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Review Article

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Phytochemicals as Safe Agents for Prevention of Cancer: Recent Advances in Cancer Therapy

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Abstract

Cancer has been known as one of the genetic disorder and also as second cause for death in developed countries and/or even in developing countries. It has been estimated to be 26 million new cases of cancer and 17 million cancer death yearly. Some phytochemicals have been known to have anticancer activity and on the other hand modern medicine lacks effective drugs against certain types of cancers. Flavonoids are placed in the nucleus of mesophyll cells and inside centers of reactive oxygen species group. Alkaloids are known class of ring compounds nitrogen having organic compounds which have a broad range of anticancer properties. In this review article, we have described some phytochemicals and also possible mechanisms for prevention of cancer.

Keywords: Alkaloids, Anticancer, Phytochemical

Introduction

Cancer has been known as one of the genetic disorder [1] and also as second cause for death in developed countries [2]. The estimations have been shown that cancer is almost reason for 13% of total deaths and its global distribution is variable in the different populations due to aging and growth of the world population [3, 4]. It has been known by 100 types of cancer and classified by their cells [5]. I t has been reported that 14.1 million new patient with cancer exception those with skin cancer other than melanoma [6]. It has been estimated to be 26 million new case of cancer and 17 million cancer death yearly [7]. Despite significant progresses, cancer has been yet known as an aggressive killer in all over worldwide. Surgery, chemotherapy and radiotherapy are common procedures for treatment of

cancer [8]. Such treatments have limitations such as side effects including fatigue, pain, diarrhea, nausea, vomiting, and hair loss [9] and could be also caused gradual resistance of cancer cells against treatment [10]. It has been shown that by half of cancer enduring in the United States exploit components derived from the various parts of plants or nutrients, singly and as adjuvant treatment in alongside chemotherapy and/or radiation therapy [11-13]. From long years ago, natural herbal medicines have been applied in order to prevention and/or treatment of different diseases [14]. Phytochemicals makes them appropriate for food consumers [15-17]. Studies have approved anticancer activities of phytochemicals [18-22]. Natural compounds of plants belonging to different groups including alkaloids, diterpenes, diterpenoquinone, purine-based compounds, lactonicsesquiterpene, peptides, cyclicdepsipeptide, proteins, macrocyclicpolyethers, etc [23]. Some phytochemicals have been known to have anticancer activity and on the other hand modern medicine lacks effective drugs against certain types of cancers, including metastatic pancreatic adenocarcinoma and castration-resistant prostate cancer [23]. In this review article, we have described the use of phytochemicals for prevention of cancer and review the previous published studies and present implications for it.

A brief of phytochemicals

The Greek term "phyto" in phytochemicals is originated from plant [24, 25]. Phytochemicals has been defined as bioactive, non-nutrient, and naturally present in plant compounds which are found especially in fruits, vegetables, and whole grains. It has been estimated to be 5000 especial phytochemicals in grains, fruits and vegetables but a large number are not yet known and must be known before understanding their health advantages in whole foods [26]. Phytochemicals present in plant substances have increased interest among researchers, food production and also for pharmaceutical industry and/or for their uses in the prevention of human health. They are divided into different groups including polyphenols, organosulfur compounds, carotenoids, alkaloids, and nitrogen-containing compounds [27]. Some phytochemicals has also been known as effectors of biologic processes and also have ability for influencing on disease risk through complementary and overlapping mechanisms [27]. Phytochemicals can penetrate and delay promotion multistep carcinogenesis [29] and also postpone the progression of precancerous cells into the malignant ones [29, 30].

Phenolics

The phenolics as secondary metabolites are broadly in plants especially in fruits [31]. They are known to have 1, 2 and/or more aromatic rings [32]. They have antioxidant properties and prevent against cancers. Their profitability could be attributed to their regular consumption and bioavailability [33]. They are precursors for flavonoids and tannins [34, 35]. Hydroxycinnamic acids and their derivatives in fruits and vegetables are resulted from p-coumaric acid (PCA), caffeic acid (CA), and ferulic acid (FA) [36]. Flavonoids are known as main class of phenolic structures that have antioxidant activity [37]. Such phytochemicals are connected in order to decrease the risk of main chronic diseases and largely identified in fruits, vegetables, and other plant foods [38]. They are divided into flavonols, flavones, flavanols (catechins), flavanones, anthocyanidins, and isoflavonoids that have one heterocyclic C ring [39]. The chemical structure of flavonoids relies on their functional group, rate of hydroxylation, other substitutions and conjugations, and rate of polymerization [40]. Functional hydroxyl groups present in flavonoids act in antioxidant activity through scavenging free radicals and/or through chelating metal ions [41, 42]. Flavonoids are placed in the nucleus of mesophyll cells and inside centers of reactive oxygen species group. Some possible

mechanisms have been suggested for the effect of flavonoids in the initiation and encourage the stages of the carcinogenicity such as effects on development and hormonal activities, including: (1) Down regulation of mutant p53 protein, (2) Stopping cell cycle arrest, (3) Prevention of tyrosine kinase activity, heat shock proteins and expression of Ras proteins [43]. Organosulfur structures are known as organic structures that could be identified by their sulfur having functional groups [44]. Daily consumption of organosulfur components could improve bioactive characteristics particularly in relation with cardiovascular health [45].Some organosulfur components were evaluated based on their ability for prevention carcinogenesis promoted through N-nitrosodiethylamine and the best was observed in diallyl disulfide [46]. Some organosulfur structures in *Allium* genus have been shown anti-cancer activity [47].

Carotenoids

Carotenoids are known as natural pigments which have received attentions. More than 600 different carotenoids have been recognized in nature. They may be originated from plants, microorganisms, and/or animals. They have a skeleton of isoprene units containing 40-carbon [48]. Carotenoids can react with free radicals and produce radicals [49]. The α-carotene has been known to have strong protective factor. The β-carotene present in green leafy vegetables act as an antioxidant, but it has prooxidant effects in high levels and particularly in high oxygen tension [2]. Antioxidant activity of carotenoids could be attributed to antioxidant activity.

Alkaloids

Alkaloids are known class of ring compounds nitrogen having organic compounds which have a broad range of anticancer properties [50]. Such structures have activity in prevention of cancer by inhibition of enzyme to poisomerase activity that is involved in DNA imitation, induction of apoptosis and gene expression of p53 gene [51, 52]. Alkaloids have similar structure neurotransmitters in the central nervous system of human beings. With regards to alkaloids and research in relation with their role for treatment of wild propagation of cells, they have been used as an efficient chemo preventive substance [53, 54]. Amaryllidaceae alkaloids, betalain alkaloids, diterpenoid alkaloids, indole alkaloids, isoquinoline alkaloids, lycopodium alkaloids, monoterpene and sesquiterpene alkaloids, peptide alkaloids, pyrrolidine and piperidine alkaloids, pyrrolizidine alkaloids, quinoline alkaloids, quinolizidine alkaloids, steroidal alkaloids, tropane alkaloids, and miscellaneous alkaloids have been known as the major class of Alkaloids [47]. Catharanthus alkaloids have been used as adjuvant treatment for chemotherapy in treatment of breast cancer, ovarian cancer, non-small cell lung cancer, and soft tissue sarcoma (orphan). Catharanthus alkaloids have also been used for therapy of acute lymphocytic leukaemia, malignant lymphomas such as Hodgkin's lymphoma and non-Hodgkin's lymphoma, multiple myeloma, idiopathic thrombocytopenic purpura and solid tumours, such as metastatic testicular cancer, Ewing's sarcoma, foetal rhabdomyosarcoma, primary neuroectodermal tumours Wilms' tumour, and retinoblastoma [23].

Overview on mechanisms of phytochemicals for prevention and treatment of cancer

Cancer has been known as one of several-mechanism carcinogenesis process, which includes several steps such as mutagenic, cell death and epigenetic by associated stages: initiation, promotion, and progression [55, 56]. Cells in humans and other organisms are broadly found in a range of oxidizing agents that are essential for life in several cases [57, 58]. Carcinogenic substance, such as environmental pollutants, dietary mutagens and radiation, will

cause to produce ROS and/or reactive nitrogen species (RNS), that react with cellular molecules such as proteins, lipids, and DNA for promotion of carcinogenesis. Regular consumption of phytochemicals directly alleviate ROS/RNS levels and removes carcinogenic reactive intermediates through dietary phytochemicals intake not only scavenge ROS/RNS directly but also eliminate carcinogenic reactive intermediates indirectly transcription factor Nrf2 [nuclear factor erythroid2 p45 (NF-E2)-related factor 2] by involving with antioxidant system. It has been accepted that if Nrf2 is to be released from Kelch-like ECH related with protein 1 (Keap1) and transferred intonucleus, Nrf2 is associated with antioxidant responsive elements (AREs) in the promoter/enhancer site of step II detoxification and antioxidant enzyme genes with the Maf protein. On the other hand, reactivation of Nrf2 could be corrected through supplementation of phytochemicals by epigenetic modifications including DNA methylation and histone correction.

Conclusion

Although, cancer is very complex and certainly cannot treat by nutrient interventions but the use of safe compounds such as phytochemicals can help to some extent in the treatment and prevention of cancer. Regular consumption of phytochemicals can prevent and decrease costs. We recommend to daily use of phytochemicals for prevention of cancer for therapeutic and treatment.

Ethical Considerations

Compliance with ethical guidelines

There was no ethical considerations to be noted in this article.

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Authors' contributions

All authors contributed toward data analysis, drafting and revising the paper and agreed to be responsible for all the aspects of this work.

Conflict of interest

The authors declared no conflict of interest.

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