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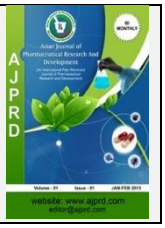

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Review Article

An Updated Assessment of the Use of Bioactive Chemicals Derived From Plants in Treatment of Colon Cancer

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A B S T R A C T

The third most common type of cancer brought on by dietary, environmental, and hereditary causes is colon cancer. It is generally established that plant-based substances can regress colon cancer in a variety of ways, including by slowing the growth of tumors, controlling the negative effects of chemotherapy and radiation therapy, and acting at the molecular level. Carnosic acid, oleanolic acid, rosmarinic acid, emodin, eugenol, anthricin, flavonoids, polyphenol compounds, caffeic acid, catechins, saponins, polysaccharides, triterpenoids, alkaloids, glycosides, phenols, quercetin, luteolin, kaempferol, and luteolin glycosides are just a few of the numerous bioactive phytochemicals found in medicinal plants. Through a variety of mechanisms, including the blockage of cell cycle checkpoints and the activation of initiator and executioner caspase, these bioactive chemicals can inhibit the proliferation of tumor cells. Because of its anti-inflammatory, antioxidant, and anti-cancer qualities, traditional medicines have been utilized to treat cancer all over the world. Thisall bioactive chemicals derived from plant are used in treatment of colon cancer "

Keywords: Colon Cancer, Epidemiology, Pathophysiology, medicinalplants.

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INTRODUCTION

Colorectal cancer (CRC) is a leading cause of death in the US and globally, accounting for over 1 million deaths annually [1]. CRC can be prevented by detecting and removing precancerous lesions before they proceed to malignancy and metastasis, as most cases start with adenomatous or serrated polyps [2]. In 2020, it is anticipated that about 1.9 million new cases of colorectal cancer and 930,000 fatalities occurred globally.[3] There was significant geographical heterogeneity in incidence and fatality rates. Incidence rates were highest in Europe, Australia, and New Zealand, while fatality rates were highest in Eastern Europe. By 2040, the burden of colorectal cancer will rise. Annually, there are 3.2 million new cases (a 63% increase) and 1.6 million fatalities (73% increase). [2]. Early diagnosis, adequate staging, and successful multimodal treatment have increased the overall 5-year survival rate for CRC from 20% in 1971-75 to almost 50% now. [4-6] recently, there has been a greater emphasis on employing nanotechnology to create unique and tailored medicine delivery methods. The unique eualities of nanosized drug delivery systems, which result from the small particle size and huge surface area of the vesicles, may contribute to improved passive targeting.properties for the pharmaceuticals. Furthermore, the latter aids in the maintenance of more drug-loaded vesicles in tumor cells by increasing permeability and retention. They improve dosage efficacy and reduce negative effects. [7] It assists in employing chemotherapy at low quantities, which eliminates most of the constraints in traditional chemotherapy.[8] In recent years, numerous research supported the use of secondary metabolites as cancer chemo preventive and therapeutic agents. The epidemiological studies also showed how dietary practices can help prevent cancer and other disorders. The information. According to this research, including certain items in one's diet can lower one's chance of developing cancer and dying from it by more than 30% [9-11]

The pathophysiology of colon cancer is influenced by genetic mutation, environmental or lifestyle factors, or poor dietary practices. The carcinogenesis of colorectal cancer (CRC)

involves three main mechanisms: Microsatellite instability, chromosomal instability, and Cp Gisl and methyl at or phenotype [12]. Environmental factors hat increase the risk of colon cancer includes nutritional factors that contribute to obesity and energy intake. Inducing cell cycle check point arrest at the G1phase, G1/Sphase, S-phase,andG2/M phase to enhance apoptosis; decreasing the expression of PI3K (phosphoinositide 3-kinase), AKT (Ak strain transforming), and MMP (matrix metalloproteinase); inducing the expression of several cell cycle inhibitors like p53, p21, and p 27; and inducing the expression of apoptotic markers like BCL 2-associated agonist of cell death, BCL2-associated X protein (BAX), Caspase 3, Caspase 7, Caspase 8, and Caspase 9 protein are just a few of the ways they can slow the growth of colon cancer [13].By encouraging apoptosis and cell cycle arrest, the use of natural sources like berries, grapes, plums, pomegranates, green tea, cruciferous vegetables, soybean, tomatoes, garlic, turmeric, ginger, olive, whole grains, and mushrooms can prevent the development and carcinogenesis of colon cancer[12] The approximately 35,000 herbal bioactive components that are derived from plants, marine life, and other sources reduce the negative side effects of using contemporary cancer treatment methods like chemotherapy and radiation therapy. The most dependablesourceofbioactivechemicalsfornaturalremediesthat supplementmedicationsin alternative systems as a sustainable method of treating colorectal cancer is medicinal plants. With less dangers and adverse effects, the terpenoids, saponins, volatile oils, flavonoids, phenolics, quinones, and alkaloids have astrongcy to toxic effect on colorectal cancer cells [8]. One of the most effective methods for treating colon cancer is chemotherapy. However, because to the absence of contemporary diagnostic equipment and the limited facilities and accessibility, its use is still quite limited in developing nations, particularly in rural areas [14]. One of the most effective methods for treating colon cancer is chemotherapy. However, because to the absence of contemporary diagnostic equipment and the limited facilities and accessibility, its use is still quite limited in developing nations, particularly in rural areas [15].

Epidemiologyofcolorectalcancer:

Colorectal cancer is the third most deadly type of cancer in the US. An estimated 134,490 new cases of colorectal cancer (70,820 in men and 63,670 in women) and 49,190 colorectal cancer deaths (26,020 and 23,170 in men and women, respectively) are anticipated in 2016. Only prostate and lung cancer rank higher than colorectal cancer in terms of new cases in men (8% of all new cancer cases), while in terms of new cases in women (8% of all new cancer cases), colorectal cancer comes in third place. In the same way, only lung and prostate cancer are predicted to kill more American menthan colorectal cancer in 2016, and only lung and breast cancer (each accounting for 8% of all cancer deaths) are predicted to kill more American women [18-22]. Except for non-melanoma skin cancer, it makes up 9.7% of all cancers. Due to a fast-paced lifestyle and a major change in dietary habits, developed nations account for more than half of all cases. Patients over 50or 60 at diagnosis account for most instances [23]. Asia has the highest number of common instances of colorectal cancer (CRC), although having a lower prevalence rate than other Western nations.[24]Global cancer statistics show that 9.9 million fatalities and 19.3 million new cases of colorectal cancer were attributed to the disease in 2020. CRC has a 10% incidence rate and a 10% fatality rate. [24]

attributed to CRC is 9.4%. The Global CRC Burden Study Report states that 0.94 million individuals will lose their lives to CRC globally in 2020, and 1.93 million people have received a CRC diagnosis. An investigation into the prevalence of CRC in India has been conducted.This study shows that the incidence of colorectal cancer (CRC) roseby5.8%per 100,000 people between 2004 and 2005 and 6.9% between 2012 and 2014 [25-27].

Pathophysiology:

Anupdated evaluation of plant-derived bioactive chemicals in the treatment of colon cancer [8] as people age, a polyp—a noncancerous growth—may appear on the inner wall of the colon or rectum. If polyps are not treated right away, they can become fatal. Early diagnosis and excision of pre-neoplastic adenomas can prevent colorectal cancer in its early stages. Numerous polyps, including tubular adenomas, villous adenomas, tubulovillous adenomas, serrated adenomas, hyperplastic, and inflammatory adenomas, have been discovered in colon cancer. [29-30] Adenoma or adenomatous polyps are tissue growths that have a high risk of developing into cancer. The majority of colorectal malignancies begin as abnormal crypts and develop into early adenoma. When seen in a villus' histology, this further develops into an advanced adenoma and grows beyond 1 cm [31]. The process used to find anomalies in the large intestine is called a colonoscopy. The colon's bulge-like form makes it easy to find polyps during a colonoscopy. Only 90% of polyps are easily detected by colonoscopy, andthe remaining 10% have different formations. Conventional adenomas are homogeneous and difficult to distinguish from the section's normal histology. However, these polyps' diverse molecular biology can identify which adenomas will develop into colorectal cancer. In contrast to guaiac-based hemoccult tests, a few screening methods have previously been developed for identifying colorectal cancer (CRC) in its early stages [32-33].

Limitation

This study was conducted in an environment where many of the chemicals tested had not had their toxicity assessed. One of the work's drawbacks is the absence of this information. Researchers should continue this work immediately in order to ascertain the level of safety of these chemicals. Since we don't know what shape a medicine can take during its transfer into a living organism—active, inactive, less active, or metamorphosis into a harmful form—the lack of information or in vitro work done with these chemicals is another key constraint. Researchers should investigate this more in the future to obtain comprehensive information (both in vitro and in vivo data) on these compounds that have been examined.

Table 1: List of bioactive compounds, their sources and their activities.

Compound	Plant Source	Extract Source	Activity	References
Anthocyanin- richphenolics	*Podocarpuselatus*	Fruit	Alters mitochondrial pathwaysand Blocks the S phase of the cell cycle	34
Berberis	*Berberis Lycius*	Root	Antioxidant and cytotoxicity effect	35
Phenolic compounds	*Pisumsativum*	leavesand buds	Potentcytotoxic effect against colon cancer cells	36
Ellagicacid	*Terminalia ferdinandiana*	Kernels	Reducesoxidative stress by free radical scavenging activity	37
Withanolides	*Withania somnifera*	Leaves	Down regulates inflammatory pathways control MAP kinase signal ling, modifies JAK-STATpathway	38
Flavonoids	*Morusalba*	Leaf	Inducecellcycle arrest and apoptosis	39
Rosmarinic acid (phenolic compounds)	*Salviaofficinalis*	Leaf	Iinhbitit the growth of HCT15 and CO115 by Down regulating the MAPK/ERK Signalling path way	41
Eugenol	*Moringaoleifera*	Leaves,bark and seed	Induceapoptosis By cell cycle arrest at the G2/M phase	42
Anthricin (flavonolignan)	*Chamaecyparis obtuse*	Leaf	Causesapoptosis by activating the JNK signalling pathway	34.
Methoxytabersonine	*Melodinus axillaris*	Leaves	a moderate activity against colorectal cancer on HCT116, with an IC50 value of 25.3 µM	
Quercetin	*Oleaeuropaea*	Fruit	arrestscellcycleat S phase	41
Vandrikidine	*Catharanthus roseus*	leaf	effective against bacteria and displayed cytotoxicity against A549 lung cancer cells, and the IC50 values ranged from 5.6 to 77.1 µM	42
Fusiformine A	Melodinus fusiformis	bark	its cytotoxic activity evaluated against the growth of human tumor cell lines (HL-60 and A-549) showed moderate cell growth in hibitory activity with IC50 values of 9.80 and 12.38 µM, respectively	43
3-Oxotabersonine	Melodinus axillaris	leaves	against colorectal cancer HCT116 cells with an IC50 of 22.6 µM,	44
Venalstonidine	Melodinus axillaris	Plant	a moderated activity on colorectal cancer HCT116 with an IC50 of 47.7 µM	45
(–)-Larutienine	Melodinusaxillaris	leaves	showed moderate activity against HCT116 colorectal cancer cells, with an IC50 value of 26.1 µM	46
Solasonin	Solanum nigrum	leaf	markedly suppressed the proliferation of CRC cells. The IC50 values of solasonin on SW620, SW480, andMGC803cellswere, respectively, 35.52, 44.1, and 46.72 µM.	47
Berbamine	Berberis amurensis	plant	It has been demon strated that berbamine could inhibit CRC cell line growth and presented an inhibitory effect on the ability of migration and invasion in CRC cells.	48
Anthricin (flavonolignan)	*Chamaecyparis obtuse*	Leaf	Causesapoptosis by activating the JNK signalling pathway	49
11-Methoxytabersonine	*Melodinus axillaris*	Leaves, bark and seed	a moderate activity against colorectal cancer on HCT116, with an IC_{50} value of 25.3 µM	50
Nitidine Chloride	Zanthoxylum nitidum (Roxb.)	Root	This compound inhibited the proliferation of RKO(2µM),HCT116(3.5 µM), and HT29 (6 µM) cells and also has the ability to strongly suppress cell proliferation at high concentrations; its significant colony inhibition of HT29 cells has been demonstrated	51
GB7 Acetate	Galbulimima belgraveana	bark	This compound showed activity that suppressed the proliferation and colony-forming ability of CRC (HCT116) cells, with an IC50 value of 97.75 µg/mL.	52
Berberine	Berberis spp	Root	It demonstrated a moderate activity against HCT116 (10.30 µg/mL)	53
Boldine	Peumus boldus	leaf	showed a moderated activity against HCT116 (IC50 = 37.87 µg/mL) [21].	54

Worenine	Coptis chinensis	plant	inhibited colorectal cancer cell growth [CRC (HCT116 and SW620; 18.30 and 15.19 μM, respectively.)], proliferation, cell cycle progression, and the Warburg effect by targeting HIF-1α in vitro	55
Chaetocochin J.	Chaetomium sp.	leaf	showed that it had a strong proliferation inhibition effect with the IC50 value to CRC cells around 0.5 μM. In addition, chaetocochin J	56
Scandine, Melodinine W2 and 3-oxo-11-Methoxytabersonine	Melodinus axillaris	leaves	They have demonstrated their moderated anti-colorectal cancer (HCT116) activity with IC50 = 42.9, 37.7, and 24.4 μM, respectively	57

CONCLUSION

It is the good of humanity, stricter oversight and regulation should be in place because plant- derived bioactive chemicals have been employed as natural treatments for cancer and other diseases. Many plant bioactive substances have anti-carcinogenic qualities, including polyphenols, flavonoids, alkaloids, caffeic acid, saponins, polysaccharides, glycosides, and triterpenoids.Theseincludeapoptosisinductionagainstcoloncancerandinhibitory effects on angiogenesis, inflammation, and the growth of cancer cells. The main purpose of these substances is to stop the growth of tumor cells and start apoptosis through various mechanisms. Colon cancer can be effectively prevented and treated by using these components from medicinal plants. However, before these may be utilized to treat colon cancer, further carefully monitored clinical trials are needed. Obtaining pure herbal substances to evaluate their efficacy against cancer cells in in vitro and in vivo models is one of these procedures. However, there are still certain problems with investigating the most effective phytochemical substances for cancer treatment. Finding possible chemicals, their bioavailability, and their target tissue action is a complicated process that calls for more sophisticated analytical and technological techniques.

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