

Anti-Inflammatory and Anti-Cancer Properties of Selected Green Leafy Vegetables - A Review

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Abstract

Green leafy vegetables are edible leaves of plants and are important components of a balanced diet. They are consumed alone or alongside other dishes as sauces or soups. Green leafy vegetables are packed with nutrients predominantly bioactive compounds that have been reported to promote a healthy state and ameliorate disease conditions. These bioactive compounds exert antioxidant, anti-inflammatory and other biological activities. Non-communicable diseases including cancers, cardiovascular and metabolic diseases have been reported to be aggravated by inflammation and oxidative stress. This paper, therefore, aimed to provide the scientific validation for the selected green-leafy vegetables as anti-inflammatory and anti-cancer agents. Databases including PubMed, Google Scholar and ScienceDirect were used to perform the search. The reviewed vegetables include *Vernonia amygdalina*, *Corchorus olitorius*, *Talinum triangulare*, *Telfairia occidentalis*, *Gongronema latifolium*, *Moringa oleifera* and *Celosia argentea*. Although the antioxidant, anti-inflammatory and cytotoxic properties of these vegetables were presented, detailed studies from multiple researchers were scanty. Therefore, further studies on these vegetables are encouraged to have sufficient data to ascertain scientific validation for anti-inflammatory and anti-cancer claims.

Keywords: anti-inflammatory; anticancer; antioxidant; green leafy vegetables; oxidative stress

Introduction

Oxidative stress is a global phenomenon that describes the imbalance between the number of pro-oxidants and antioxidants in favour of pro-oxidants [1]. Pro-oxidants notably reactive oxygen species and reactive nitrogen species such as nitric oxide, singlet oxygen, lipid peroxides are elevated in the state of oxidative stress in contrast to reduced levels of endogenous antioxidant defence molecules such as superoxide dismutase, glutathione peroxidase, catalase, etc. [2]. A lot of the natural processes that take place in the human body generate free radicals which are the culprits of oxidative stress. Free radicals are necessary for some biological processes that are essential for life, acting as signal molecules at low concentrations in cellular pathways [3], however, excessive generation of free radicals causes the damage of tissue macromolecules (proteins, lipids and DNA) leading to structural modifications as well as cellular dysfunctions [4,5].

High amounts of free radicals have been implicated in the outset of many diseases including cancer; a disease that has been reported to result from

DNA damage thus affecting the cell cycle⁶. The development of cancer is an intricate process that implicates oxidative stress, inflammation and genetic makeup, which are triggered by both exogenous and endogenous factors [7,8]. Elevated oxidative stress in cancer cells is aggravated by metabolic changes and mitochondrial dysfunctions, thereby enhancing the expression of the cell survival protein - nuclear factor erythroid 2-related factor 2 (NRF-2) which encourages the progression of cancer [6].

About 25% of all cancers have been associated with inflammatory reactions [9]. Cancer cells are in a hyperactive state of oxidative stress as a result of increased metabolism and ROS [10]. Reactive oxygen and nitrogen species within the inflammatory microenvironment, damage tissue macromolecules including proteins, DNA and lipids. Accumulation of the damaged cells leads to the generation of cancer stem cells [10]. This process facilitates the recruitment of inflammatory cytokines such as interleukin-6, which in turn aggravates the generation of superoxide (O₂^{•-}) and nitric oxide radicals through the inducible nitric oxide synthase (iNOS) and nicotinamide adenine dehydrogenase (NADH) pathways.

Furthermore, at the level of gene expression, reactive oxygen/nitrogen species and pro-inflammatory cytokines stimulate the expression of DNA methyltransferase-1 protein leading to DNA methylation of tumour suppressor genes [11].

Free radicals are degraded by the body's natural defence system, supported by exogenous antioxidant compounds such as vitamins, minerals, and some phytochemicals including polyphenols, flavonoids and others [6]. Plants are beneficial to humans for the management of diseases owing to the presence of phytochemicals (bioactive compounds) present in them [12]. There are epidemiological shreds of evidence for the role of bioactive compounds in combating human diseases such as cancer, diabetes, cardiovascular diseases and others [13]. Green-leafy vegetables are important components of a balanced diet and they are rich in many beneficial bioactive compounds including terpenoids and polyphenols. The anti-inflammatory and anticancer properties of seven green-leafy vegetables including *Vernonia amygdalina*, *Corchorus olitorius*, *Talinum triangulare*, *Telfairia occidentalis*, *Gongronema latifolium*, *Moringa oleifera* and *Celosia argentea* were reviewed in this paper. The objective of this review is to provide scientific validation for the selected green-leafy vegetables as anti-inflammatory and anti-cancer agents, with the hope of promoting their cultivation, utilisation and consumption.

Methodology

Scientific databases including ScienceDirect, PubMed and Google Scholar were used to search for available literature on the selected green-leafy vegetables for anti-inflammatory and anti-cancer properties. Keywords including "anticancer", "anti-inflammatory", "green-leafy vegetables", "Nigeria", "*Vernonia amygdalina*", "*Corchorus olitorius*", "*Talinum triangulare*", "*Telfairia occidentalis*", "*Gongronema latifolium*", "*Moringa oleifera*" and "*Celosia argentea*" were used for the search.

Results and discussion

Information about the plants presented includes; family, scientific and common names, phytochemicals present and biological activities reported. Seven green leafy vegetables commonly consumed in soups or sauces along with staple meals whose anti-inflammatory and anticancer properties have been reported were identified. These vegetables include *Vernonia amygdalina*, *Corchorus olitorius*, *Talinum triangulare*, *Telfairia occidentalis*, *Gongronema latifolium*, *Moringa oleifera* and *Celosia argentea*.

***Vernonia amygdalina*:** *Vernonia amygdalina* is a shrub popularly grown in Africa both for its medicinal and culinary properties. It belongs to the family- Asteraceae, and is commonly called 'bitter leaf'. As the name implies, the shrub has a characteristic bitter taste which can be reduced by washing and discarding the water several times before use for culinary purposes, but for medicinal purposes, the bitter extract is consumed rather than being discarded. In Nigeria, extracts of bitter-leaf are used to manage many diseases including diabetes, malaria, hypertension, cough, blood tonic, etc¹⁴. Phytochemicals present include flavonoids, saponins, tannins, oxalates, sesquiterpene lactones, phenolic acids, xanthenes, etc. [15]. Biological activities reported for *V. amygdalina* include antibacterial, antimalarial, antifungal, anticancer, antioxidant, hypoglycaemic, hepatoprotective, analgesic, antihypertensive, etc [16]. The cytotoxicity of *V. amygdalina* against 4T1 breast cancer cells showed that the n-hexane, ethyl acetate and ethanol fractions exerted an inhibition concentration of 1860.54±93.11, 25.04±0.36 and 1940.84±96.37 µg/ml respectively [16]. Furthermore, Johnson et al. reported that methanol extract of *V. amygdalina* exerted a cytotoxic effect on PC-3 Human Prostate Carcinoma cells, using the trypan blue test, cell morphology analysis and the MTT assay [17]. In an earlier report, extract of *V. amygdalina* exerted apoptotic effects on MCF-7 breast cancer cells [18].

The ability of extract of *V. amygdalina* to modulate oxidative stress in cancer cells has also been reported.

***Corchorus olitorius*:** *Corchorus olitorius* is a popular vegetable in Nigeria and West Africa, it is commonly called 'ewedu' by the Yoruba people. The plant belongs to the Malvaceae family and its English name is 'Jute' [19]. The leaves serve as a vegetable in a variety of soups and are slimy. Traditionally, the leaves of *Corchorus olitorius* are used to treat headaches, stomach problems, general pains, fevers, gonorrhoea, tumours and chronic cystitis [20,21]. It has also been used as a diuretic, purgative, and is employed to ease labour pains and delivery. Jute leaf contains good amounts of antioxidants like vitamin E, A, and C; and its antioxidant potential is highly employed in the management of many diseases including diabetes, heart disease as well as hypertension [22]. Phytochemicals present include alkaloids, saponins, cardiac glycosides, phenols and flavonoids, chlorogenic acids, phytol and monogalactosyldiacyl glycerol [21,23]. The biological activity carried out on the extract of *Corchorus olitorius* against cancer cell lines HeLa (cervical), HL460 (lung) and PC-3 (prostate), showed mild cytotoxicity at ≥800µM [21]. Ethanol extract of *Corchorus olitorius* exerted a reductive effect on viable cells based on results obtained from MTT assay carried out on MCF-7 breast cancer cell line [24].

***Moringa oleifera*:** *Moringa oleifera* L of the family- Moringaceae, is a perennial angiosperm plant. The plant is native to the Himalayan region but is however currently domesticated in most tropical and sub-tropical countries of the world including Saudi Arabia [25]. Moringa leaves are edible and can be added to salads, rice or pasta or other dishes, soups. The leaves can be juiced, fried or steamed. Moringa leaf powder can also be used as a tea, added to beverages, sprinkled on food or taken in capsules. In folklore, various parts of the plant are employed in the treatment of diseases including ear and dental infections, hypertension, anaemia, cancer, diabetes, skin infections, respiratory infections and others [26]. Moringa leaves are a rich source of both micro- and macro-nutrients including digestible proteins, minerals, vitamins and phytochemicals such as alkaloids, cyanogenic glycosides, oxalates, saponins, phytates and tannins [27]. Some bioactive compounds reported conferring anticancer benefits including isopropyl isothiocyanate, eugenol, D-allose, and hexadecenoic acid ethyl ester [28], have been identified in the ethanol extract of the leaves. Biological activities reported for moringa leaves include antioxidant, anticancer/antitumor, antidiabetic, antilipidemic, hepatoprotective and anti-inflammatory effects [29]. Cytotoxicity studies carried out on breast and colorectal cancer cell lines (MDA-MB-231 and HCT-8 respectively) using ethanol extract of leaves of moringa showed significant anticancer effect²⁸. Treatment of both cancer cell lines with ethanol extract of moringa leaves showed a 90% decrease in cell motility assay; while an 80-90% decrease in anchorage-dependent colony formation was also observed. Furthermore, it was reported that the apoptotic ability of the extract was observed in the late phase of the cell cycle [28]. Recently, the reports of Khor et al. showed that moringa leaf extracts were effective against the proliferation of Kasumi-1 leukaemia cells [30]. Three extracts-absolute ethanol, 50% ethanol and aqueous extracts of the leaves were used for cell viability study using the MTT assay and it was observed that the absolute ethanol extract exerted the highest inhibitory effect on Kasumi-1 cells with an IC₅₀ of 10 µg/mL when compared with the 50% ethanol and aqueous extracts (25 µg/mL and >400 µg/mL) respectively [30].

***Talinum triangulare*:** *Talinum triangulare* is a herbaceous perennial plant belonging to the family Portulacaceae, and it is widely used as a vegetable [31]. It is commonly called waterleaf, "ebe dondo" in Bini and "gbure" in Yoruba. *T. triangulare* is used locally for the management of some non-communicable diseases such as obesity and cardiovascular diseases [32]. Other reports indicate its use in the treatment and prevention of liver disease and cancer [33]. Phytochemical analyses

reveal the presence of tannins, saponins, flavonoids, cardiac glycosides and alkaloids [34]. Various extracts of *T. triangulare* were reported to contain significant amounts of flavonoids and phenolic acids and were able to stimulate nitric oxide production as well as inhibit leukaemia cancer cell proliferation [33]. There is a need for more research on the antioxidant and anti-inflammatory properties of this vegetable.

Telfairia occidentalis: *Telfairia occidentalis* is a tropical plant widely cultivated in West Africa for its palatable and nutritious leaves and edible seeds. The common names of the plant include fluted pumpkin, fluted gourd and ‘ugu’ and it belongs to the Cucurbitaceae family [35]. Pumpkin leaves are used to prepare soups and sauces either alone or in combination with other vegetables. The leaves can also be blended and the juice extracted for use as a medicinal drink. Traditionally, extracts of the leaves of *Telfairia occidentalis* have been used to treat/manage anaemia, convulsion, hypercholesterolemia, liver disease, hypertension, diabetes and to boost immunity [35,36]. Magnesium, calcium, zinc, sodium, lead, iron and copper are the predominant mineral components of fluted pumpkin leaves while identified phytochemicals include tannins, flavonoids, alkaloids, saponins and phenols³⁵. Biological activities reported for *Telfairia occidentalis* include anti-inflammatory, anticancer, antioxidant, antidiabetic, haematological, analgesic, hepatoprotective, antimicrobial, antimalaria and male fertility enhancement [37].

Gongronema latifolium: *Gongronema latifolium* commonly called “Utazi” belongs to the family Asclepiadaceae. The vegetable is well known in Nigeria and other African countries for its medicinal and nutritive properties. The leaves of *G. latifolium* has a characteristic bitter-sweet taste when used in soups, and it is also used as a spice for local bear³⁸. In Nigerian folklore, the leaves of *G. latifolium* are reportedly used to treat malaria, anorexia, nausea, diabetes, constipation and hypertension [39]. In some other African countries, a decoction of the leaves of *G. latifolium* is used to treat dysentery, cough, dyspepsia, malaria, asthma and stomach problems [40]. Phytochemical compounds identified in the leaves of *G. latifolium* include saponins, resins, flavonoids, alkaloids, glycosides, terpenoids, steroids, phytate, anthranoids, anthraquinones, cyanogenic glycoside, glycosides, phlobatannins, hydroxymethyl anthraquinones, polyphenols, reducing compounds, tannins, oxalate, cardiac glycosides, β -sitosterol, essential oils, lupenyl esters, pregnane esters, hydrogen cyanide, phytosterols, terpenes, anthocyanidins [40,41]. Biological activities reported for *G. latifolium* leaves include hypoglycemic [42], nephroprotective [43], hypolipidemic [44], hepatoprotective [45], antioxidant [46], anti-inflammatory [47], haematological [48], anticancer [49], electrolyte balance [50], anti-ulcer [51], immunomodulatory [52], antimicrobial and tissue regenerative properties [40]. Aqueous and methanol extracts of the leaves of *G. latifolium* were subjected to established methods for testing acute inflammation and it was observed that both extracts significantly inhibited the carrageenan-induced paw oedema, acetic acid-induced vascular permeability and leukocyte migration [53]. Furthermore, Iweala et al. subjected extracts of the leaves of *G. latifolium* to *in vitro* anticancer tests against human lung carcinoma (A-549) and human breast adenocarcinoma (MCF-7) [49]. They reported that the dichloromethane extract of *G. latifolium* leaves exerted the strongest inhibitory effect against A-549 and MCF-7 with IC₅₀ of 9.57 and 6.51 μ g/mL respectively [49]. Also, the antioxidant properties of the plant which could contribute to the anti-cancer and anti-inflammatory properties of the plant have been reported. *In vitro*, the ethanol extract was reported to inhibit DPPH [49] while enhanced antioxidant defence against oxidative stress in alloxan-induced diabetic rats was reported by Ojo et al. [54]

Celosia argentea: *Celosia argentea* of the family- *Amaranthaceae*, is a vegetable plant popular grown and consumed in Nigeria. It is known as “soko” in Yoruba, Western Nigeria, and there are usually two varieties- red and green [55]. In Chinese and Indian folklore, different parts of the

plants have been used to treat fever, diarrhoea, mouth sores, itching, wounds, jaundice, gonorrhoea, snakebite, glandular swelling, uterine bleeding, leucorrhoea and inflammation [56,57]. Phytochemicals analysis revealed the presence of saponins, alkaloids, cardenolides, cardiac glycosides, flavonoids and phenolics [55]. Biological activities reported for *C. argentea* include antihypertensive, antidiabetic, hepatoprotective, antibacterial, antioxidant, anti-mitotic, anti-inflammatory and immunostimulatory activities [58,59]. The flavonoid fraction of the leaves of *C. argentea* was reported to exert anti-inflammatory effects on carrageenan-induced rat paw oedema and cotton pellet-induced chronic inflammatory models at a dose of 10 mg/kg body weight of rats [55]. Furthermore, Adebajou et al. reported that extracts of *C. argentea* exerted moderate inhibition against nitric oxide production in RAW 246.7 cell line used for studying anti-inflammatory responses [57]. Nitric oxide (NO) is a significant molecule in signal transductions and is critical in inflammatory reactions. Excessive generation of NO and other reactive species causes tissue damage leading to various diseases such as cancers, cardiovascular disorders and atherosclerosis [60]. Cytotoxicity evaluations of *C. argentea* using MTT assay showed increased cell proliferation rather than inhibition, and as such, the plant is recommended for cell regeneration therapies as in wound healing [57].

Conclusion

Leafy vegetables are valuable food materials that supply enormous nutrients to humans. They contain numerous phytonutrients that can be harnessed to combat diseases associated with oxidative stress and inflammation. The growing rate of cancer incidence cannot be overemphasised and currently, there is no cure for cancer. Promoting the consumption of these vegetables can help to reduce the risk of these diseases. Furthermore, promoting the consumption of these vegetables will enhance their cultivation and increase revenue generation for farmers.

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Conflict of interest

There is no conflict of interest among the authors

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