which includes *Cedrus duham* species, *Papaver somniferum* L, *Cupressus sempervirens* L*, Glycyrrhiza glabra* L, along with *Commiphora myrrha* Engl. Such drugs (Table 1) were originally applied in raw types involving teas, powders, dressings, and tinctures [7].

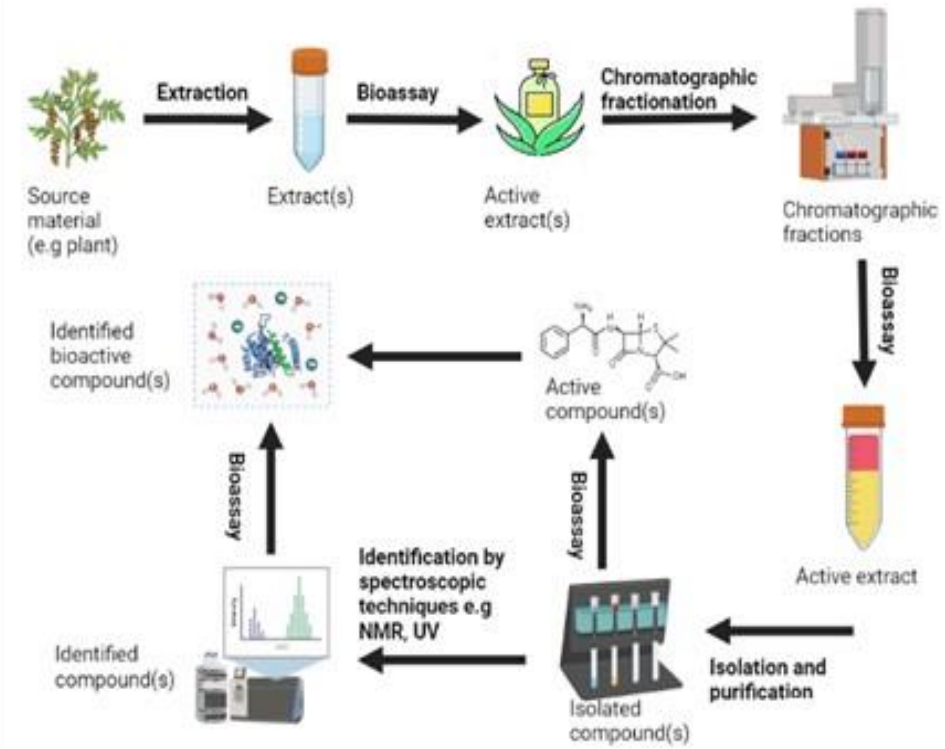

Fig. 1. Timeline for discovering natural drugs.

Table 1. Drug compounds isolated from medicinal plants [6].

Drug	Plant	Activity
Taxol	*Taxus brevifollis*	Anti-cancerous
Morphine	*Papaver somniferum*	Narcotic and powerful pain reliever
Serpentine	*Rauwolfia serpentia*	Hypertension
Quinine	*Cinchona* sp.	Antimalarial
Vincristine	*Catharanthus rosesus*	Anti-cancerous

2.1. Secondary Metabolites of Plants

The therapeutic power of plant components is predominantly because of the blend of components designated as the secondary metabolites of plants (SMoPs). SMoPs are a distinct biochemical cluster of elements formed through plant cells via secondary metabolic paths (derivatives of the primary metabolic paths). Contrary to the primary metabolites being tangled in the key metabolic pathways which are fundamental for subsistence secondary metabolites of plants are not needed for life as well as development, however, they portray significant tasks in interspecies defense besides antagonism. Currently, there are two hundred thousand diverse secondary metabolites of plants being isolated as well as recognized. SMoPs are categorized as shown in (Figure 2) for their chemical

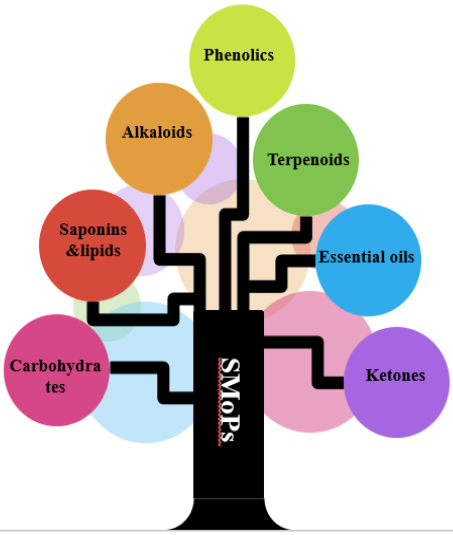

Fig. 2. Categorization of secondary metabolites of plants.

arrangements otherwise biosynthesis paths [8].

2.2. Antioxidants

Antioxidants have been reported to stop oxidative damage instigated by free radicals. All organisms are protected from the attack of free radicals by the defense processes which search as well as stabilize the free radicals nonetheless while the formation speed of free radicals surpasses then oxidative stress is created. It is a detrimental process that can harm cell structures involving lipids, DNA, as well as proteins. So, there is an upsurge in the application of naturally occurring antioxidants and their use in cosmetics, medicine, foods, or raw materials instead of man-made materials [8]. The antioxidant depicts a defense approach to which the body of a human is safe from free radicals which create oxidative harm. However, free radicals' abundance advances toward cellular stress which ultimately harms cellular structures as well as their functions, DNA, and proteins. Reactive oxygen species commonly known as ROS are a class of reactive compounds, free radicals, as well as ions produced through oxygen. Medicinal plants have emerged as possible natural antioxidant sources, producing a variety of anti-oxidative chemicals with medicinal and therapeutic characteristics. Antioxidant-containing drug formulations are commonly used to treat and prevent a wide range of infectious and complicated disorders. Antioxidants are said to protect against oxidative stress stimulated via reactive oxygen species as well as free radicals. Natural antioxidants come in a wide range of compositions, physical and chemical characteristics, processes, and action sites. Antioxidant activity has been documented in medicinal plants that are high in flavonoids, vitamins, polyphenols, and anthocyanins [9].

3. CONSEQUENCES OF SYNTHETICAL MEDICATIONS

Chemical or synthetical pharmaceuticals may have stronger or faster effects than herbal remedies, but they also come with a slew of consequences and hazards. Herbal medications are thought to be free of such side impacts for the reason that they have been used by millions of people around the world for thousands of years to treat a variety of ailments [10].

3.1. Expensiveness of Synthetic Drugs

In comparison with synthetic medicines, herbal remedies are less expensive. Medicinal plants continue to make a meaningful contribution to current prescription pharmaceuticals by providing key ingredients which can be used to make new ones [11].

4. IMPORTANCE OF MEDICINAL PLANTS IN LONG-TERM HUMAN HEALTH

For thousands of years, civilization has relied on therapeutic plants as a resource of medications. Early human beings were completely reliant on plants intended for all their medical requirements, including restraint to diseases, therapy, along with various forms of medication, and have been using plants as pharmaceuticals for millennia. The usage of medicinal plants has had a spiritual impact during the course of the evolution of individual society, as well as varied perspectives over conceptions of wellbeing coupled with sickness that each culture's existence embraces. For almost 3,000 years, a huge variety of vegetation has been employed in the medical field techniques for instance traditional medicine in India, Africa as well as China with the majority of them containing medicinal properties according to Western (Figure 3). Moreover, some more herbs were being employed by various civilizations for thousands of years while being more unlikely to be validated by dint of Western criteria. The importance of therapeutic (medicinal) vegetation on the well-being of humans is undeniable. The World Health Organization identifies 252 medications as fundamental in addition to essential, 11 % of the total are exclusive of plant derivation and a high portion of it is synthesized via natural precursors. Digoxin, quinine, and quinidine derived through *Cinchona spp*., vinblastine along with Vincristine, isolated *viz Catharanthus roseus*, atropine as of *Atropa belladonna*, as well as *Papaver omniferum* provide morphine along with codeine are some of the medications derived from natural sources. Natural origin medications account for 60 % of anti-cancer along with medications (anti-infectious) now in the marketplace otherwise appearing in experimental trials. These plants offer chemicals for the formation of innovative medications, and biomimetic synthesis, along with the detection

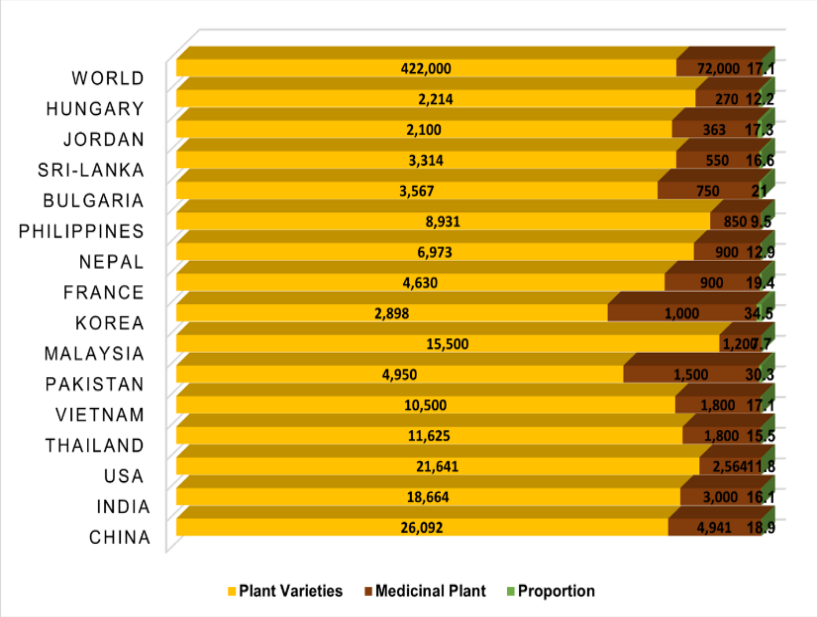

Fig. 3. Worldwide usage and proportion of medicinal plants [5].

of new therapeutic characteristics which are not previously associated with identified molecules [11].

4.1. Effectiveness of Herbal Medicines

The fact is that plant remedies can be utilized in the treatment of some ailments when traditional medicine fails and that medicinal plants are effectual, mild, as well as much of the time specialized in their role over the organs of humans [10].

5. CANCER

Cancer is a life-threatening disease caused by aberrant cell proliferation in the human body. The normal function of the damaged organ is significantly interrupted as a result of the abnormal proliferation, which may end in the patient's mortality. Mutations in two types of genes are commonly responsible for cancer: cancer-inducing oncogene and tumor-suppressing genes are genes that play a significant impact in tumor suppression. To metastasis, cancer cells normally spread throughout the body via blood arteries and lymphatic systems. Traditional therapies have included botanicals (medicinal) from the dawn of time on this planet. Because medicinal plants have therapeutic benefits, are less poisonous, and are less expensive than conventional ailments, 80 percent of the world's population, particularly those in rural areas, are directly dependent on them. Many natural metabolites or subtly modified metabolites generated from plants have anticancer properties, indicating that these plants can be used to treat cancer [13]. Natural compounds or derivatives account for 48.6 % of all cancer medicines that have been registered since the 1940s [1].

Previously, 24.6 million cancer survivors, 10.9 million new cancer cases, as well as 6.7 million fatalities due to cancer were reported each year throughout the globe. According to statistics from the World Health Organization, globally, 14.1 million new cancer cases and 8.2 million deaths have been reported in 2012, with an estimated 70 % surge in new cancer cases over the following two decades [13]. The coronavirus disease 2019 (COVID-19) pandemic, on the other hand, in 2020, had a detrimental impact on cancer detection and treatment. Healthcare facility closures have reduced access to care and fears of exposure to COVID-19 caused delays in treatment and diagnosis, which could cause a brief drop in cancer incidence followed by an increase in advanced-stage cancers along with, a higher death rate. However, owing to the halt in the dissemination of population-centered surveillance data, it would take several years to determine these and other pandemic-related secondary effects on the population. For instance, cancer mortality and incidence data are available for 2018 and 2019, correspondingly [14].

5.1. Medicinal Plants possessing Chemotherapeutic Properties

After significant research on medicinal plants with chemotherapeutic potential over many years, (*Alhagi pseudalhagi, Aphanamixis polystachya*, *Calamus rotang, Cirsium rhinoceros, Aphanamixis polystachya, Annona squamosa, Terminalia arjuna, Polygonum cuspidatum, Euphorbia jolkinin, Centella asiatica, Bupleurum kaoi, Stephania tetrandra, Ochrosia elliptica, Labill Ophiorrhiza mungos, Ornithogalum umbellatum* (*Ornithogalum*). *Taxus brevifolia* is a species of *Taxus Tabernaemontana divaricata, Scandinavian, Paederia, Elephantopus scaber, Impatiens balsamina, Coix lachryma, Rhei Rhizoma, Taxus wallichiana, Moringa oleifera, Vitex negundo*, and a variety of other plants are among them). Scientists were successful in discovering anti-cancer phytochemicals (Table 2) [15] such as eugenol, silymarin, allicin, catechins, curcumin ursolic acid, anethol, ellagic acid, lycopene, resveratrol, 6-gingerol, S-allyl cysteine, capsaicin, along with others. [16].

5.2 Phytochemicals as cancer treatment: a unique approach

Phytochemicals are compounds found in therapeutic (medicinal) plants that hinder cancer development and development. According to studies, the plant kingdom contains over two hundred fifty thousand different plant varieties, but 10 % of them have been explored and intended for the cure of numerous ailments. Phytochemicals along with their counterparts can be discovered in a variety of plant components, including the flower stigmas, pericarp, sprouts, fruits, seeds, roots, rhizomes, stems, leaves, embryos, and bark are all examples of plant parts, and a variety of pharmacological effects. Saponins, gums, minerals, taxanes, flavonoids, lignans, vitamins, glycosides, alkaloids, oils, terpenes, biomolecules, and other primary and secondary metabolites all play a part in the process of either blocking or activating cancerous cell activation proteins, signaling pathways (Figure 4) [17] (cycloxigenase, CDK4 kinases and enzymes (matrix metalloproteinases) MMP, Cdc2, COX-2 (Cycloxigenase), CDK2), topoisomerase enzyme, B cell lymphoma 2 (Bcl-2), cytokines, automates target of rapamycin (mTOR), MAPK/ERK, PI3K, Akt, (tenecteplase) TNK via inducing DNA repair (p21, p27, p51, and p53 genes) as well as their products (protein), Bax, Bak, Bid proteins, accelerating enzymes that defend the body (Caspase-3, 7, 8, 9, 10, 12) forming antioxidant enzymes (antioxidant activity) e.g. glutathione peroxidase (GPxn), glutathione (GSH), as well as glutathione S-transferases (GST). As a result, they have a high anti-cancerous impact in the context of effectiveness [18]. Recent studies revealed that medicinal plants and the bioactive substances they contain had been thought to be important agents in treating breast cancer through various processes. Asthma, scrofula, and other respiratory conditions are commonly treated with *Citrullus colocynthis*. Additionally, it is used to treat cancer, leukoderma, splenomegaly, blockage, dyspepsia, urine incontinence, and weakness. *C. colocynthis*, which has cytotoxic activity and is thought to be helpful in the treatment of cancer, contains cucurbitacins as well. Rameshbabu et al. looked at the antiproliferative effects of methanolic and aqueous

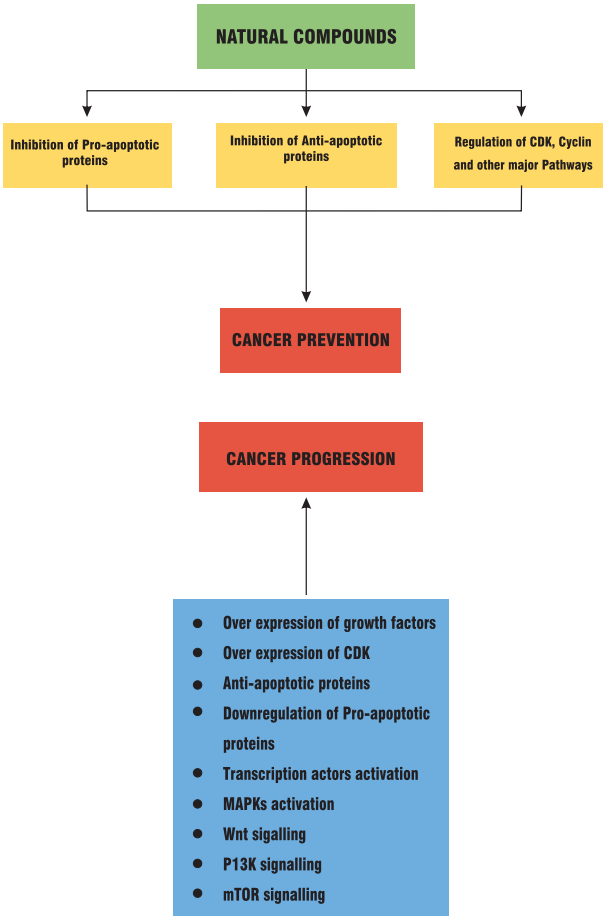

Fig. 4. Utilization of natural compounds for cancer prevention [17].

Table 2. List of medicinal plants with anti-cancer properties [15].

Anticancer chemical compounds	Molecular process of anti-cancerous activity	Medicinal plant
Apigenin	Impacts leptin or leptin receptor path, as well as stimulates cellular apoptosis via initiating (p38) mitogen-stimulated protein kinases (MAPK) path.	*Petroselinum crispum, Moringa peregrine*
Betulinic acid	Provokes mitochondrial apoptosis path.	*Betula alba, Ziziphus mauritiana* Lam.
Genistein	Hinders tyrosine kinase enzymes via inhibition of DNA topoisomerase (II), as well as engages in c-Jun N-terminal kinases (JNK) path for the promotion of activity of AP-1.	*Glycine max, Lupinus albus, Flemingia vestita*
Crocetin	Inhibition of nucleic acid formation generates apoptosis as well as delays developmental factor signifying paths, and enhancement of the anti-oxidation process.	*Crocus sativus L., Saffron crocus*
Diindolylmethane or Indole 3-carbinol	Epigenetic performance of cancerous cells via modulation of the receptor tyrosine kinase, PI3K, or Akt signaling paths as well as modification of invasion and metastatic angiogenesis.	Cabbage as well as mustard family.
Phenoxodiol	Boosts the apoptosis process, and inhibits anti-apoptotic elements quantity.	*Glycine max* (L) Merr.
Protopanaxadiol	Halts the cell in the G0 or G1 stage of the cell cycle phase.	*Panax ginseng* CA. Mey.
Curcumin	Intervenes with NF-κB to regulate tumor cell development via management of multiple cells signaling paths involving cFLIP, c-IAP1, cyclin D1, c-myc, XIAP, Bcl-2, and Bcl-x.	*Curcuma longa.*
Camptothecin alkaloids byproducts (irinotecan along with topotecan)	Apoptosis induction through telomerase complexes suppression.	*Saussurea lappa, Camptotheca acuminate* Decne
Indigo (meisoindigo along with indirubin)	Promotion of cell differentiation apoptosis, as well as tumor growth inhibition.	*Indigo naturalis*
Flavopiridol	Cell cycle progression inhibition in malignancy.	*Dysoxylum binectariferum, Amoora rohituka*
Homoharringtonine and Harringtonine	Inhibition of protein synthesis in melanoma.	*Cephalotaxus* species
Salvicine as well as saprorthoquinone	Inhibition of DNA topoisomerase (II).	*Salvia prionitis*
Roscovitine	Hinders histone deacetylates action in cancerous cells in addition to that activates SIRT1.	*Vitis vinifera, Raphanus sativus*
Podophyllotoxin (etoposide plus teniposide)	Topoisomerase (II) enzymes inhibition.	*Podophyllum emodi, Podophyllum peltatum*
Vincristine combined with vinblastine	Blockage of cell development employing preventing microtubule formation.	*Vinca rosea* Linn., *Catharanthus rosea* (L.) G. Don

extracts from several *Anastatica hierochuntica* (L.) components, including the seeds, stems, as well as leaves. The outcomes demonstrated that following treatment with both extracts, procaspase-3 expression and MCF-7 cell viability both dropped. Additionally, both extracts increased the expression of genes associated with apoptosis and the cell cycle, including Bax, TP53, and CDKN1A [19].

According to investigations, flavonoids can prevent the growth of tumor cells by preventing the production of ROS and suppressing the activity of the enzyme's xanthine oxidase, cyclooxygenase-2, and 5-lipoxygenase, all of which are crucial for the growth and progression of tumors. Kaempferol demonstrated antiproliferative and apoptotic efficacy against human osteosarcoma, stomach (SGC-7901), and lung (A549) carcinoma cells in a different investigation. Hesperidin also exhibits hepatoprotective and anticancer properties against the growth of hepatocellular carcinoma. Human epithelial colorectal adenocarcinoma cells treated with cyanidin demonstrated both an inhibition of proliferation and an induction of apoptosis [17]. Triterpenoid saponin tubeimoside-V, a substance from the plant *Bolbostemma paniculatum*, was studied following the plant's extraction and fractionation, which enabled isolation and characterization. It demonstrated the clearing of glioblastoma cells through apoptosis and acted as an antitumor chemotherapeutic [20]. Paclitaxel (PTX), a well-known first-line chemotherapy treatment/ therapy for cancer diseases like ovarian and breast cancer, is the most frequent herbal medicinal ingredient isolated from (Rehd) *T. chinensis*. The compounds vindesine, vincristine, vinorelbine, and vinblastine are found in *Vinca rosea*. The Food and Drug Administration (FDA) has approved and granted licenses to all of these vinca alkaloids, which were the first all-natural substances to enter clinical trials across a number of tumors. It is known that utilizing these alkaloids in low concentrations disrupts microtubular function, while administering them in high dosages results in cell cycle arrest and apoptosis. Currently, these alkaloids are used to treat a number of tumors [21]. Anthocyanins and phenolic acids, the primary active components of mulberries, have been demonstrated to inhibit cell proliferation in a variety of cell lines, including MCF7 cells. *M. nigra* reduces mutant p53 levels in HT-29 cells, which results in cell death through a caspase-3-independent mechanism [22]. In lung cancer cells like H1650 and A549, *Polygonum cuspidatum* extracts block free radical molecules like DPPH (2,2-diphenyl-1-picrylhydrazyl) and hydroxyl. *Toona sinensis* leaf extract inhibits the production of ROS and causes apoptosis in lung adenocarcinoma cells, particularly H441 [23].

6. CONCLUSION

It is challenging to standardize a specific medication treatment for a patient because tumorigenesis depends on a variety of pathways and diverse sets of mutations. Chemotherapy addresses important problems such as medication resistance, side effects, and the return of the disease. Combinatorial therapies shed some light on the fact that monotherapies don't always work for cancer patients and have the potential to cause several negative effects. It has been observed that even after successfully treating those cancers, some of the cells stay excluded and trigger tumor recurrence because the tumor is made up of different types of cells. Long-term usage of medicines or radiation therapy renders cancers resistant to these treatments, which lowers their effectiveness. In order to lessen side effects and ultimately regulate the resistance developed by the tumors, an alternate therapy would therefore involve combining the aforementioned therapeutic modalities. These include any chemotherapeutic drug combinations as well as any combination of two therapies, such as radioimmunotherapy or radiochemotherapy. Its primary goal is to interfere with the homeostasis of tumor cells by focusing on aspects that can increase therapeutic effectiveness and inhibit or postpone the development of acquired resistance. Natural compounds would be an excellent choice and could possibly inspire the development of new drug candidates since they might be employed as new discoveries in the drug discovery process. The main task at hand is to refine these natural compounds' pharmacokinetic qualities such that in vivo tests on humans might rely on their safety and effectiveness. It is imperative to research the role of natural substances as cancer cures due to the different negative effects of conventional cancer therapy alternatives. Since they have fewer negative side effects, the use of these compounds for treating carcinogens has become more significant in drug delivery. Future research on these phytochemicals appears to be both promising and active. Compared to manufactured medications, these are less harmful and more helpful. In this review paper, we attempted to condense the list of some of the plants and naturally occurring substances produced from plants that have anticancer qualities for different malignancies, which would eventually lead to some

novel compounds and be approved for use in the treatment of cancer.

7. CONFLICT OF INTEREST

All authors declare no conflict of interest.

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Abbreviations:

FDA: Food and Drug Administration
M.Ps: Medicinal Plants
SMoPs: Secondary Metabolites of Plants
ROS: Reactive Oxygen Species.