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Review

Medicinal plants with anti-colorectal cancer bioactive compounds: Potential game-changers in colorectal cancer management

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ABSTRACT

Development and identification of molecular compounds capable of killing or inhibiting transformed cells promoting carcinogenesis without inducing toxic effects to the normal cells are of utmost significance. A systematic review was conducted in screening for important literature was extensively performed by searching the Web of Science, Ovid, BMC Springer, Elsevier, Embase, and MEDLINE databases for optimum selectivity. Google Scholar was also used to supplement information. Pharmacotherapeutic biomolecules active against colon cancer carcinogenesis in *Musa acuminata* and *Musa balbisiana* (bananas), *Punica granatum* L (pomegranate), *Glycine max* (Soybean), *Brassica oleracea* L var. italica Plenck (Broccoli), and *Hibiscus rosa-sinesis* and *Hibiscus sabdariffa* (hibiscus) were evaluated. Signaling pathways like phosphatidylinositol 3-kinase (PI3K), mitogen-activated protein kinase (MAPK), protein kinase B (AKT), and nuclear factor-kappa B (NFκB) correlate the mediation of COX-2 expression. Increased levels of COX-2 are correlated with the occurrence and progression of colon cancer. Natural antioxidants in herbal plants including polyphenols and carotenoids inhibit the oxidation of lipids, proteins, and nucleic acids and thereby preventing the initiation of oxidizing chain reactions. These bioactive compounds should be considered an important dietary supplement.

1. Introduction

Colorectal cancer is among the most common malignancy but the third prime cause of cancer-associated mortalities in both men and women especially in developed countries [1]. Significant advances have been achieved in the knowledge of molecular activities leading to the formation of adenomatous polyps (cancer precursors) and cancer. Numerous colorectal tumors are sporadic but a substantial percentage (5–6%) have a distinct genetic association [1]. Epigenetic changes via aberrant promoter methylation and exertion of histone modifications play a key role in the origin and proliferation of colon cancers. Reversal of epigenetic marks using compounds targeting aberrant transcription factors, co-activator, co-repressor interactions, and histone-modifying activities, gives insightful possibilities where the epigenome of cancerous cells can be manipulated with probable therapeutic advantages [2].

Surgery and chemotherapeutic interventions are the most used forms of treatment for colon cancer due to the lack of scientifically explored alternatives. However, the development and identification of molecular compounds capable of killing or inhibiting transformed cells promoting carcinogenesis without inducing toxic effects or being toxic to the normal cells are of utmost significance [3]. In light of this, management with dietary supplements derived from plants is beginning to receive due recognition as the most potent approach to lessen the burden of colorectal cancer-associated mortality [4]. Plants have significant bioactive compounds essential for growth and development in almost all living organisms. They are widely consumed as food and for their medicinal values in virtually all cultures. However, their pharmacological properties and efficacy are poorly understood. Most phytochemicals with determined bioactive potential have been associated with plants [5]. Nearly all phytochemicals established in plants are classified into four biochemical classes: terpenes, alkaloids, glycosides, and polyphenols [5].

Different plant organs have demonstrated substantial medicinal

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properties such as hypoglycaemic antioxidant and antitumor potentials [6]. It has been cited that 50% of cancer management options are derived from biologically active agents common in plants [7]. Ethnopharmacological studies should be encouraged to investigate the more appropriate technique of plant selection, extraction, chemical formulation, and dose calculation to ascertain and attain extensive benefits from these medicinal plant species [7]. A study performed using *Cassia fistula* demonstrated that the herb's seeds and fruits exhibited active repression of cancerous cells derived from the colon, breast, and liver [6].

Bioactive molecules common in bananas have demonstrated extensive cancer inhibitory and anticancer activities via various mechanisms such as cytotoxicity, apoptosis of cancerous cells, cell cycle arrest, anti-inflammatory and antioxidant effects [8]. A cluster of matrix metalloproteinases (MMPs) termed gelatinases (MMP-2 and MMP-9) is greatly correlated with tumor invasion through degradation of the cellular matrix, and the subsequent release of cancerous cells through proteolysis [1,9]. Cruciferous vegetables contain sulforaphane which is a compound in plants with anticancer-established properties. Sulforaphane adequately prevents cancer cell growth and enhances apoptosis in colorectal cancer cells and additionally inhibits histone deacetylase associated with tumor development [10]. A meta-analysis study demonstrated an existing inverse association between higher consumption of leguminous plants and the risk of developing colorectal cancer. In the study, of all the leguminous plant species observed, soybeans and legume fibers portrayed a distinct association with a lowered risk of colorectal cancer (CRC) development [11].

Juice extracts from pomegranate and purified ellagitannins on colorectal cancer have demonstrated that they prevent the stimulation and proliferation of colorectal cancer cell lines [12]. More studies have intimated that a polyphenol-enriched extract of *Hibiscus* (*Hibiscus sabdariffa)* largely inhibited and curtailed cell migration and invasion of colonic cancerous cells [13]. Pharmacological research of the genus *Hibiscus* has demonstrated that some species of the plant have the essential bioactive ability as antihypertensive, hepatoprotective, anti-diarrheic, anti-inflammatory, antipyretic, antidiabetic, anti-convulsant, anti-spermatogenic, anti-tumor, anti-helminthic immunomodulator, antimutagenic agents, and antioxidant [14]. A separate study has elucidated that ethanol extract of *Cordyceps militaris* (fungi) was significantly cytotoxic to CRC and actively inhibited tumor growth and development in the xenograft model [15]. The anticancer bioactivity of *Cordyceps militaris* was correlated to stimulation of cell cycle arrest together with mitochondrial-mediated cell death. The study further reported that the ethanolic extract induced cell cycle arrest in G2/M phase, and that it significantly increased early apoptosis on the cell-lines. In addition, the use of *Cordyceps militaris* increased the expression of p53, cleaved caspase 3, cleaved caspase 9, cleaved PARP, Bad, Bak and Bim [15].

It is with increased dependence on synthetic CRC treatment options that this paper sought to review plants and a fungus with bioactive agents and with specific potency against CRC growth and development. The reviewed plants were bananas, pomegranate, leguminous plants, hibiscus, and cruciferous vegetables. They are used either as food or for their medicinal values. They will play a pivotal role in CRC management. The reviewed plants are easily accessible and cheap compared with the excruciatingly high cost that comes with CRC treatment. This paper, therefore, underpins a strong foundation for ethnopharmacological scrutiny and exploration of active phytochemical compounds common in plants that are natural antioxidants, as alternatives to overreliance on synthetic antioxidants for empirical CRC treatments. Cancer management agents are classified as antibiotics, alkylating agents, mitotic inhibitors, antimetabolites, platinum compounds, hormone therapeutics, and biological response modifiers [16] as demonstrated with their associated target cancers in Table 1, below.

Table 1
Anticancer management agents and associated cancer they treat [16].

S/N	Anticancer Agents	Treated Cancer Type
1	Alkylating	Breast, multiple cancers, myeloma sarcoma, lung and ovarian
2	Antibiotics	Colorectal, lung cancers, prostate, breast, and ovarian
3	Antimetabolites	Leukemia, intestinal tract cancers, breast, pancreatic and ovarian
4	Mitotic inhibitor	Breast, myeloma, leukemia, ovarian, lymphoma, and lung
5	Platinum compound	Testicular, lung, head, neck, ovarian, bladder, and colon cancers
6	Biological response modifier	Malignant melanoma, breast (trastuzumab), and non-Hodgkin lymphoma
7	Hormone therapies	Prostate, endometrial (uterine), and breast cancers

2. Methods

2.1. Electronic databases

To encapsulate numerous publications for identifying primary studies assessing the influence of phytochemical compounds on colorectal cancer carcinogenesis, screening for relevant literature was extensively performed by a systematic review [17] through the Web of Science, Ovid, BMC Springer, Elsevier, Embase, and MEDLINE databases for optimum selectivity. Google Scholar was also used to supplement information. However, articles in google scholar were verified for authenticity by interlinking the articles with their corresponding existing publisher.

2.2. Review question and the screening criterion

A review question was formulated to facilitate the search criterion. The structured question was: "*Are phytoconstituents in medicinal plants actively potent in inhibiting colorectal cancer?*". As an initial step, the authors independently screened only English research titles and abstracts from primary studies for possible inclusion in the study, guided by the formulated review question [17,18]. All studies on other types of cancers other than colorectal cancer, and studies with plants that exhibited high levels of cellular toxicity and adverse reactions we technically excluded from the study. Titles and abstracts meeting the minimum satisfactory threshold were enrolled for full-text article scrutiny and subsequently used to generate the required analytical data for the present review, upon being deemed appropriate by five independent authors. Independence of authors when making the final decision on adoption of the enrolled articles, was necessary to minimize potential risks of bias [17,18]. From a significant pool of 6402 titles and abstracts screened, only 106 full-text articles met the inclusion criteria threshold.

2.3. Systematic search strategy

A systematic search strategy was drafted to enhance a comprehensive review. "Colorectal cancer", "colon cancer", "adenomatous polyps", "colorectal tumor", and "colon tumor" terms were combined with either of the following MeSH terms: "Anti-tumor", "anti-cancer", "bioactivity", "biological activity", "phytochemicals", "pharmacological activities". These terms were strictly combined with either of the following plant term or fungus terms: "banana", "pomegranate", "leguminous plant", "legumes", "Hibiscus", "*Hibiscus sabdariffa*", "cruciferous vegetables", "cruciferous".

Table 2
Taxonomic classification of the banana species [21].

Kingdom:	Plantae
Class:	Monocotyledonae
Order:	Scitamineae
Family:	Musaceae
Genus:	Musa
Section:	Eumusa
Species:	*Musa acuminata* (AA), *Musa balbisiana* (BB)
Groups:	AAA dessert and highland beer and cooking bananas AAB plantains and dessert bananas ABB cooking bananas

Table 3
Descriptive characteristics *of Musa acuminata* and *Musa balbisiana* [22].

Plant part	*Musa acuminata*	*Musa balbisiana*
Pseudostem color	Heavily marked with black or brown blotches	Blotches very slight or absent
Petiolar canal	Margins erect or spreading, with scarious wings below, not clasping pseudostem	Margin inclosed, not winged but clasping pseudostem
Peduncle	Usually downy or hairy	Glabrous
Pedicels	Short	Long
Ovules	Two regular rows in each loculus	Four irregular rows in each loculus
Bract shoulder	Usually high (ratio < 0.28)	Usually low (ratio > 0.30)
Bract curling	Bracts reflex and rollback after opening	Bracts do not reflex
Bract shape	Lanceolate or narrowly ovate, tapering sharply from the shoulder	Broadly ovate, not tapering sharply
Bract apex	Acute	Obtuse
Bract color	Red, dull purple, or yellow outside; pink, dull purple, or yellow inside	Distinctive brownish-purple outside; bright crimson inside
Color fading	Inside bract color usually fades to yellow towards the base	Inside bract color usually continuous to base
Bract scars	Prominent	Scarcely prominent
Free tepal of male flower	Variably corrugated below the tip	Rarely corrugated
Male flower color	Creamy white	Variably flushed with pink
Stigma color	Orange or rich yellow	Cream, pale yellow, or pale pink

3. *Musa acuminata* Colla and *Musa balbisiana* Colla species of medical importance

3.1. Botanical and morphological description

Bananas are elongated fruits found in herbaceous flowering plants of the genus *Musa*. Bananas occur in varying sizes, colors, and firmness, but are commonly elongated and curved, with a soft flesh with an abundance of starch. Their outer covering may be green, purple, red, brown, or yellow when ripe. Fruits occur in clusters and hang from the top of the herbaceous plant. The two common parthenocarpic varieties of the bananas of significance in this review are *Musa accuminata* Colla and *Musa balbisiana* Colla [8]. The three known genera belonging to the Musaceae family are *Musa, Ensete,* and *Musella* [19], with the *Musa* genus established to consist of 65 species of cultivated and wild bananas and plantains [8]. Bananas are mainly perennial herbs. They are grown in most tropical and subtropical countries and are a source of staple food for most communities globally. Their parthenocarpic nature exposes their vulnerability to widespread pathological diseases [20]. Tables 2 and 3 below show the taxonomic classification and the distinctive features of the two banana species of interest in this review.

3.2. Phytochemicals present in different organs

Phytochemicals are significant biomolecular compounds common in

Table 4
Phytochemicals present in different parts of the banana herb.

Plant parts	Category	Phytochemicals from various banana cultivars	Extract	Ref.
Ripe fruit	Phenolic acids	Octadeca-9,12,15 trienoic acid Octadeca-9,12-dienoicacid	Dichloromethane	[25]
		Vanillic acid Caffeic acid Ellagic acid	Acetone	[26]
Peel		13-octadecanoic acid	Methanol, oil	[22, 27, 28]
		Palmitic acid Oleic acid Linoleic acid Methyl palmitate Methyl oleate Methyl linoleate Stearic acid Carvacrol Pentadecanoic acid Palmitoleic acid Benzoic acid		
Leaves		Tannic acid	Ethanol, acetone, petroleum ether	[29]
		Cinnamic acid Ferulic acid	Leaf powder	[30]
Bract		Delphinidin-3-rutinoside Cyanidin-3-rutinoside Petunidin-3-rutinoside Peonidin-3-rutinoside Malvidin-3-rutinoside	Methanol	[31, 32]
Seeds		Leucoanthocyanidin	Acetone	[22]
Pulp of banana fruit		Gallic acid	Not specified	[33]
Overripe fruit		Protocatechualdehyde	Not specified	[34]
Sap		Hydroxycinnamic acid Caffeoylquinic acid	Ethanol	[35]
Ripe fruit	Flavonoids	Quercetin	Pulp	[33, 34]
		Proanthocyanidin Catechin Gallocatechin Epicatechin Procyanidin	Methanol	[33]
		(+) Catechin hydrate	Acetone	[26]
Sap		Apigenin Myricetin Kaempferol	Ethanol	[35]
Ripe fruits	Glycosides	Endo-b-1,3-glucanase (Ban-Glu)	Pulp	[36]
	Triterpenoids	a-tocopherol	Dichloromethane	[25]
		Cycloartenol	Dichloromethane	
	Sterols	Campesterol Stigmasterol	Dichloromethane	
Peels		b-sitosterol Pyrogallol	Methanol	[37]
Rhizome		(S)(+)-naproxene 2-methoxy-9-phenyl-phenalen-1-one	Methanol, oil	[24]
Rhizome, Root		Anigorufone	Methanol	[27]
Fruit		2-pentanone	Not specified	[24]
Ripe fruit	Carotenoids	Ascorbic acid Retinol a-carotene b-carotene Zeaxanthin		[27]
Peel	Lignan	Sesami Epi-sesami	Methanol, oil	[38]
Ripe banana		Sitosteryl glucoside (Sitogluside)	Not specified	[39]

Plate 1. Pomegranate flower.

numerous medicinal plant species and are essential in enhancing human wellbeing. They have a huge influence in medical research as they constitute important beneficial properties such as preventing different physiological abnormalities [23]. Most phytochemical compounds in the diet could potentially prevent colon carcinogenesis by influencing biochemical activities in the colonic mucosa [24]. The significance of *M. acuminata* C as a medicinal herb of medical importance is associated with its bioactive compounds such as phenolics, biogenic amines, carotenoids, phytosterols, and volatile oils, commonly found in the stem, pseudostem, fruit, leaf, sap, inner trunk, flower, root, and inner core [8]. The chemical compound of the lipophilic extract of the ripe pulp of banana is majorly associated with *Musa acuminata* and *Musa balbisiana* species [25]. These bioactive compounds are listed in Table 4 below.

3.3. Anti-colorectal cancer properties

Cyclooxygenases (COX) are enzymes associated with the production of lipid prostaglandins and are therefore of critical significance for biochemical processes in the body [24]. Cyclooxygenases 1 (COX-1) modulate homeostasis whereas Cyclooxygenases 2 (COX-2) are influenced and play a crucial role in inflammatory processes [40]. At minimal levels, COX-2 is expressed in the colon, but it may be influenced by cytokines, tumor necrosis factors, growth factors, and lipopolysaccharides under stressful conditions. Increased levels of COX-2 are correlated with the occurrence and progression of colon cancer [24,40]. Synthetic COX-2 inhibitors have been established to have adverse side effects and thus natural inhibitors could be explored as alternative forms of chemoprevention therapies in colon cancer management. Flavoring compounds such as 2-pentanone found in bananas have proven inhibitory activity toward COX-2 [41]. Natural antioxidants present in bananas such as polyphenols and carotenoids inhibit the oxidation of lipids, proteins, and nucleic acids and thereby inhibiting the initiation of oxidizing chain reactions. Consequently, synthetic antioxidants such as butylatedhydroxyanisole and butylatedhydroxytoluene have recently been established to be carcinogenic and results to adverse side effects [26]. Banana fruits well-ripened possess enhanced anti-cancer potential while the dark spots found in fully ripened bananas produce a constituent known as Tumor Necrosis Factor (TNF) with the ability to terminate cancerous tumors as well as inhibit the growth of cancerous cells [42]. The antioxidant activity in banana plants is critical because of their free radical scavenging capacity, prevention or inhibition of peroxidation, and the chelating transition metals property [22,29].

4. Pomegranate (*Punica granatum* L)

4.1. Botanical and morphological description

The species name of pomegranate is classified as *Punica granatum* L. It has an abundance of seeds ranging from 200 to 1400 [12].

Table 5
Taxonomic classification of *P. granatum* L [45].

Domain	Eukaryota
Kingdom	Plantae
Phylum	Spermatophyta
Subphylum	Angiospermae
Class	Dicotyledonae
Order	Myrtales
Family	Punicaceae
Genus	Punica
Species	*Punica granatum* L

Table 6
Phytochemicals present in *P. granatum* L.

Plant organ	Phytochemical compound	Ref.
Seeds	sugars, polyunsaturated (n-3) fatty acids, vitamins, polysaccharides, polyphenols, and minerals	[46]
Dried seeds	punicic acid, the 18-carbon fatty acid, isoflavone genistein, phytoestrogen coumestrol, sex steroid estrone.	[46]
Seed coat	delphinidin-3-glucoside, delphinidin-3,5-diglucoside, cyanidin-3-glucoside, cyanidin-3,5-diglucoside, pelargonidin-3-glucoside, and pelargonidin-3,5-diglucoside with delphinidin-3,5-diglucoside being the major anthocyanin	[46, 47]
Stems and roots	Alkaloids: pseudopelletierine, isopelletierine, and N-methylisopelletierine, Anthocyanidins Pelargonidin, Gallic acid, ellagotannins and Ellagic acid	[43]
Peels	polyphenols, prodelphinidins, catechins, tannins	[48]
Leaves	Brevifolin carboxylic acid, Brevifolin carboxylic acid-10-monosulphate, 1,2,3-Tri-O-galloyl-β-D-glucose, 1,2,4-Tri-O-galloyl-β-D-glucose, 1,2,6-Tri-O-galloyl-β-D-glucose, 1,4,6-Tri-O-galloyl-β-D-glucose, 1,3,4-Tri-O-galloyl-β-D-glucose, 1,2, 4, 6-Tetra-O-galloyl-β-D-glucose 1,2,3,4, 6-Pent-O-galloyl-β-D-glucose, 3,4,8,9,10-pentahydroxy-dibenzo[*b*,*d*]pyran-6-one 1-(2,5-dyihydroxy-phenyl)-pyridium chloride	[49]
Juice	Cyanidin-3-glucoside Cyanidin-3,5-diglucoside Cyanidin-3-rutinoside Delphinidin Delphinidin-3-glucoside Delphinidin 3, 5-diglucoside Pelargonidin 3-glucoside Pelargonidin 3,5-diglucoside	[49]

Pomegranates grow well in subtropical climates to semi-arid mild--temperate. It is made up of a neat, rounded shrub or small tree that can grow to 20 or 30 ft. It's a deciduous plant but its leaves persist in some areas. The tree trunk has a red-brown bark that turns gray with time. Leaves are glossy, leathery, and narrow. The plants' flowers have attractive scarlet, white or variegated flowers that are over an inch with 5–8 petals with a red, fleshy, tubular calyx that remains on the plants' fruit, Plate 1. It is both a self-pollinating plant species and an insect cross-pollinated plant. The base of the fruit is a prominent calyx. The interior of the fruit is partitioned and well separated by membranous walls and white, spongy, tissue packed with sacs filled with pink, red or white pulp or aril. In each sac, there is one hard or soft seed [43].

They are adequately adapted to environments with hot summers and cool winters [43]. A humid climate adversely affects the formation of fruit. The tree can be severely injured by temperatures below 12° F Juice from pomegranate is collected by crushing seeds that have been established to contain polyphenols such as Gallo, ellagitannin, and flavonoids [12]. *Punica granatum* L is consumed in different forms such as juice, wine, or as a jam [43]. The taxonomic classification is highlighted in Table 5. The red color of the juice extract has been associated with anthocyanins [44].

Table 7
Taxonomic classification of soybean (*Glycine max*) [59].

Domain	Eukaryota
Kingdom	Plantae
Phylum	Spermatophyta
Subphylum	Angiospermae
Class	Dicotyledonae
Order	Fabales
Family	Fabaceae
Subfamily	Papilionoideae
Genus	Glycine
Species	*Glycine max*

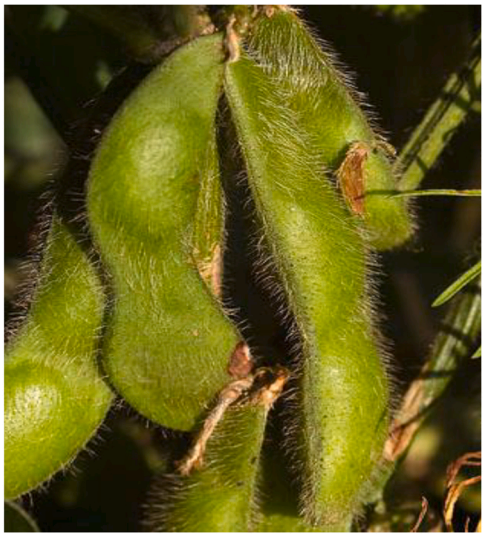

Plate 2. Soybean in pods.

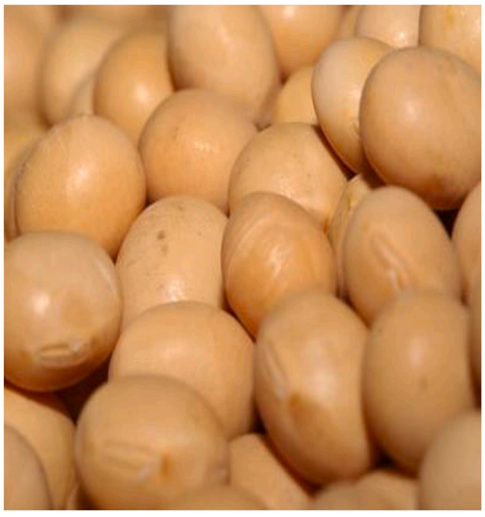

Plate 3. Soybean seeds.

4.2. Phytochemicals present

The main phytochemical present in *Punica granatum* L is the polyphenols which include flavonoids, hydrolyzable tannins, and condensed tannins. Hydrolyzable tannins (ellagitannins and gallotannins) are the most predominant polyphenols and represent about 92% of the plant's antioxidant activity [44,46]. Anthocyanins from *P. granatum* L have been determined to possess higher antioxidant properties than vitamin E

Table 8
Taxonomic classification of broccoli [75].

Hierarchal classification	Characteristics
Kingdom	Plantae – plants
Subkingdom	Tracheobionta – vascular plants
Superdivision	Spermatophyta – seed plants
Division	Magnoliophyta – flowering plants
Class	Magnoliopsida – dicotyledons
Order	Capparales
Family	Brassicaceae – mustard family
Genus	*Brassica* L. – mustard
Species	*Brassica oleracea* L. – cabbage
Varieties	*Brassica oleracea* L. var. *italica* Plenck – sprouting broccoli

Plate 4. Photo showing the head of harvested broccoli.

(α-tocopherol), β-carotene, and ascorbic acid [47]. Table 6 below shows the phytochemical compounds present in different organs of pomegranate.

4.3. Anti-colorectal cancer properties of Punica granatum L

P. granatum has demonstrated atherosclerotic and antioxidant characteristics because of its significant quantities of polyphenols including punicalagin, ellagic acid, ellagitannins, and also flavonoids such as luteolin glycosides, quercetin, and kaempferol [50]. Other studies have also demonstrated the induction of programmed cell death of colon cancer cells by punicalagin from *P. granatum* juice [51]. In addition, ellagitannins, gallotannins, and ellagic acid common in pomegranate have also been cited to induce apoptosis in the colon cancer Caco-2 cells [49]. Further, the intrinsic pathway of cell death happened when the mitochondrial cytochrome c leakage in the cytosol was induced by punicalagin and ellagic acid [51]. The consumption of pomegranate seed oil has been determined to largely inhibit the proliferation of colonic adenocarcinomas.

Tumor occurrence has been found to have enhanced aspects of peroxisome proliferator-activated receptor-gamma protein in the non-cancer mucosal [52]. COX-2 expression adjustment by *P. granatum* juice extract is a significant mechanism for colorectal cancer anti-proliferative activity of the juice, evidently correlated with the presence of polyphenols. Signaling pathways like phosphatidylinositol 3-kinase (PI3K), mitogen-activated protein kinase (MAPK), protein kinase B (AKT), and nuclear factor-kappa B (NFκB) correlate the mediation of COX-2 expression. The adjustment of NFκB process is mediated by P13K through AKT [12]. In mesangial cells, phosphatidylinositol 3-kinase (P13K) stimulation caused increased cell proliferation and COX-2 expression. *P. granatum* juice extract, therefore, inhibits NFκB activation, AKT processes, and finally the expression of COX-2 in colonic carcinoma cells [12,53]. Adams et al. [54] pre-treated HT-29 colon cells with pomegranate juice, total pomegranate tannins, as well as punicalagin, and their results showed that COX-2 expression was significantly decreased in a dose-dependent fashion. Kasimsetty et al. [55] treated HT-29 cells with urolithins/ellagitannins (pomegranate constituents) and reported that they caused apoptosis since they induced

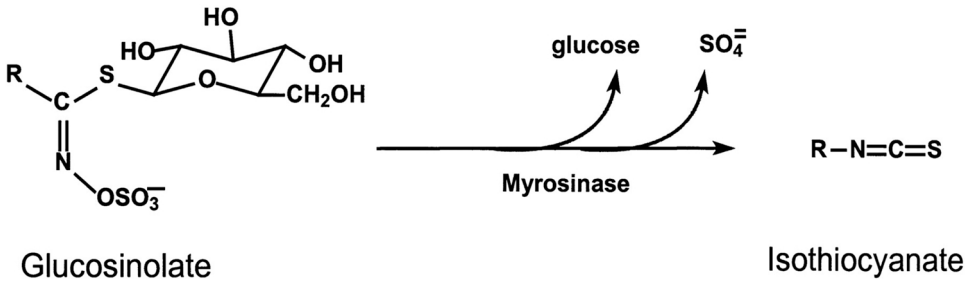

Fig. 1. Transformation of glucosinolates to isothiocyanates by plant myrosinase [78]. Broccoli seeds are major sources of glucoraphanin, glucoiberin, glucoerucin, 4OH-glucobrassicin, and glucoibervirin. Gut microbes also have an inherent capacity to transform glucoraphanin into sulforaphane.

Table 9
Classification of *Hibiscus rosa-sinesis* and *Hibiscus sabdariffa* [84].

Domain	Eukaryota
Kingdom	Plantae
Phylum	Spermatophyta
Subphylum	Angiospermae
Class	Dicotyledonae
Order	Malvales
Family	Malvaceae
Genus	Hibiscus
Species	Hibiscus rosa-sinensis, *Hibiscus sabdariffa*

caspase-3-like activity in a dose-dependent fashion. It has been demonstrated that pomegranate juice exerts a strong activity in inhibiting the expression of inflammatory cytokines interleukin-1 β (IL-1β) and IL-6 in periodontal therapy [46]. Other studies have demonstrated that pomegranate extracts scavenge free radicals and reduce macrophage oxidative activity, and lipid peroxidation, and increase plasma antioxidant capacity [43]. Oxidative stress yields toxic chemical metabolites which have been correlated with the initiation and promotion of cancer carcinogenesis [49]. It is therefore beneficial to adopt the use of natural antioxidants from *P. granatum* for colorectal cancer management. In addition, the dried pericarp of the fruit and the juice extract is regarded as important for the management of colic, colitis, headache, diuretic, menorrhagia, oxyuriasis, and acne, piles, oral infections, and allergic dermatitis [49].

5. *Glycine max* (soybean)

5.1. Botanical and morphological description

Glycine max is a plant commonly known as soybean. Soy food dietaries and isoflavones have received significant attention recently for their potential ability the prevention of osteoporosis and cancer [56]. Soybean is among the most beneficial oilseed and the least expensive source of plant protein globally [57]. It is the only legume classified under the genus Glycine as shown in Table 7. Its pods are characterized by a furry surface as shown in Plate 2. The seeds are also demonstrated in Plate 3 below [58].

5.2. Active biomolecules present in Glycine max

Polyphenols are naturally occurring antioxidants and studies have demonstrated that *Glycine max* is richly endowed with these bioactive molecules especially isoflavones [60]. In addition, soybean has low quantities of other antioxidant bioactive compounds such as tocopherol, saponin, phytate, and vitamin C [61]. In general, the active

Plate 5. Photos showing 5petalled *Hibiscus rosa-sinesis* growing in different colors.

Plate 6. Photo showing red calyx with 5 sepals and yellow flowers of a *Hibiscus sabdariffa* L plant.

Table 10
Active biomolecules present in hibiscus.

Class	Phytochemical compound	Ref.
Anthocyanins	Cyanidin-3-sambubioside	[14]
	Delphinidin-3-sambubioside	[82, 86–89]
	Delphinidin-3-glucoside	
	Cyanidin-3-glucoside	
Flavonoids and phenolic acid	Gallic acid	[14]
	Chlorogenic acid isomer I	[82, 86–89]
	Chlorogenic acid	
	Chlorogenic acid isomer II	[90]
	5-Hydroxymethylfurfural	
	Methyl gallate	
	2-O-trans-Caffeoyl-hydroxicitric acid	
	5-Caffeoylquinic acid	
	Myricetin-3-arabinogalactoside	
	Protocatechuic acid	
	3-Caffeoylquinic acid	
	Protocatechuic acid glucoside	
	Kaempferol-3-p-coumarylglucoside	
	Quercetin	
	Caffeic acid	
	Ellagic acid	
	Galloyl ester	
	Coumaroylquinic acid	
	Quercetin-3-sambioside	
	Feruloyl quinic acid derivative	
	Kaempferol-3-glucoside	
	Quercetin-3-rutinoside	
	5-O-Caffeoylshikimic acid	
	Myricetin	
	Catechin	
	Gallocatechin	
	N-Feruloyltyramide	
	Leucoside(kaempferol-3-O-sambubioside)	
	Quercetin-3-glucoside	
	Kaempferol-3-O-rutinoside	
	4-Caffeoylquinic acid	
	Quercetin derivative	
	Caffeoylquinic acid isomer	
	Tiliroside	
	Feruloyl derivative	
	Methyl (AS in Methylepigallocatechin)	
Organic acid	Hibiscus acid glucoside	[14]
	Hibiscus acid 6-methyl ester	[82, 86–89]
	Hydroxycitric acid	
	Hibiscus acid	

biomolecules common in the plant are Bowman-Birk inhibitor, Kunitz trypsin inhibitor, isoflavone-deprived soy peptide, hemagglutinin, neutral PR-5 protein, ferritin, peroxisomal proteins, SbPRP protein, defense proteins such as calmodulin, beta-glucan-binding protein, disease resistance protein, l unasin, and glysojanin [62]. Enzymes such as tyrosine ammonia-lyase and phenylalanine ammonia-lyase and, defense-related enzymes, cysteine proteinase, isocitrate lyase, isoflavone synthase, chalcone reductase, and vast tone reductase [62]. UDP-glucose such as flavonoid 3-O-glucosyltransferase, isoflavone conjugate-hydrolyzing beta-glucosidase, beta-glucosidase, anticarcinogenic daidzein-rich fraction, polysaccharides, glyceollins, and isoflavones, genes associated to 2-oxoglutarate-dependent dioxygenases, 5′-adenylylsulfate reductase, and also ATP sulfurylase, glycinin derivatives such as e-Phe-Leu and Trp-Leu, and Val-Leu-Ile-Val-Pro [62, 63].

5.3. Anti-colorectal cancer properties

Soybeans are distinctively unique among the leguminous plants since they are an aggregation source of isoflavones and anthocyanins. Genistein is the most plentiful form of isoflavones common in soybean and is largely associated with the anticancer properties of soybean [64]. Isoflavones can potentially bind to estrogen receptors because they are structurally like endogenous estrogen and therefore inhibit hormone-related carcinogenesis [11]. The consumption of legume fiber is largely correlated with a decreased risk of colon cancer as demonstrated by other studies [11]. Other researchers [65] similarly found that consumption of soybeans was connected to a nearly 21% reduction in the risk of developing colon cancer among women. This result is linked to the metabolic and structural similarities of isoflavones in soy to estrogens in mammals. Genistein influences the tyrosine-specific protein kinases through its inhibitory potency which are associated with the proliferation of cancerous cells and therefore attenuate their growth and development. Genistein further redesigns the replication of DNA and hence repairing the injurious damages inflicted by the mutagen [66]. The other anticancer activities of genistein are related to the modulation of apoptosis through the inhibition of cell death. Soybean-derived gma-miR159a has been demonstrated to be assimilated by mammals and inhibit colon cancer and colitis, which is a significant pointer that soybean miRNAs can improve quality of the intestinal health through a long-term diet consumption [67]. The TCF7 gene is wrongly activated during colon cancer development which could be a significant target for colon cancer prevention and similarly its treatment. Of great importance is that endogenous miRNAs such as miR-34a, miR192, and miR6852 among others are associated with TCF7 gene regulation and therefore inhibiting the occurrence and development of colon cancer [67].

Polyphenolic bioactive compounds such as quercetin have demonstrated significant prophylactic and therapeutic activities against colon cancer, with its non-mutagenic potential and demonstrated low toxicity. The chemotherapeutic activity of quercetin has been achievable through inhibition of cell proliferative potential, promotion of cell cycle arrest, and induction of cell apoptosis [3]. More studies have shown that the rate of colon cancer incidence is low in Asian countries and this has been associated with their appropriate intake of sufficient amounts of soybean [64]. Soybean polypeptides and their soluble sugars cause programmed cell death activities on colorectal cancer cells, in a concentration-dependent manner through the generation of reactive oxygen species (ROS) and mitochondrial dysfunction, stimulating caspases and splitting the polymerase protein chains [68].

Most lifestyle-related diseases such as colonic cancer are largely correlated with the oxidative injurious damage poised by free radicals by oxidizing biomolecules [61]. Considering this, the presence of natural antioxidants in soybean is an important dietary supplement that could significantly lower the risks and incidences of colon cancer by scavenging these free radicals in the body. It has been demonstrated in other studies that mimicked gastrointestinal digestion activity of germinated *Glycine max* bioactive proteins increases its antiproliferative activity against cancerous cells by the initiation of programmed cell death (apoptosis) and down-regulation of target cancerous genes [69]. Peptides are known to inhibit the release of pro-inflammatory agents in lipopolysaccharide (LPS) induced macrophages, while the digestive

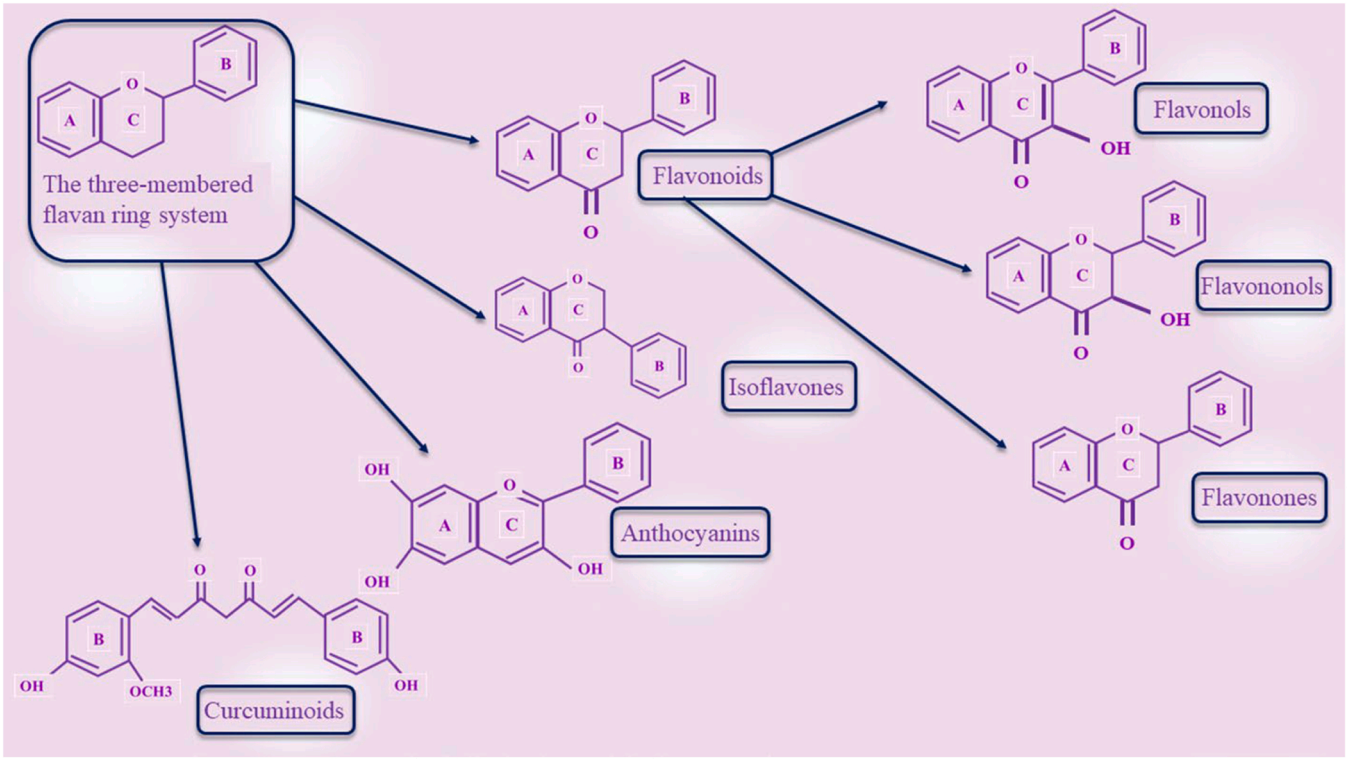

Fig. 2. Polyphenolic compounds with a three-structural flavan-ring system. Mechanisms of polyphenols are largely dependent on the availability of the benzene ring-bound hydroxyl groups and the structural molecular organization of polyphenols.

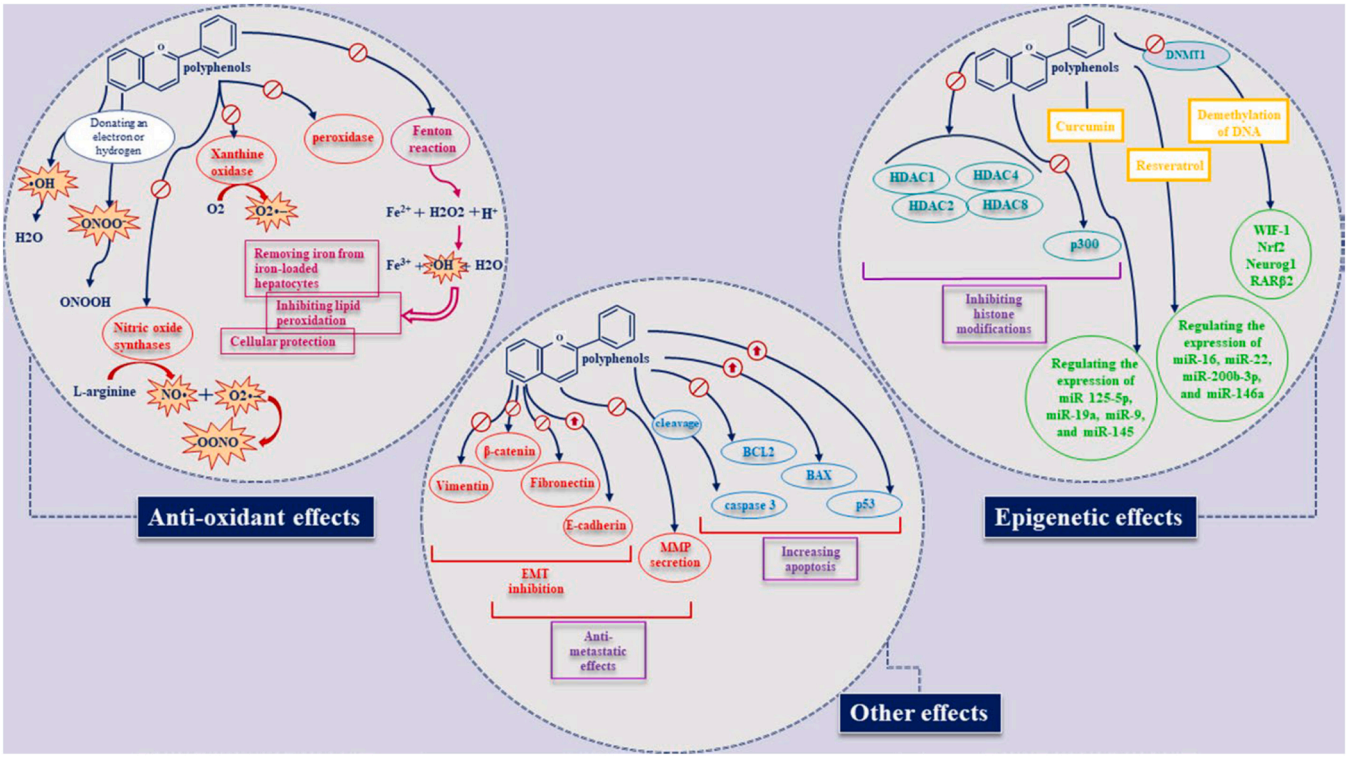

Fig. 3. Anti-cancer polyphenolic effects: antioxidant effects, epigenetic effects, apoptotic effects, and anti-metastatic effects. Polyphenols elicit these modulatory effects and hence inhibiting the growth and proliferation of cancer.

process promotes the transformation of food dietary nutrients to physiologically bioactive compounds [70]. A separate study further observed that pepsin-pancreatin compounds from ungerminated *Glycine max* proteins decreased the inflammatory activities of macrophages to lipopolysaccharides by preventing the expression of iNOS and COX-2 [70]. High oleic acid (OA) soybean lines have demonstrated active properties

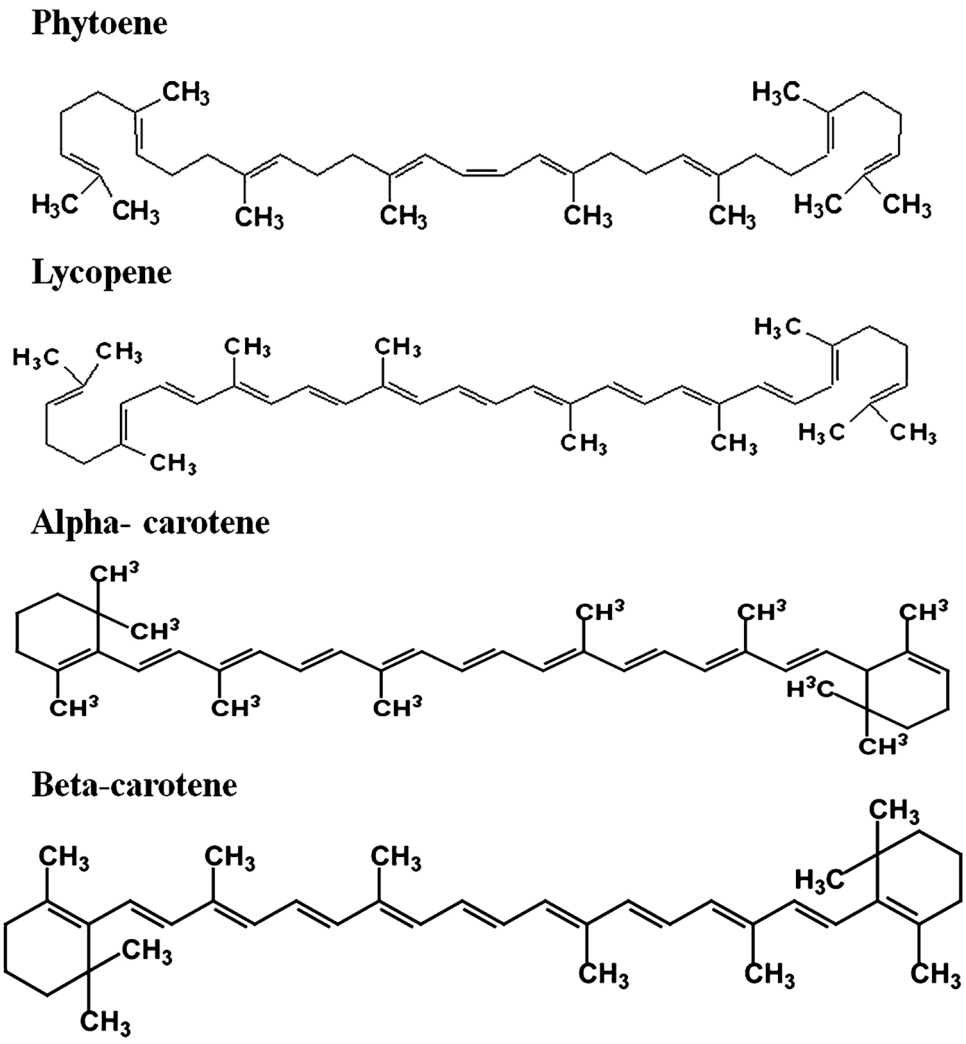

Fig. 4. Different structures of phytochemical carotenoids; phytoene, lycopene, Alpha-carotene, and Beta-carotene. Carotenoids are classified as tetraterpenoids and are fundamentally synthesized in plants and other photosynthetic organisms, and by non-photosynthetic bacteria, molds, and yeast. Lycopene has been thought to inhibit atherogenesis and carcinogenesis [101].

of inhibiting cancer cell growth in cancer cell lines and have proven potential nutraceutical use against human colonic cancer [71]. Active metabolites in soybean, therefore, inhibit cancer cell growth and proliferation, influence cell differentiation, promotes apoptosis, inhibits angiogenesis, and function as a tyrosine kinase inhibitor [72]. This study therefore equivocally supports the idea of the chemo-preventive ability of peptide molecules derived from soybean against human colorectal cancer and inflammation.

6. Cruciferous vegetables

Cruciferous vegetables such broccoli, cabbage, cauliflower, and Brussels sprouts constitute significant levels of sulforaphane which has anti-cancer therapeutic properties [73]. Of all the cruciferous vegetables, broccoli sprouts have the highest concentration levels of sulforaphane because the biomolecular compound originates in the seed and it is not manufactured in the broccoli plant as it grows [74]. Notably, it has scientifically been established that one sprout carries all the sulforaphane that is commonly available in a full-grown broccoli plant [74]. Plants associated with the family Cruciferae and genus Brassica such as cauliflower and broccoli have significant quantities of isothiocyanates largely occurring as their glucosinolate precursors e.g., 4-methylsulfinylbutyl isothiocyanate or sulforaphane. These precursors actively stimulate phase 2 enzymes [74]. This review focuses on broccoli sprouts due to their proven high concentration levels of the sulforaphane biomolecular compound compared to other cruciferous plant vegetables.

6.1. *Brassica oleracea L var. italica Plenck (Broccoli)*

6.1.1. *Botanical and morphological description*

Broccoli is a plant belonging to the family Brassicaceae previously referred to as Cruciferae, Table 8. Plants belonging to the genus Brassicaceae have a vast history of being cultivated for their edible leaves, fleshy stems, roots, inflorescence, or oils commonly extracted from the seeds [75]. Broccoli has plenty of green fleshly endowed flower heads (primary inflorescence) arranged like a tree, with branches emerging from a thick consumable stem. The large mass of heads is covered with numerous leaves [76] as shown in Plate 4. Broccoli has plenty of nutritional properties such as a good source of vitamins A, C, and niacin, in addition to mineral elements such as potassium, calcium, sodium, magnesium, and fiber [76]. The average size for harvesting the leafy head of broccoli is approximately 16 cm in diameter [76,77].

6.2. *Phytochemical compounds present in broccoli*

Phytochemicals present in broccoli are significant in enhancing the human immune system. They include glucobrassicin; kaempferol, polyphenols; flavonoids and phenolic acids, and carotenoids;

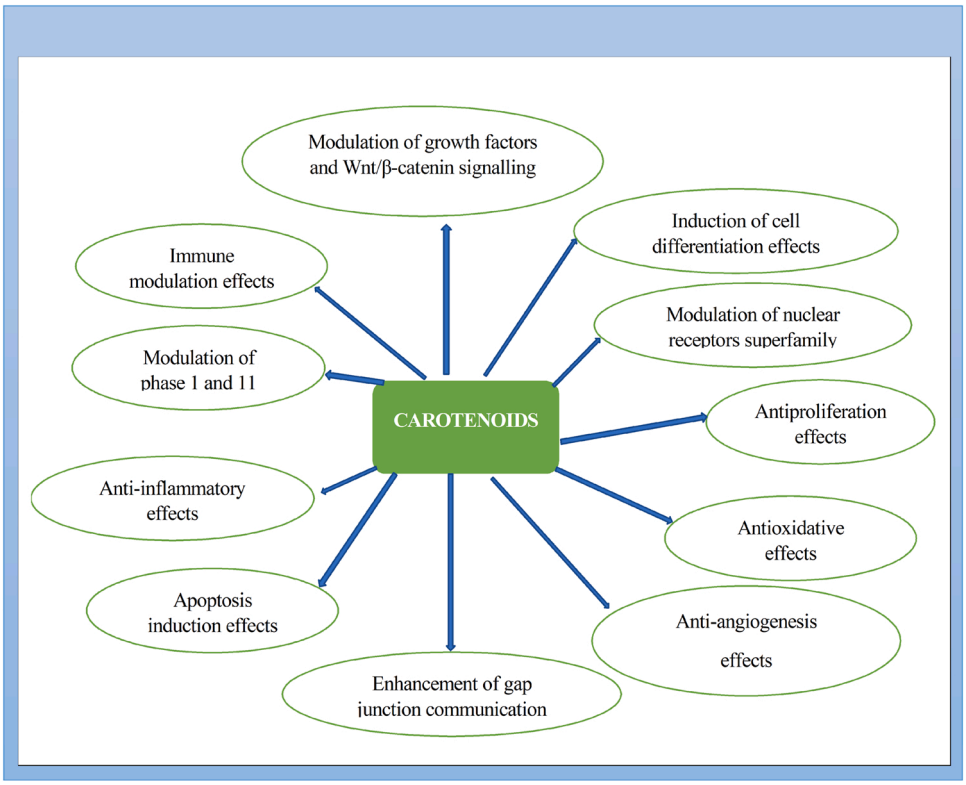

Fig. 5. Different mechanisms of cancer chemotherapy by carotenoids. Transformation of numerous proteins demonstrate that the initial influence involves modulation of transcription. This modulation may occur through other transcription factors or at the level of ligand-activated nuclear receptors.

Table 11
Different carotenoids and their significant effects in the body.

Carotenoids	Significance	Effects elicited
α-Carotene	Antioxidant; Provitamin A activity	Reduced risk of certain cancers; Immunity enhancement; Stimulate cell to cell communication;
Lycopene	Antioxidant	Reduced risk of certain cancers; Reduced risks of certain cardiovascular diseases, osteoporosis and diabetes
β-Cyptoxanthin	Antioxidant; Provitamin A activity; Anti-inflammatory effects	Prevents risks of certain cancer and cardiovascular conditions; Immunity enhancers
Lutein/ Zeaxanthin	Photosynthetic pigment; anti-photosensitizing agent; antioxidants; and blue light filters	Decreased risk of cardiovascular disease and certain cancers; reduced age-related muscular Degeneration and cataract
Astaxanthin	Coloration; antioxidant	Decreased risk of certain cancers, diabetes, cataract, and cardiovascular diseases
Canthaxanthin	Coloration; antioxidant	Decreases risk of some cancers, immune enhancement.
Focoxanthin	Antioxidant	Antiallergic, anti-obese, anti-inflammatory, anticancer and anti-osteoporotic activities

zeaxanthin, and beta-carotene. The seeds contain a rather substantial amount of glucosinolates and glucoraphanin specifically compared to the leaves and the inflorescence tissues of the plant [75]. Broccoli seeds are the most suitable sources of glucoraphanin besides being constituents of other forms of glucosinolate such as glucoiberin, glucoerucin, 4OH-glucobrassicin, glucoibervirin [73–75]. Sulforaphane is often produced upon the transformation of glucoraphanin (a glucosinolate) by the enzyme myrosinase upon an injury to the plant as demonstrated in Fig. 1. Further, it has also been demonstrated that glucoraphanin may equally be transformed to sulforaphane by gut microorganisms [78].

6.3. *Pharmacological activity of broccoli against colorectal cancer*

Glucosinolates (glucobrassicin) biomolecules are largely distributed in the genus Brassica and have stimulated substantial interest regarding their perceived role in cancer control and prevention [75]. Broccoli has numerous quantities of sulforaphane that inhibit cancerous growth by induction. The induction activity emerges principally from glucoraphanin (the glucosinolate of sulforaphane) where these sprouts have relatively low levels of indole glucosinolates and are possible tumor promoters [74]. These phytochemical antioxidants common in broccoli neutralize the unstable molecules (free radicals) that promote cell damage. Isothiocyanates such as sulforaphane and indole-3-carbinol are associated with enhancing detoxifying enzymes and function as antioxidants, hence reducing oxidative stress [74,75], which inhibits chemical metabolism of the potential carcinogens [78].

Notably, most isothiocyanates have been supported by substantial evidence to be potential inducers of phase 2 proteins [79]. This approach has been found effective in reducing the risk of exposure and susceptibility to carcinogens. However, besides detoxifying electrophiles, phase 2 proteins exert versatile, enduring, and substantial catalytic antioxidative protection [79].

Observed lyophilized sprouts demonstrated substantial proapoptotic and selective cytotoxic effects against colon carcinogenesis, without harmful or toxic effects on normal human cells [80]. Broccoli sprouts with their abundant presence of polyphenolics and sulforaphane, the florets, and leaves have all demonstrated potent chemo-preventive properties against colorectal carcinogenesis [81], and this study therefore strongly supports their incorporation as significant natural antioxidant dietary supplements.

7. *Hibiscus rosa-sinesis* and *Hibiscus sabdariffa* L (hibiscus plants)

7.1. Botanical and morphological description

The genus (Malvaceae) comprises more than 300 species of either annual or perennial herbs, trees, or shrubs [82]. *Hibiscus rosa-sinensis* is a bushy, evergreen perennial shrub growing as tall as 2.5–5 m (8–16 ft) and 1.5–3 m (5–10 ft) wide, with solitary, red flowers, and glossy leaves. It has a tap root system. The flowers are 5-petaled and are 10 cm in diameter, with orange-tipped red anthers. They can occur in different colors: white, orange, peach, yellow, pink, red, or can be purple which are 4–18 cm broad. The leaf is simple, alternate, stipulate, serrate, petiolate, glabrous, and apex acuminate with multicostate reticulate venation. The fruit is mostly abortive. *Hibiscus rosa-sinesis* is traditionally grown for its large bell-shaped blossoms [83]. *Hibiscus sabdariffa* L also known as roselle is an ideal and perfect crop for developing countries because it is easy to grow and can be intercropped for consumption as food and fiber [82].

Hibiscus sabdariffa L is an annual, bushy, and erect herbaceous subshrub that can grow up to 8 ft tall, with smooth cylindrical and typically red stems. The leaves of the plant are alternate, 3–5 in, and are 7.5–12.5 cm in length, green with red coloring venules and long or shortened petioles. The leaves of the plants are simple; lower leaves are 3–5 or could even be 7 lobed, while the margins of the leaves are toothed. Flowers are borne singly in the leaf axils and are about 12.5 cm wide, yellow, have maroon eyes as they buff, and turn pink as they continue to wither. They consist of a typical red calyx, with 5 large sepals with an epicalyx of 8–12 slim, bracts (or bracteoles) at the base, Table 9, Plates 5 and 6 [82].

7.2. Phytochemicals present in hibiscus

Hibiscus consists of numerous active biomolecules ranging from anthocyanins, flavonoids, phenolic acids, and organic acids [80,82] as summarized in Table 10. The plants contain substantial amounts of organic acids such as citric acid, hibiscus acid, malic acid, hydroxycitric acid, and tartaric acids as major constituents, while ascorbic acid and oxalic acid as the minor constituents [82]. It has been established through studies that cyanidin-3-sambubioside (cyanidin-3-O-(2-O-b-D-xylopyranosyl)-b-D-glucopyranoside), delphinidin-3-sambubioside (delphinidin-3-O-(2-O-b-D-xylopyranosyl)-b-D-glucopyranoise) and cyanidin-3-glucoside as the most abundant anthocyanins in leaves and flowers of *Hibiscus sabdariffa* L [85].

7.3. Pharmacological activity of both species against colon carcinogenesis

The main compounds of *Hibiscus sabdariffa* L significant in the context of its pharmacological potential are anthocyanins, organic acids, polysaccharides, and flavonoids [82]. On the other hand, *Hibiscus rosa-sinesis* plant extract has been cited to possess numerous medicinal and anticarcinogenic properties due to its hypolipidemic and antioxidant effects [91]. The flowers have been demonstrated to have a high pharmacological potential for hypertension and pyrexia management [92].

Chronic inflammation and oxidative stress are often associated with chronic diseases including colon carcinogenesis [93]. These processes together are involved in the stages leading to tumourigenesis such as cellular transformation, proliferation, promotion, angiogenesis, metastasis, and survival [93,94]. As previously reviewed, hibiscus constitutes numerous quantities of polyphenolic compounds that act as excellent antioxidants [93]. In addition, anthocyanins do not only have antioxidant potential but also have a role in mediating other crucial physiological functions associated with carcinogenic suppression [14]. These bioactive polyphenols actively scavenge on reactive free radicals (ORFs) that could otherwise cause inflammation along the colonic mucosa membrane. It has been documented that OFRs begin a chain reaction that could cause damage to biological macromolecules including carbohydrates, lipids, proteins, and nucleic acids, causing an imbalance of the body's homeostasis [95]. Hibiscus extracts have been found to significantly inhibit the migration and possible invasion of the human colorectal cancer cell DLD-1, and similarly induced suppression of metastasis through downregulation of the associated FAK signaling and CD44/c-MET signaling [13].

Overexpression of CD44 has been established to correspond with tumor metastasis in different forms of cancers [96]. More studies suggest that the expression of CD44 is essentially upregulated in colorectal carcinogenesis and correlates with the observed poor clinical manifestation [97]. The role of CD44 in metastasis is associated with interaction with tyrosine kinase (enzyme) receptors such as c-MET, which is an oncoprotein commonly linked with tumor progression, migration, invasion and proliferation. In addition, more expression of CD44 and the induced activation of c-MET can significantly promote FAK phosphorylation and the downstream signaling that enhances cell motility [96,97]. Notably, hibiscus adequately downregulates CD44 and c-MET expression while inhibiting FAK signaling processes such as paxillin, Akt, RhoA, Rac1, Cdc42, thus suppressing DLD-1 cell metastatic ability [13]. Hibiscus protocatechuic acid has been shown to confer an efficacious agent by inhibiting the carcinogenic activity of azoxymethane in the colon [14]. The ethanolic extracts of these plant species have proven effective in inhibiting the mutagenicity influenced by heterocyclic amines in the *Salmonella* microsome assay and thus inhibiting the formation of colon tumors at the initiation stage. Further, chloroform and ethyl acetate extracts obtained from the leaves of these plants decreased the mutagenic activity conferred by 1-nitropyrene in HeLa cellular cells in a dose-response process exhibiting an antiproliferative effect [14]. Hibiscus is therefore an important plant that potentially deters the growth and proliferation of malignant colorectal cancer cells.

7.4. The molecular mechanism of polyphenols and their anti-cancer effects

The diverse mechanisms of polyphenols are largely dependent on the availability of the benzene ring-bound hydroxyl groups, which confer the scavenging ability of free radicals [98], and also on the structural molecular organization of different polyphenols [99]. Flavonoids are numerous and diversely varied based on their hydroxylation pattern, conjugation potential between the aromatic rings, methoxy groups, and glycosidic moieties [100]. Their nuclear structural polymerization produces tannins and other important reactive species. Flavonoids and their subsequent derivatives of benzo-ɣ-pyrone are widely distributed in plants [99]. Notably, the antioxidative potential of polyphenols occurs either through the scavenging of reactive free radicals or through the formation of a blockade against their generation [98].

Reactive nitrogen species (RNS) and reactive oxygen species (ROS) are the major free radicals that principally cause and propagate oxidative stress in human cells. Oxygen is a substantive reactive element that is likely to become part of potentially injurious cellular molecules often regarded as "free radicals." These free radicals can attack the normal cells resulting in structural and functional loss [101]. Oxidative stress can exert injurious effects on large molecules like proteins, lipids, and DNA causing an elevated risk for cancer [101]. The benzene ring of polyphenols is significantly involved in scavenging peroxyl, hydroxyl, and peroxynitrite radicals [100]. 3′4′-catechol and unsaturated 3-OH arrangement are the known determining structural organization against peroxynitrite [102]. Figs. 2 and 3 demonstrate the schematic polyphenolic molecular compounds with three-structural flavan-ring systems and their subsequent molecular mechanisms eliciting anticancer effects.

7.5. Molecular mechanisms of cancer chemotherapy by carotenoids

Because chemotherapy is a significant strategy in the management of

cancer, molecular mechanism-based cancer chemotherapy using carotenoids is becoming a more attractive approach [103]. Carotenoids are classified as tetraterpenoids and are fundamentally synthesized in plants and other photosynthetic organisms as well as by non-photosynthetic organisms such as bacteria, molds, and yeast [104]. Lycopene is a structured biomolecular singlet oxygen extinguisher that has demonstrated tumor suppressive potency on mice in vivo and human cells. It is a more efficient antioxidant with a singlet-oxygen-extinguishing potential compared to ß-carotene tocopherol [101]. The molecular mechanisms of tumor chemoprevention by carotenoids derived from plants are changes in pathways resulting in apoptosis or cell growth. The associated mechanisms include regulatory mechanisms of cell cycle progression, hormone and growth factor signaling, immune modulation, and cell differentiation [103]. Biomolecular carotenoids such as β-carotene, α-carotene, β-cryptoxanthin, lutein, lycopene, zeaxanthin, neoxanthin, violaxanthin, canthaxanthin, fucoxanthin, astaxanthin, and siphonoxanthin have been established to be potent against growth and proliferation of different cancerous cells such as colon, breast, liver, prostate, leukemia and cervical cancer [101].

Colon cancer mostly develops in inflamed tissues, demonstrating that inflammation of body tissues is significantly correlated with cancer development [105]. It is therefore evident that chronic inflammatory conditions cause an increased incidence of carcinogenesis [103,105]. Therefore, suppressive inhibition of inflammatory cytokine expression is directly associated with inhibition of cancer development. The associated inflammatory cytokines are IL-1β, IL-6, and TNF (tumor necrosis factor). The expression of cytokine is majorly regulated by NF-kB. Studies have demonstrated that astaxanthin prevents the expression of the above inflammatory cytokines and NF-kB, and consequently inhibited inflammatory-associated colorectal cancer development in mice [106] (Figs. 4, 5 and Table 11).

8. Conclusion and future recommendations

Plants have significant bioactive compounds essential for growth and development. They are widely consumed as food and for their medicinal values in virtually all cultures. The reviewed plants in this study constitute active phytochemical compounds such as Quercetin polyphenols and carotenoids among other active biomolecules that inhibit the growth and development of colorectal cancer. Synthetic COX-2 inhibitors have been established to have adverse side effects and thus natural inhibitors occurring in such plants could be explored as alternative forms of chemoprevention therapies in colon cancer management. Natural antioxidants including polyphenols and carotenoids inhibit the oxidation of lipids, proteins, and nucleic acids and thereby preventing the initiation of oxidizing chain reactions. These bioactive compounds should be considered an important dietary supplement that could significantly lower the risks and incidences of colon cancer by scavenging on unstable molecules that could initiate carcinogenesis. To avert heavy dependence on synthetic antioxidants for empirical CRC treatments, this article provides a strong basis for ethnopharmacological investigation and exploration of active phytochemical constituents that are prevalent in the reviewed plants and are natural antioxidants. More studies should however be done to determine and classify the dose levels necessary to produce sufficient preventive therapy.

Author contributions

All the authors contributed significantly to the development, review, and editing of the manuscript. All authors approved the submission of the manuscript.

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Conflict of interest statement

The authors declare no conflict of interest.

Data Availability

Data will be made available on request.

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