CHEMOPREVENTIVE ROLES OF MEDICINAL FOODS AGAINST ENVIRONMENTAL CARCINOGENS-INDUCED CANCERS

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Abstract – Objective: *Cancer remains the major cause of death globally apart from cardiovascular diseases. Behavioural and dietary risks could trigger up to 70% of new cancer cases in the next 20 years based on speculations. The risk of cancer is becoming more rampant mainly because of various environmental carcinogens which are responsible for their initiation and progression. Consideration has now been given to the roles of medicinal foods as cancer chemo-preventive agents.*

Materials and Methods: *Cancer treatments and / or management can be overwhelming, hence prevention is pivotal to decrease incidence and mortality rate. We reviewed some medicinal foods with potential chemo-preventive and pharmacological activities. Frugal chemo-prevention, using natural products was considered due to some factors such as availability and cost-effectiveness; this is very important when we consider the current state of the economy of many countries worldwide considering the cost of herbs, spices and foods that are known universally.*

Results: *The anti-cancer, antioxidant, anti-inflammatory properties of medicinal foods, their bioactive compounds, mechanism of action as well as their possible chemo-preventive roles against various forms of cancer such as lung, breast, prostate cancers with high incidence and mortality driven by environmental pollutants and carcinogens were explored.*

Conclusions: *In this current review, we pointed out the chemo-preventive possibilities of some medicinal / functional foods on environmental carcinogens - induced cancers in a bid to enhance plant medicines and compounds for possible drug development.*

KEYWORDS: *Chemo-prevention, Medicinal foods, Pharmacological properties, Drug development, Antioxidant, Anti-inflammatory.*

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INTRODUCTION

Cancer is one of the major causes for death worldwide apart from cardiovascular diseases. Behavioral and dietary risks could trigger up to 70% new cases based on speculations in the next 20 years. Cancer is associated with uncontrolled proliferation of cells which invade, destroy and metastasize to neighboring cells. Cancer is caused by many factors and carcinogenesis is enhanced by risk factors which play cogent roles in increasing the chances of cancers. The modifiable risks of cancer include tobacco, occupational exposure, air pollution, polluted water, alcohol, poor diet and nutrition, ionizing radiation, hormones, infectious agents, etc. All of them constitute the environmental carcinogens including chemicals such as arsenic, asbestos, wood dust, benzene, chromium, viruses such as Epstein Barr virus, human papilloma virus and radiation such as radon, uranium. All these environmental carcinogens induce the initiation, promotion, progression and metastases of common cancers such as lung, breast, prostate, liver, cervical, skin etc.

The beneficial role of medicinal foods is seen in the prevention, treatment and management of various cancers and they cannot be underestimated because of the bioactive compounds found in these plants and plant products. Medicinal foods have been described as foods that contain nutrients with medical or physiological benefits. Actually, any food with known disease-preventing or health-promoting property other than nutrient provision is now considered as a functional/medicinal food. Foods in these categories are soy, garlic, turmeric, chestnut, tomato, dietary fibre, pepper etc. Embedded in these functional foods are various bioactive compounds that exhibit various anti-cancer properties via molecular mechanisms which include inhibition of cell proliferation, tumour microenvironment changes, induction of apoptosis, enhancement of tumour suppressor gene like p53, modulation of signaling network and reactive oxygen species (ROS) generation.

In this review, the chemo-preventive properties of medicinal/functional foods on environmental carcinogen-induced cancers were investigated and information about the risks, incidence and mortality of various cancers was given. Some medicinal/functional foods, their bioactive compounds, their mechanism of action and safety dose as well as future directions of these functional foods as plant medicines and potential candidate for drug development were also presented.

CANCER

Cancer is one of the world's greatest causes of death; in the year 2018 alone about 9.6 million deaths occurred and in 2020 this number accounted for almost 10 million deaths globally. New leading cancers incidence in 2020 included breast, lung, colon and rectum, prostate, skin and stomach cancers while new leading cancers in mortality include: lung, colon and rectum, prostate, liver, stomach and breast cancers[1]. Worldwide, about 1 of 6 deaths is related to cancer and about 70% of cancer mortality occurs in middle- and -low-income countries. Cancer is a conventional term for a large group of diseases that has great impact on any part of the body. Malignant tumors and neoplasms can also be used at times to describe them. One unique characteristics of cancer is the fast production of abnormal cells that grow beyond their natural restrictions, and then attack and invade other parts or organs of the body, the last phase of which is referred to as metastasis; this significantly causes most deaths from cancer.

Approximately 33% of cancer mortalities are caused by five important dietary and behavioral risk factors which are obesity, lack or reduced consumption of vegetables and fruits, physical inactivity, alcohol and tobacco consumption. Tobacco consumption is a major risk factor when considering cancer-related death which is about 22%[2]. Infections that could occur as a result of cancer are Human Papilloma Infection (HPV) and hepatitis, which account for about 25% of cancer cases in middle and low-income countries[3]. Terminal-stage presentation, inability to gain access to early diagnosis and treatment are common. In 2017, around 26% of low-income countries declared pathology facilities that are accessible to the public. More than 90% of high-income countries recounted available and functional treatment services unlike the 30% of nations with low income. There is a disturbing increase in the economic impact of cancer globally, the sum-total of cancer economic cost yearly in 2010 was about US$ 1.16 trillion[4].

CANCER RISKS FACTORS

Cancer occurs as a result of transformation of normal cells into tumor cells in a multilevel process starting from the development of a pre-cancerous lesion to a malignant tumor as end result. The interplay between a person's genetic factors and other external factors includes the following:
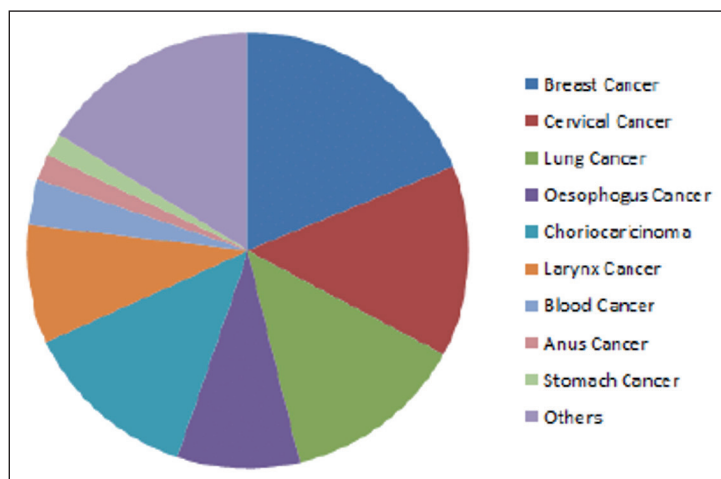1. Physical carcinogens like ionizing and ultraviolet radiation;

Fig. 1. Distribution of common cancer types.

2. Chemical carcinogens like contents of tobacco smoke, arsenic (a water contaminant), asbestos, and aflatoxin (a food contaminant);
3. Biological carcinogens like bacteria or viruses, and other infection causing pathogens.
4. Tobacco-use (such as smokeless tobacco and cigarettes).

Tobacco-use is a major risk factor for cancer, causing almost 22% cancer related mortality all over the world. It is important to note that about 15% of cancer diagnosis in 2012 was reported to be caused by carcinogenic infections, Human papillomavirus (HPV), *Helicobacter pylori*, Hepatitis B and C infection, and Epstein Barr infection[3]. Even Hepatitis B and C virus and other HPV types predispose people to liver and cervical cancer, respectively. Accumulation of several risk factors including compromised cellular repairs mechanisms occur as ageing sets in.

INCIDENCE AND MORTALITY OF MAJOR CANCERS

Incidence is the number of new cases that arises in a given geographic region at a specified time, reported either as total number of cases yearly or as rate per 100, 000 people annually. Rates are used to estimate the average risk of cancer development in a year and approved comparisons between countries and regions. While mortality means the number of deaths taking place in a stated area and period, and number of deaths per 100,000 people annually. Mortality is the product of the rate and the fatality rate (the extent of patients' death); therefore, mortality rates estimate the average risk of death in the population from a specific cancer in a given year[1].
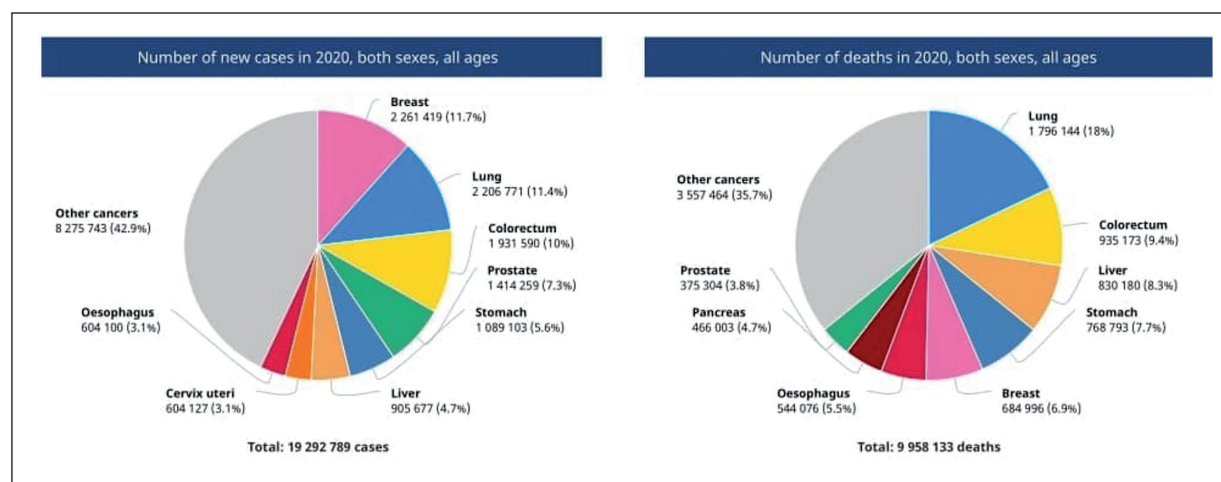

Fig. 2. Pie Charts showing the distribution of deaths and cases for the top 10 cancers in 2020[1].

GLOBAL CANCER BURDEN

In 2020, approximately 19.3 million new cases and 10 million mortalities were announced. 1 of every 5 men and 1 of every 6 women globally developed cancer in their lifetime, and 1 out of 8 men and 1 out of 11 women died as a result of cancer. Globally, the total of people who are alive during 5 years of their cancer diagnosis, named the 5-year prevalence, is approximately 20.6 million. The burden of cancer increases as a result of population growth, ageing and direct link between some types of cancer and socio-economic development.

Global pattern for both sexes includes the following:

- In 2020, Asia was reported to have the highest incidence and mortality globally, because almost 60% of the world population is found in this region.
- In Europe, 22.8% cancer incidence and 19.6% of cancer mortality global statistics were recorded.
- 13.3% of the world's population is found in America, the cancer incidence is 20.9% and mortality is 14.2% globally.
- In Asia, cancer mortality is (58.3%) while in Africa is (7.1%) because of high incidence of cases (49.3 and 5.7%, respectively). Higher mortality rates and higher frequency of specific cancer-types are observed in these regions mainly because of poor prognosis, late diagnosis and treatment[1].
- Nigeria had 115,950 new cases of cancer and 70,327 mortality cases in 2018.

Gender based cancer pattern globally: In men: Lung cancer has 14.5% incidence cases and 22.0% mortality rates.
- (13.5%) prostate cancer incidence
- (10.9%) colorectal cancer occurrence
- (10.2%) liver cancer incidence
- (9.5%) stomach cancer death rate (Global Cancer Observatory, 2018).

Death rates of certain cancers in women are lung cancer (13.8%) and colorectal cancer (9.5%), cervical cancer for both incidence (6.6%) and mortality (7.5%).

ENVIRONMENTAL CARCINOGENS AND CARCINOGENESIS

The main cause of cancer is exposure to environmental pollutants/carcinogens. It is only on few occasions that environmental constituents have been linked to human cancer[5]. Some certain molecular markers identified in malignant tissues are progressively used to pinpoint environmental causes of cancer, disqualifying some presumed cancer agents, leading to the discovery of tumours causes that were missed in customary epidemiology studies.

FATE OF ENVIRONMENTAL POLLUTANTS AND CARCINOGENS

As the use of synthetic materials keep increasing, a good number of these synthetic compounds are constantly in the environment because of slow

TABLE 1. Summary statistics of the five most frequent cancers in Nigeria in males, females and both sexes.

|	*Male*	*Female*	*Both Sexes*
Population	99 277 846	96 597 394	195 875 239
Number of new cancer cases	44 928	71 022	115 950
Age-standardized incidence rate (World)	89.1	119.4	103.8
Risk of developing cancer before the age of 75 years (%)	9.8	12.5	11.1
Number of cancer deaths	28 414	41 913	70 327
Age-standardized incidence rate (World)	60.4	75.5	67.7
Risk of developing cancer before the age of 75 years (%)	6.5	8.4	7.4
5-year prevalent cases	74 284	136 768	211 052
Top 5 most frequent cancers excluding non-melanoma skin cancer (ranked by cases)	Prostate Colorectum Non-Hodgkin lymphoma Liver Stomach	Breast Cervix uteri Colorectum Ovary Non-Hodgkin lymphoma	Breast Cervix uteri Prostate Colorectum Non-Hodgkin lymphoma

Fig. 3. The various stages of carcinogenesis and interventions strategies of medicinal foods.
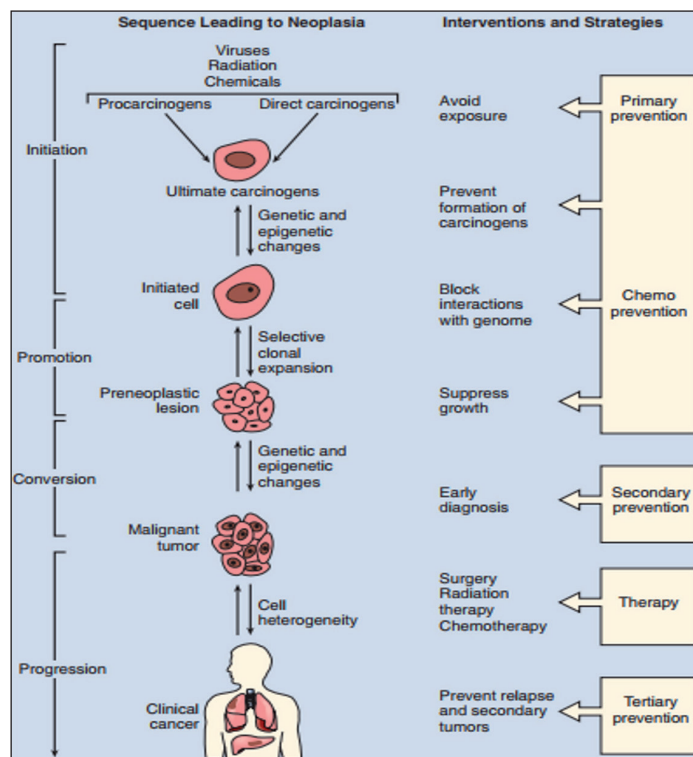
degradation or pseudo persistent because of steady release to the environment. These materials are a threat to the health of people, water bodies and land's biological systems because of their toxicity.

Statistics on their occurrence, transport, breakdown, toxicity, and bioavailability are needed to safeguard our natural habitats and human health from the destructive impacts of these pollutants[6].
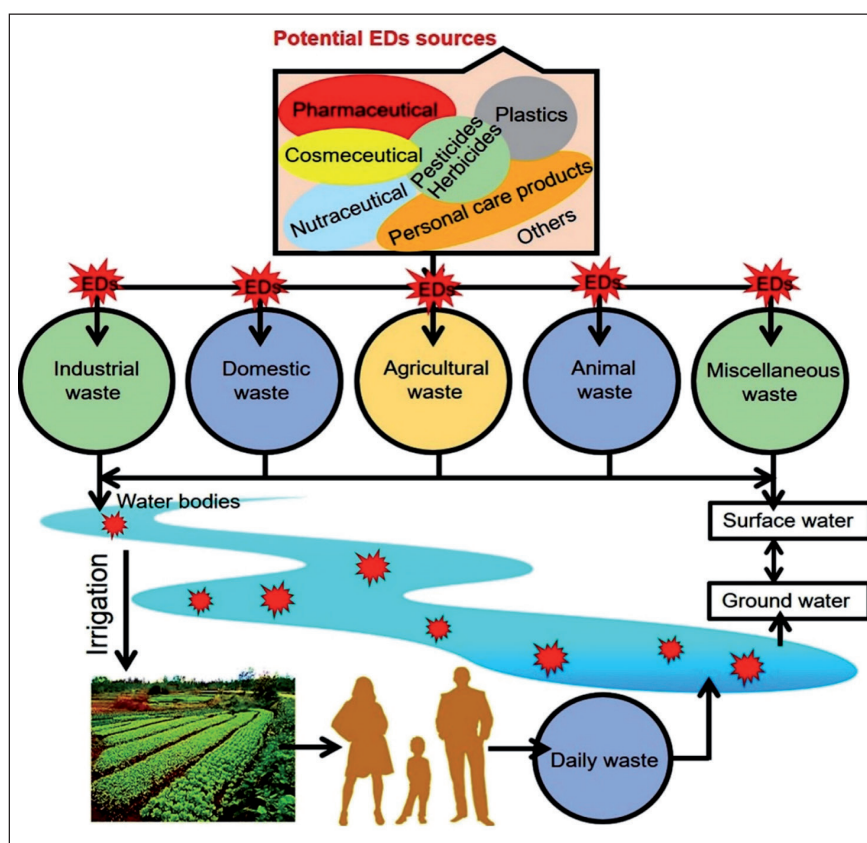
Fig. 4. Overview of Emerging contaminants/Pollutants Routes.

Emerging Environmental Pollutants (EPs) point out a lot of synthetic chemicals (beautifying agents, pesticides, drugs, personal family care items and poisonous heavy metals) that are broadly utilized and crucial for current society worldwide[7,8]. These pollutants are very harmful, mutagenic and carcinogenic, their build-up presents serious threat to the earth (biosphere, hydrosphere, lithosphere etc.)[9-11]. Successful breakdown and evacuation of these pollutants have arisen as a significant burden for environmental researchers and biotechnologists.

CARCINOGENESIS

It is presently known that carcinogenesis consists of different variables that range from exposure to chemicals, alterations in proto-oncogenes and tumor suppressor genes because of exogenous and endogenous etiologies, and strict guideline or activities of numerous basic signaling pathways needed for normal homeostasis in the cell.

Exposure to environmental chemicals can be converted by xenobiotic metabolizing enzymes to reactive intermediates resulting in the formation of DNA adducts, and if not fixed by DNA repair enzymes, irreversible changes in critical genes will be seen. This leads to precancerous cells development. Under normal circumstances, molecular pathways controls apoptosis and cell proliferation, in turn inhibiting the development of a tumor[12,13]. Environmental xenobiotics may cause mutagenesis forming reactive intermediates that brings about adduct formation with gene encoding normal signaling proteins that inhibits initiation of apoptosis[14].

MEDICINAL FOODS

A novel relationship involving food and health in daily life has been shown by the specific health effects of functional foods[15]. Functional foods, among several definitions have been defined by the combined action of the European Commission on Functional Food Science in Europe, as food produce with vital nutritional impact having beneficial effects on more than one role of the human organism, therefore enhancing the physical and general conditions likewise reducing the danger of emerging diseases. The volume of intake and variety of functional foods must be in consonance to its usual acceptance for nutritional purposes.

Recent report has shown that medicinal foods have huge significance lately their therapeutic potential in different pathologies such as neurodegenerative disease, diabetes and cancer[16-18]. Functional foods as the name implies, comprise of food sources that are of

dietary significance and are associated with resolving the body's diseased condition. They have been noted for their valuable roles in cancer prevention and treatment. Various functional foods that have been gotten from different sources, for example, plants, animals and microbial sources, are reported to have observable anticancer effects with changing mechanisms of action such as apoptosis induction, anti-metastatic, anti-proliferative, anti-angiogenic, scavenging of free radicals, inhibition of matrix metalloproteinases etc.[19]. Functional foods revealing anticancer potential include ginseng, garlic, vegetables, berries, cereals, dairy products, beverages and many others.

Functional foods which are fortified with special constituents with valuable physiological effects were first used in Japan. In order of significance, the foods had to fulfil nutritional needs such as constitute natural ingredients, be part of the diet on a daily basis and when taken, have a specific function in human, for example:
- Improve biological defense mechanism
- Inhibition or recovery of several pathological conditions
- Maintain both the mental and physical condition
- Delay aging[20]

The new speculation of functional foods as natural or processed foods having both essential or non-essential organically active constituents in precise quantity give a clinically verified and documented health advantage for the management, treatment or prevention of a chronic diseases, was described by the functional food center[21].

POTENT MEDICINAL FOODS IN THE MANAGEMENT OF VARIOUS CANCERS

Chestnut

Extract of chestnut has antioxidant properties, protective role against gastric, prostate and breast cancer[22]. Ethanolic chestnut extract has a huge adverse effect on the development of gastric cancer cells, when juxtaposed with crude extract of chestnut having no effect and surprisingly the aqueous chestnut extract showed cancer promoting effect. The inner shell and flesh of chestnuts (as well as the flowers and leaves), and uncooked and processed chestnut gives antioxidant effect. The extract's chemo-preventive efficacy is dependent on their extraction medium and applied dose[22].

Soy

In the studies done on soy and cancer risk, ample consideration and attention was given to breast cancer. Studies concentrated on possible prevention
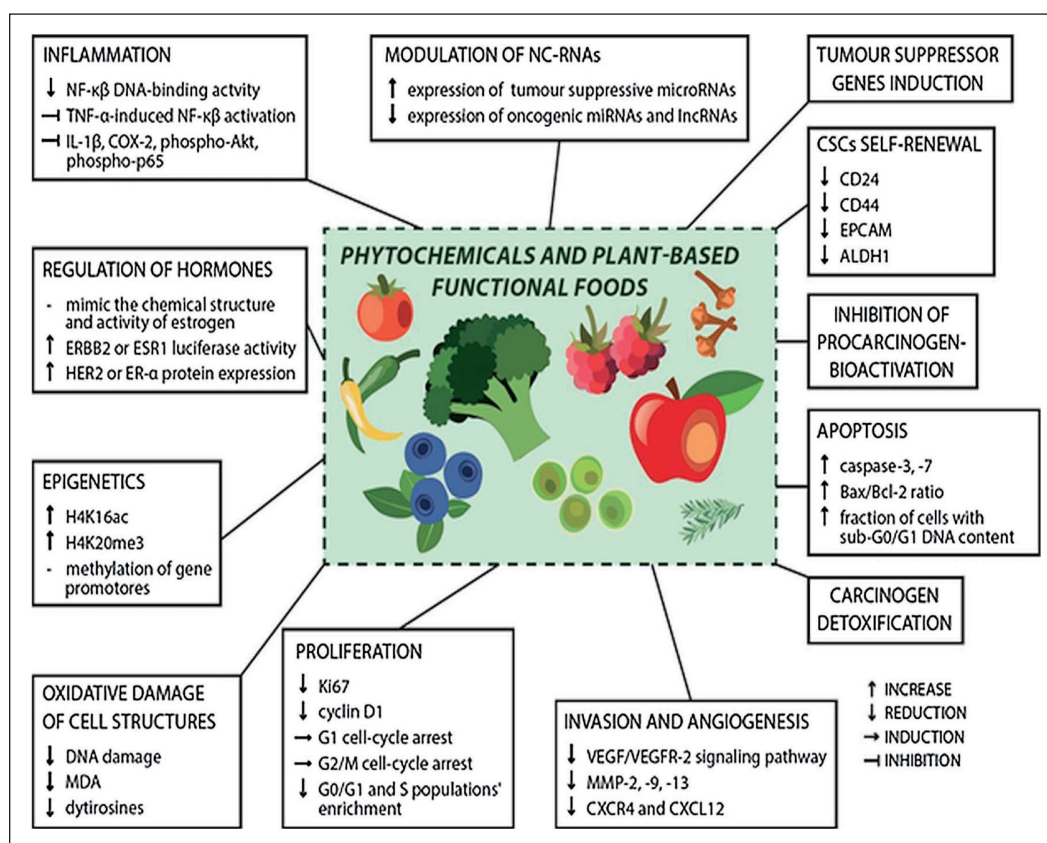
Fig. 5. Mechanism of action of Plant-derived Phytochemicals.

exhibited by Isoflavones to lessen the breast cancer risk, particularly among postmenopausal women placed on drug treatment with tamoxifen as soy did not interact with the drug efficacy[23]. In any case, it is proposed that soy does not affect the direct consumers[24], yet more helpful to early consumers, when it comes to preventing cancer[25]. This demonstrates why soy consumption among teens is associated with decreased risk of breast cancer especially in premenopausal women[26] interestingly, another research discovered no relationship in premenopausal and an inverse relationship among postmenopausal women[27]. Soy consumption particularly in high quantities decreased colorectal cancer risks since the result of soy treatment relies truly upon the amount (dose) consumed or administered[28].

Garlic

Garlic, which is in the Allium class of vegetables, is a sulfur-containing active compound, protective against the initiation and/or progression of various cancers[29]. Diallyl trisulphide prevented the growth of prostate cancer [30] and the invasion of the lung in a transgenic mouse model of prostate cancer[31]. This effect was dependent on the dose, the higher the dose the greater the benefit derived.

The diallyl prevented prostate cancer progression at 1 mg and 2 mg administered to the mice three times each week when compared to control. The organo-sulphur compound acts by limiting androgen receptor expression[32], which is effectively associated with the advancement of prostate cancer. Other forms of garlic like garlic oil have been defensive against liver cancer [29]. Liver cancer initiated by environmental carcinogen such as N-nitrosodiethylamine, which is commonly detected in certain tobacco products and foods was prevented in a rat model; rats and humans have the same pathophysiology when it comes to prostate cancer. This points out the chemo-preventive effect of garlic oil against the cancers. It was also discovered in another study that garlic supplement could reduce cancer of the blood[33]. Recent report shows that it is effective against gastric cancer[34].

Tomato

Lycopene is one of the potent bioactive components in tomato[35]. Studies recommend that lycopene has chemo-preventive agent against cancers especially prostate cancer[36], breast cancer, lung cancer and gastric cancer[37]. Tomato is shown to be effective against cancer of the liver caused by

environmental carcinogens in a rat model. Dieth-ylnitrosamine-induced and non-alcoholic steato-hepatitis-induced early liver cancer was inhibited in rats by lycopene containing tomato extract[38]. Correspondingly, death from prostate cancer was accounted for in a study carried out on rats administered with very little tomato powder [39].

Red pepper

Capsaicin (a bioactive compound in pepper) in an *in-vitro* study worked as an anti-cancer agent by preventing the metastasis of cancer cells of the skin to other body parts exhibiting its chemo-preventive activity[40]. Another study carried out on gall bladder cancer patients, pointed out that they were administered with more red pepper than the controls but capsaicin was not related with their cancer, but another compound named aflatoxin was responsible [41].

Dietary fiber

Dietary fiber prevents constipation by gathering stool, increasing the stool water content [42]. It has been predicted to have huge impact on the col-orectal cancer risk. In a similar study, dietary fiber was effective in the prevention of colorectal cancer amongst clans at the risk of the chronic diseases' development[43]. In the colon, dietary fiber has direct action on the intestinal wall thus decreasing the pressure on alimentary canal walls. Likewise, dietary fiber-rich diets have been linked with a decreased breast cancer risk in post-menopausal women[44]. These include cauliflower, broccoli, Brussels sprouts, cabbage, fledglings, and greens (turnip, kale, mustard, collard). In an *in-vitro* research, phenethyl isothiocyanate (3 µM) from cruciferous vegetables was proposed to have chemo-preventive effect as its inhibitory role affected human breast cancer cell lines [45]. A case-control study that compared fruit with cruciferous vegetables demonstrated cruciferous vegetables to be essentially connected with a decreased risk of lungs cancer among smokers. This relationship was considerably more established in heavy smokers (the individuals who took more than 20 cigarettes day by day) and momentary smokers (those with under 30 years of smoking)[46].

THERAPEUTIC AND PROTECTIVE MECHANISMS OF PHYTOCHEMICALS

The mechanisms proposed for fruits and vegetables influence on human cancers are different and complex. Different phases of carcinogenesis might be inhibited and diverse *in-vivo* or *in-vitro* frameworks are utilized to demonstrate these inhibitory effects in pre-clinical studies. For that reason, describing the bioactive constituent of the products of these plants and collections of *in-vitro* and animal study information before clinical examinations is important. Phytochemicals, because of their dietary source, are assumed to be safer and better tolerated with generally low toxicity.
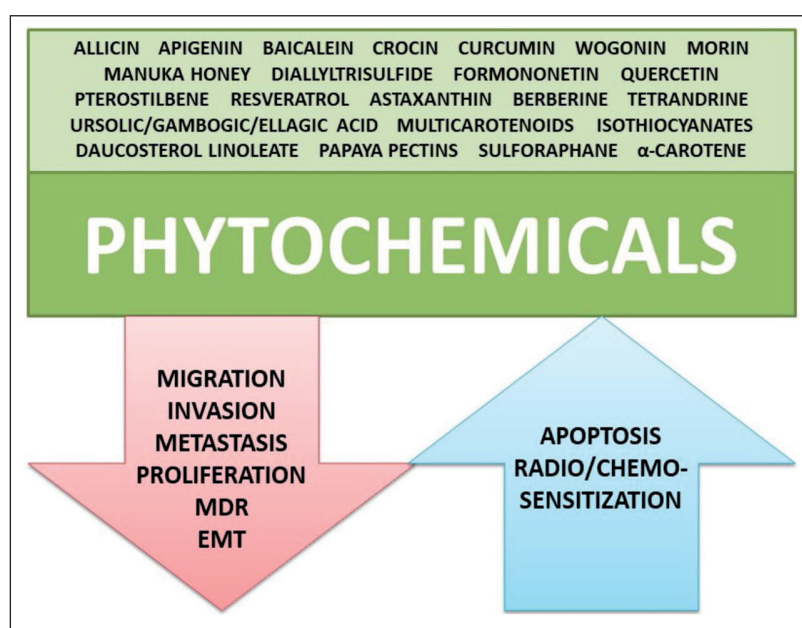

Fig. 6. Anticancer and anti-metastatic effects of phytochemicals.

OXIDATIVE STRESS MODULATION

Healthy cells maintain complex redox homeostasis between the levels of reactive oxygen species (ROS) and reactive nitrogen species (RNS) balanced by the antioxidant defence system. RNS/ROS are results of normal cellular metabolism with physiological functions at low and moderate concentrations[47]. Oxidative stress is caused by imbalance in the cell's redox status, and this could be the reason for the pathophysiology of some diseases, such as cancer.

In cancer, oxidative stress caused by chemical and physical agents, inflammation and disease can directly damage DNA prompting tumor development [48]. It also changes the conformation and function of protein. Phytochemicals are commonly recognized for their antioxidant property through counteracting activity against destructive effects of oxidation *in-vitro* by quenching ROS generation. Similarly, phytochemicals also enhance the expression of genes that detoxify receptive species, metabolize toxic compounds, and maintain cellular homeostasis. Phytochemical's capacity to repress chemical-induced carcinogenesis in mice models has been a foundation for their chemo-preventive activity. An interruption in tumor progression has been revealed, upon simultaneous effective use of 12-O-tetra decanoylphorbol-13-acetate (TPA) and phenolic compound, for example, caffeic acid, curcumin, chlorogenic acid, ferulic acid and ursolic acid or resveratrol[49].

INHIBITION OF INFLAMMATION

The continuous inflammation and inflammatory mechanism have been noticed as the basis of many diseases, for example, chronic aging. Stud-ies have also given critical proof to show a positive connection between inflammation and cancer[50]. Chronic inflammatory conditions are stimulated by various factors, for example, microbial infection, autoimmune diseases, obesity etc.[51]. Underlying infections or inflammatory responses have been connected to almost 15-20% of cancer-related mortalities[52]. Various phytochemicals have been shown to invade the inflammation related pathways, clarifying their cancer preventive activity[53]. Curcumin is a notable anti-inflammatory agent[54] with its impact on inflammation being mediated by numerous mechanisms, for example, up-regulation of transforming growth factor beta1 (TGF-β1) and down-regulation of cyclooxygenase-2 (COX_2) and inducible nitric oxide synthase (iNOS)[55], also regulation of interleukin-1 receptor (IL-1R)/toll like receptors (TLR) pathway[56].

Resveratrol is another known anti-cancer agent[57], with anti-inflammatory activity (Inoue and Nakata 2015). It prevents the formation of pro-inflammatory cytokines [tumor necrosis factor-alpha (TNF-α) and interleukin (IL)- 6/8], miR-155, miR-663 and anti-inflammatory cytokines[58]. Resveratrol has been shown to affect the pro-inflammatory events activated by IL-1beta[59]. Various signaling pathways play a critical function in inflammation, cancer initiation and progression. Signaling via nuclear factor kappa-light-chain-enhancer of activated B cells (NFκB) is a well examined pathway that is associated with cancer[60]. Generally, phytochemicals like curcumin, EGCG, resveratrol, honokiol and plumbagin influence NFκB signalling[61]. The Keap-1/Nrf 2 pathway also controls inflammation-related gene expression[62]. Nrf2 facilitates antioxidant response to several stimuli, in order to prevent oxidative damage and initiation of in-
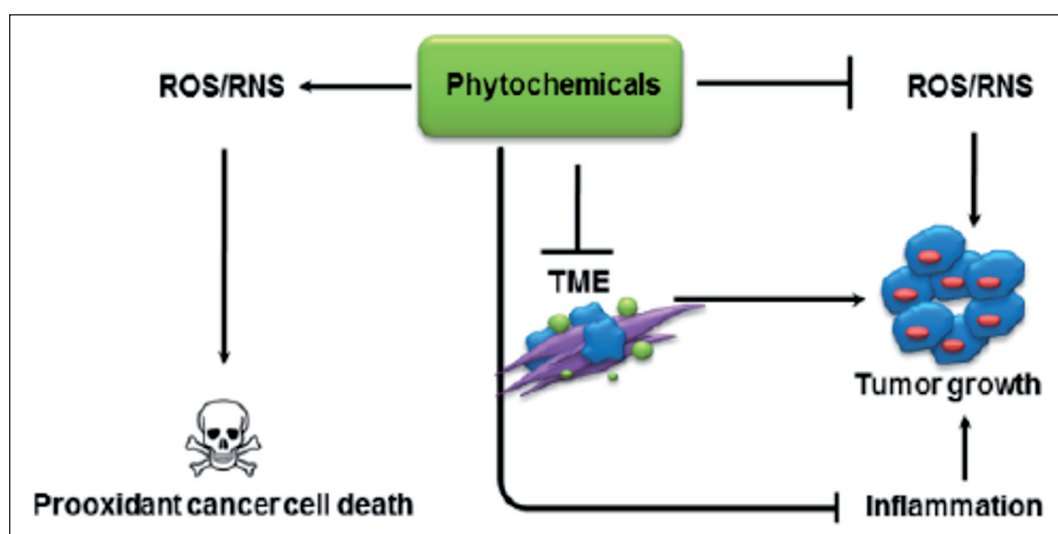

Fig. 7. Roles of phytochemicals in human malignancies.

flammatory responsive diseases, such as cancer, Keap1 causes the sequestration of Nrf2 in the cytoplasm, therefore inhibiting Nrf 2 from exhibiting its antioxidant capacities. It is then recommended that phytochemicals are effective in the targeting of Keap1 leading to the initiation Nrf2 antioxidant activity. Certainly, numerous phytochemicals are outstanding targets of Keap1/Nrf2 pathway [63].

SAFETY DOSE AND INDEX

Chemo-preventive foods contain distinctive natural and biologic agents like phytochemicals which suppresses or reverse tumor growth and development. These compounds in regulated doses may modulate signaling pathways associated with cell proliferation and apoptosis, upgrade the host immune system and repair damaged cells. As beneficial as they may be, their doses must be regulated as high dosage could have unpalatable effect on the host cells and could be harmful.

Chestnut: 300 mg of horse Chestnut seed extract twice every day. Prolonged administration of chestnut product contains toxic substance esculin which can cause dizziness, migraine, nausea, spasm. Crude and natural seed, bark flowers and leaf are unsafe.

Garlic: 1 mg/kg of a water dissolvable garlic extract taken every day for one month. Side effects: Increased bleeding, bad breath, Stomach and heart burns, asthma[64].

Tomato: dosage of tomato as treatment depends on upon a few factors, such as, the client's age, health status etc. Till date, there is no adequate scientific data to determine a suitable range of doses for tomato. Note, natural products are not in every case safe because knowledge of their doses is important. One must track important product guidelines and consult a pharmacist or doctor or other healthcare provider prior to usage [65].

Side effects: orally, red or green tomatoes, and its leaves are possibly harmless when used in the right amount found in food. A particular tomato extract (Lyc-O-Mato) is actually safe when used for not more than two months. Too much tomato leaf or green tomatoes are potentially risky symptoms noticed for usage may include mouth and throat irritation, vomiting, dizziness, diarrhoea, mild spasms, migraine, and death in serious cases.

Red Pepper: 0.075% - 8% capsaicin. Large doses taken by mouth for a long period are hazardous and can lead to liver or kidney damage and increased blood pressure.

Soy: 30 grams of Soy protein every day. Period of usage must not exceed 6 months to avoid results like constipation, swelling, nausea, allergic reactions.

Dietary Fiber: According to the Institute of Medicine, women and men need 25 g and 38 g of fiber daily, respectively. A good source of fiber has 2.5 - 4.9 grams of fiber per serving[66].

CONCLUSIONS

Environmental carcinogens are numerous and increasing as a result of human activities. Combating the environmental carcinogens-induced cancers by therapeutic/ functional foods is crucial in order to enhance the prevention, treatment and the management of these cancers. Chemo-preventive roles of these medicinal/functional foods is accomplished in various proposed mechanisms like inhibition of cell proliferation, tumor microenvironment changes, induction of apoptosis, enhancement of tumor suppressor gene like P[53], modulating signaling organization and ROS generation. Future perspective of these functional foods would be the development of plant medicines as possible candidate for drug development.

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