A review on phytochemistry and risk reduction of cancers by *Apium graveleons* (Celery), *Beta vulgaris* (Beet root), *Carota daucus* (Carrot) and *Citrus limon* (Lemon).

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Abstract

Phytochemicals are the major source of allopathic medications. They possess various potential bioactive compounds; provide therapeutic and prophylactic benefits. Cancer has become one of the most common and threatening diseases worldwide. Strategies for combating cancers are challenging; need for safe and effective chemotherapy. The aim of current review was on phytochemicals of *Apium graveleons*, *Beta vulgaris*, *Carota daucus*, *Citrus limon;* possess enormous therapeutic benefits; particularly in the prevention of the risk of cancers. Review was conducted from the literature published from January-2011 to December-2022. Scientific databases used for collecting the published literature. Chemotherapy is the most common treatment employed in the management of cancer patients; however, patient compliance is compromised due to various factors including taste, cost, and enormous side effects. Findings of review revealed that phytochemicals in the selected plants have the potential to possess chemo-preventive and chemotherapeutic activity; consuming juices of these plants can be a significant alternative for chemotherapeutic drugs that possess many side effects; usually intolerable and prevent the potential risk of cancers in healthy individuals. Hence; published data in this review confirmed the presence of anticancer activity in celery, beetroot, carrots & lemon; contain various flavonoids, polyacetylenes, and other compounds. These plants have shown significant effect on certain in-vitro cancer-cell lines. There is a need for further exploration by researchers for isolating lead compounds; show preventable and curable measures for cancers. Research work on human settings is needed to be addressed for authentication of many fatal cancers.

Keywords

Phytochemicals; cancers; chemotherapy; flavonoids; polyacetylenes; in-vitro; cell-lines.

1. INRODUCTION

The word Phytochemical is derived from the Greek word phyton; refers to plants that contain many naturally occurring chemical constituents; impart various positive and negative health benefits. Plants have been part of medication history since the beginning of the mankind; plants are used in the treatment of different ailments due to their enriched bioactive compounds, thereby providing medicinal properties to plants (Shaikh *et al.*, 2020). Not all the constituents of the plant merely impart medicinal properties but they contain various wanted and unwanted chemicals; usually active constituents are processed and isolated from the inactive compounds for therapeutic purposes (Pengelly, 2020). The most important classes of active constituents of plants, possess medicinal properties; alkaloids, tannins, flavonoids, and phenolic compounds; utilized by many researchers as a lead compounds for synthesizing medications to benefit human beings in combating different diseased conditions (Mahmood *et al.*, 2018). Isolation of active constituents from the plant material is carried out through different separation/extraction methods. The conventional methods used for this purpose; maceration, percolation, infusion, digestion, decoction and hot continuous extraction, nowadays latest techniques such as Ultrasound-Assisted Extraction, Microwave-Assisted Extraction, Supercritical Fluid Extractions and Accelerated Solvent Extraction have also been introduced that are economically feasible. In clinical practice; several plant origin drugs are in use, these drugs are; topotecan, epipodophyllotoxins, taxol, vincritine, irinotecan and vinblastine (Shukla *et al.*, 2015). Unfortunately, despite availability of these drugs, no single drug is fully effective and safe (Shukla *et al.*, 2015). With the passage of time and increase incidences of the current non-curable diseases, there is a need for the new medications to improve quality of life of many patients suffering from chronic conditions such as cancers; mediated by abnormal proliferation and differentiation of cells and the second most common cause of human death throughout the world (Yan *et al.*, 2017). Findings of several studies conducted on humans and animals; suggested that, regular use of certain naturally occurring phytochemicals as a dietary supplements can reduce the risk of cancers (J Kapadia *et al.*, 2011). The chief active constituents of these phytochemicals and their desirable properties are discussed in later part of current review.

Apium graveolens; also known as Celery is a perennial/annual plant. It has been part of traditional medicine in the treatment of various ailments (A. Khalil *et al.*, 2015; Shakib *et al.*, 2015). The main active constituents of celery are glycosides, steroids, and different types of phenolic compounds; including phototoxic furanocoumarins (Psoralen, xanthotoxin & bergapten), flavones, trace elements (sodium, potassium, calcium, and iron); beside this it also contains many essential oils, vitamins, and antioxidants (Al-Asmari *et al.*, 2017; Jung *et al.*, 2011). *Apium graveolens* seed is enriched with important flavonoids; apigenin and apiin (Al Aboody, 2021; Kooti *et al.*, 2014; Mahmood *et al.*, 2018). The flavonoids and phenolic compounds possess pharmacological properties, such as antioxidants, antibacterial, antidiabetic, anticancer, anti-inflammatory, and anti-thrombosis (Mahmood *et al.*, 2018). Plants containing antioxidants have been well known for providing cancer preventing properties due to their potential of trapping free-radical species; fresh celery leaves are a source of vitamins and flavonoids (Hennekens, 1994; Jung *et al.*, 2011).

Apigenin is one of the major flavonoids; found in abundance in the seeds of celery and possess antitumor, antioxidant, antiviral properties, studies demonstrated its cancer prevention and treatment properties through induction of apoptosis and autophagy (Al-Asmari *et al.*, 2017; Sung *et al.*, 2016).

Beta vulgaris; a biennial plant, native to the Mediterranean region, the Atlantic coast of Europe, the Near East, and an India; cultivated for its roots in early spring. It has potent bioactive compounds that contributes in the medicinal properties; being enriched with minerals, nutrients, and vitamins, it is beneficial as a dietary supplement. Different parts of the plant of *Beta vulgaris* have been used for various pharmacological effects; such as antioxidant, anti-depressant, anti-microbial, anti-fungal, anti- inflammatory, diuretic, and expectorant (El-Beltagi *et al.*, 2018; Kale *et al.*, 2018; Miraj, 2016). Red roots of this plant has been ranked as the tenth most potent vegetables with respect to antioxidant property; it has significant role in the prophylaxis of chronic diseases such as cancers, cataractogenesis, cardiovascular disease, neurodegenerative diseases, and stroke. In addition; red beets are also composed of phenolic acids, flavonoids, and ascorbic acid (El-Beltagi *et al.*, 2018; Kale *et al.*, 2018; Miraj, 2016). Red beets contains betalain pigment that imparts the dark color to the vegetable; they are mainly betacyanins and betaxanthins; studies have shown, these pigments have profound anti-inflammatory and anti-tumor activity; consumption of fresh juice of beetroot has played a vital role in the prophylactic management of several clinical conditions including coronary heart disease and cancer (Kale *et al.*, 2018). One of the studies also evaluated the cytotoxic activity of beetroot extract (J Kapadia *et al.*, 2011).

Daucus carota; a biennial plant, native to Afghanistan and Persia; carrots are one of the most common vegetables available worldwide; cultivated for their edible, healthy, and nutritious attributes; comprised of many medicinal compounds with various health benefits such as carotenoids, flavonoids, polyacetylenes (falcarinol, falcarindiol and falcarindiol-3-acetate), antioxidants such as alpha- and beta-carotene, lycopene, and lutein (Boadi *et al.*, 2021; G Zaini *et al.*, 2012; Mahmood *et al.*, 2018). Carrots have anticancer properties due to the presence of bioactive compounds such as polyacetylene; beta-carotenes have been also evaluated for inducing apoptosis in tumor cells (G Zaini *et al.*, 2012). *Daucus carota* has been suggested as an alternative treatment in the management of leukemia; induction of apoptosis and inhibition of the leukemic cell line has been tested using flow cytometry (Ademosun *et al.*, 2021).

Citrus limon; it grows on perennial tree; native to Asia particularly India and China. It is a common edible fruit that is used as a flavor in many juices, culinary and cooking. Lemon is widely distributed around the world and is almost consumed on daily basis not only for taste, but it provides many health benefits. Lemons possess bioactive compounds including flavonoids, vitamins, and essential oils that contain antioxidants and limonene which show significant anticancer activity (Osanloo *et al.*, 2022). Lemon juice has numerous pharmacological effects, which includes; antiviral, antibacterial, and antifungal and also used for alleviating pain and relieve inflammation (Amengialue *et al.*, 2016; Loizzo *et al.*, 2016).

Current review study highlights few important phytochemicals; possess enormous therapeutic benefits. Researchers can further explore lead compounds; can furnish preventable and curable measures for improving patients' quality of life.

These phytochemical plants are utilized in the form of salad and juices by many people in order to stay healthy; prevent from various diseased conditions. These phytochemicals are present in the above-stated naturally occurring plants, have the potential to possess chemo-preventive and chemotherapeutic activity; hence, consuming juices of these phytochemical plants can be a significant alternative for chemotherapeutic drugs that possess many side effects, usually intolerance for many patients. These juices can also improve quality of life in various cancer patients; prevent potential risk of cancers in healthy individuals. The review aimed to enlighten the specific anticancer and chemo-preventive potential of the above-stated plants that could be added in the form of a normal diet for both healthy and ill patients.

2. MATRIALS AND METHOD

A review on the phytochemistry of *Apium graveleons* (celery), *Beta vulgaris* (beetroot), *Carota daucus* (carrot), *Citrus limon* (lemon) and their role in the prevention of the risk of cancer was conducted from the literature published in the last ten years from January 2011 to December 2022. Google Scholar, Science Direct, Springer, PubMed, and NLM (National Library of Medicine) were the databases used for collecting the published literature associated with different herbs for their phytochemistry related to cancer prevention. More than 60 articles were downloaded from these databases. After abstracting relevant information from the studies and assessing quality, data synthesized and presented by following PRISMA flow diagram (Lindsey *et al.*, 2020). The PRISMA diagram details how studies were identified, the results of abstract screening, the results of full text eligibility assessment including a breakdown of reasons for exclusion, and details of included studies (Moher *et al.*, 2009). Therefore, abstracts of downloaded articles were reviewed and after a thorough study of the abstracts; 9 articles were rejected due to irrelevancy. The remaining articles were screened and a detailed appraisal was conducted, results were evaluated and tabulated, compared with publications of different authors and conclusions were made. All the articles were evaluated for their quality in terms of the type of journal i.e., where it has been published, data collection methods, statistical tests, significance values, and interpretations were made.

3. RESULTS AND DISCUSSION

Development of drug and innovation in technologies are continuous processes. Burden of different types of cancer and associated mortalities are major challenges for healthcare provider. Although many new drugs are developed; however, cancer is still a leading cause of mortality (Dutt *et al.*, 2019). Phytochemicals are emerging as promising safe and effective agents for the cure and treatment of many life threatening diseases (Dutt *et al.*, 2019). Plants are an important source for the drug development (Rafique *et al.*, 2020). The main limitations of currently developed plant based drugs are their adverse effects on normal cells, e.g; myelosuppression, suppression of growth of epithelial cells of gastrointestinal, respiratory and genitourinary tracts, cardiotoxicity, neurotoxicity and immunisuppression (Singh *et al.*, 2016). In the current study; the results were evaluated from previously published data and conclusions were made accordingly. Herbal treatment is a nature's gift to human for improving health (Zhang *et al.*, 2021); therefore, the main aim of study was to evaluate the presence of anti-

cancer Phytochemicals, that are nontoxic and possess no side-effects in *Apium graveleons* (Celery), *Beta vulgaris* (Beet root), *Carota daucus* Carrot) and *Citrus limon* (Lemon).

The summary of thirty-eight (38) references regarding phytochemical plants based on published data and their anti-cancer activity is shown in the Table 1.

Table 1. Phytochemicals and their Role in Cancerous Cells Prevention

Phytochemical plants (Scientific Name)	Flavonoids and other chemicals possessing antioxidant and anti-cancer activity	Role in cancer	References
Celery (*Apium graveleons)*	Apigenin and apiin	Cell-proliferation, apoptosis, autophagy	(S. S. T. Ahmed *et al.*, 2022; AL-Jumaily, 2010; Iyer *et al.*, 2019; Köken *et al.*, 2016; Sung *et al.*, 2016; Varadharajan *et al.*, 2011)
Beetroot (*Beta vulgaris)*	Flavonoids, Betalain, betanin, Betavulgarin, Betacyanin and betaxanthins	Cytotoxic activity on cancer cells, apoptosis and autophagic cell death	(M. A.-E. Ahmed *et al.*, 2012; Chandrasekaran *et al.*, 2020; El-Beltagi *et al.*, 2018; J Kapadia *et al.*, 2011; Kapadia *et al.*, 2013; Lee *et al.*, 2014; Liu *et al.*, 2020; Nowacki *et al.*, 2015; Shakib *et al.*, 2015; Venugopal *et al.*, 2017; Zein *et al.*, 2015)
Carrot (*Carota daucus)*	Flavonoids, falcarinol, β-carotene and lutein	Apoptosis, inhibition of leukemic cell-lines	(Atalar *et al.*, 2021; Daaboul *et al.*, 2017; El-Sibai *et al.*, 2014; G Zaini *et al.*, 2012; N. Khalil *et al.*, 2018; Muhammad *et al.*, 2020; Saleem *et al.*, 2018; Shakib *et al.*, 2015; Shebaby *et al.*, 2015; Shebaby *et al.*, 2014; Shebaby *et al.*, 2017; Taleb *et al.*, 2012; Tawil *et al.*, 2015; Zaib *et al.*, 2022; Zeinab *et al.*, 2011)
Lemon (*Citrus limon)*	Flavonoids and limonene	Cell proliferation, apoptosis	(Diab, 2016; G K *et al.*, 2019; Osanloo *et al.*, 2022; Salih *et al.*, 2021; Talib, 2017; Yousefian Rad *et al.*, 2020; Zhou *et al.*, 2021)

The studies reviewed in this literature confirmed the presence of various flavonoids, they are common secondary metabolites among all the above-mentioned natural bioactive plants; their higher quantity of antioxidants have significant chemo-preventive and chemo-therapeutic properties (Al Aboody, 2021). The flavonoids (apigenin and apiin) found in celery are most effective as apoptosis inducing agents to control abnormal cell proliferation.(Sung *et al.*, 2016) Among the flavonoids found in carrots; falcarinol is the major bioactive species; its bioactive levels can easily be attained through the consumption in the form of vegetable and juice (G Zaini *et al.*, 2012). According to another study; flavonoids are effective antioxidants, anti-angiogenic and stop the growth of abnormal cells (Hassan *et al.*, 2014).

Besides flavonoids certain pigments such as betacyanin and betaxanthins; present in beetroot have shown significant anti-tumor activity, betacyanins are the most common and potent anticancer constituents of the beetroot extract (J Kapadia *et al.*, 2011). Limonene found in citrus lemon has shown remarkable anticancer activities; mechanism of action is potentially related to induction of apoptosis (Osanloo *et al.*, 2022). The carotenoids â-carotene and lutein found in carrots also possessed slight effects on cell proliferation; it induces the apoptosis if present in high concentrations(G Zaini *et al.*, 2012). Moreover wild and black carrots also have been evaluated for their cytotoxic activity on various cancer cells(Atalar *et al.*, 2021; Saleem *et al.*, 2018; Tawil *et al.*, 2015). The review also included a case report published in 2015 addressing the significance of beet-root and carrot juice effect in combination with chlorambucil for the treatment of chronic lymphocytic leukemia in a female 76-year-old patient; the report concluded the beet-root and carrot juice in combination or alone showed strong effectiveness in remission of chronic lymphocytic leukemia (Shakib *et al.*, 2015).

Despite all these facts; it cannot be overlooked that efficacy of medicinal plants are based upon quality and quantity of therapeutic phytochemicals (Singh *et al.*, 2016). Unfortunately; these phytochemicals vary based upon season, altitude and latitude (Singh *et al.*, 2016). In addition; different parts of same plants contains different phytochemicals with different therapeutic role. It is possible to make anticancer drugs from these phytochemicals; however, it requires intense efforts (Singh *et al.*, 2016). Further research is required to attain more knowledge about phytochemicals and processes to explore their anti-cancer potentials.

4. CONCLUSION

Current review has been conducted to summarize published data that confirmed the presence of anticancer activity in certain phytochemical plants that contain various flavonoids, polyacetylenes, and other compounds. These Phytochemicals have shown significant effects on certain cancer cells. The literature review showed research work; carried out on in-vitro cancer-cells lines; furthermore, research work on human settings is not yet established, that needs to be addressed in combating many types of fatal cancers. Hence all the above mentioned phytochemicals have significant anticancer activity; published in the last 10 years. Consumption of juices of these phytochemicals has the potential to provide a safe alternative alone and /or in combination with chemotherapy in the management of certain cancers; can improve pa-

tient's appetite and quality of life. Furthermore; the juices are palatable and cost-effective in comparison to chemotherapy. Juice combination of these phytochemicals can improve immunity and prevent risks from cancers in healthy individuals, due to their high antioxidant and flavonoid content. Research data on these phytochemical plants is still insufficient and needs more information relevant to their effectiveness in human settings.

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