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Manipulation of different phytochemical classes against inflammation induced by radiations

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Abstract

This review represents a scientific approach regarding the utilization of phytochemicals in research work field as promising radioprotective agents. Recently, numerous studies proved the efficacy of phytochemicals as antioxidant, antimicrobial, anti-inflammatory and anticancer. Consequently, based on the previous exerted activities, phytochemicals have drawn the attention as radioprotective agents in both prophylactic and post radiation treatment protocols**.** Moreover, this collective work is basically concerning about the radiation meaning, types, effect on human health and offers a new perspective scenario about the outstanding benefits of phytochemicals, found in many plants around us and their unique radioprotective effect.

Key words: phytochemicals**,** radioprotective**,** antioxidant, anti-inflammatory, anticancer**.**

List of abbreviations

CBC	Complete blood picture
CF	clastogenic factors
COX-2	cyclooxygenase-2
HaCat cells	spontaneously transformed aneuploid immortal keratinocyte cell line from adult human skin
ICAM-1	intercellular adhesion molecule-1
IL-10	interleukin 10
JAK/STAT	Janus-kinase/signal transducers and activators of transcription
LDRT	low dose radiation treatment
MDA	malondialdehyde
MPO	myeloperoxidase
nm	nanometer
NO	nitric oxide
NF-κB	nuclear factor k-light-chain-enhancer of activated B cells
Nrf2	nuclear factor erythroid 2 related factor 2
RT	radiotherapy
ROS	*reactive oxygen species*
SOD	superoxide dismutase
TGF-β	transforming growth factor-β
TOMS	traditional oriental medicinal plants
TNF-α	tumor necrosis factor alpha
V79-4	lung fibroblast cells

1. Introduction

This review represents a scientific approach regarding the utilization of phytochemicals in research work field as promising radioprotective agents. Over the past decades, humanity went through horrible sufferings post exposure to damaging radiation consequences worldwide. Accordingly, it is the science function, especially pharmacognosy, to spread the awareness about the proper and stable consumption of phytochemicals.In addition, offering an integrated explanation to their promising role as radioprotectors.

It has been prominent that various research studies reported the effectiveness of phytochemicals e.g.curcumin, apigenin, quercetin, resveratrol, hesperidin, silibin and many others against diversity

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of diseases for instance: diabetes, hypercholesterolemia, heart impairment, kidney, hepatopathy and other countless disorders [1,2,3]. Recently, numerous studies proved the efficacy of phytochemicals as antioxidant, antimicrobial, anti-inflammatory, anticancer for many cancer types and to improve variety of neurodegenerative diseases. Furthermore, the mechanism of action by which many phytochemical compounds possesses their pharmacological activities has been clarified [4, 5].

Consequently, based on the previous exerted activities, phytochemicals have drawn the attention in this novel study trend; radioprotection in both prophylactic and post radiation treatment protocols [6, 7)]. Additionally, this collective work is basically concerning about the radiation meaning, types, effect on human health and offers a new perspective scenario about the outstanding benefits of phytochemicals, found in many plants around us and their unique radioprotective effect.

Definition of radiation

It can be defined as energy emitted from a body or source that is transmitted through a medium or space and absorbed by another body. Ionizing radiation has sufficient energy to produce ions in the matter or human body at the molecular level. That significantly causes severe body injuries including DNA damage and proteins denaturation. This doesn't mean that non-ionizing radiation is harmless to humans but the related injury is generally directed to thermal damage or in another meaning burns. However, the biological adverse reactions are to be briefly handled in the upcoming discussion [8].

Types of radiation (Fig.1)

Radiation is classified into non-ionizing which is characterized by longer wavelength, low frequency and ionizing with shorter wavelength and high frequency [9].

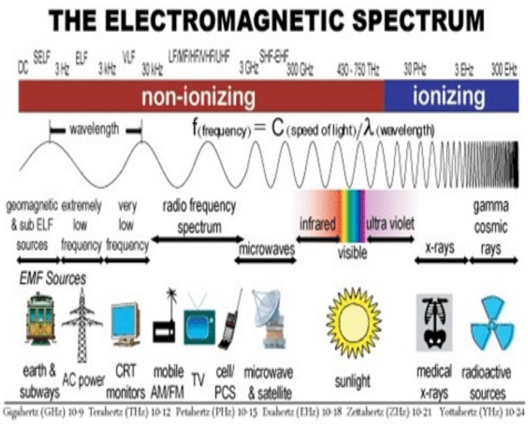


Fig1: Radiation classification according to wavelength and frequency

https://www.who.int/ionizing_radiation/about/what_is_ir/en/

Types of non-Ionizing radiation and their effect on human body [10]

- Radio waves and Microwaves (exposure to radio and microwave frequency sources can cause burns)
- Frequencies of electromagnetic radiations measured in Hertz. KHz, etc.
- Lasers beams are measured in joules (J). Eye is most sensitive organ to get injured by laser.
- Infrared light (measuring unit is nm. Mostly penetrates superficial layers of the skin, causes thermal injury, potential for damage to the eye cornea, during welding, heating, etc.).
- Visible light(400 to 750nm wavelength)
- Ultraviolet light(200nm to 400 nm Bridge between non-Ionizing and ionizing Radiation; UVA and B bands produce biologic effects on the skin and the eyes from sunburn, photosensitization reactions to skin cancers).

Types of ionizing radiation and their clinical effects [11]

1.Gamma Rays
2. X-Rays
3. Alpha Particles
4. Beta Particles
5. Neutrons

Measurement units

Rad- Conventional unit of absorbed dose of radiation per unit mass.
Gray (Gy) – 1 Gray=100 Rads

Ionizing radiation exposure limits

The annual exposure should not exceed 5rem.
Most common exposure circumstances were mainly recorded in:

- Medicine especially; x-ray.
- Nuclear power.
- Industry e.g. (food preservation).

Acute Radiation Syndrome (Over 100 rad in a single exposure): In period of 1 to 6 hours after exposure, the following symptoms could be noticed: anorexia, and GIT disturbance (nausea, vomiting and diarrhea). CBC of the causalities recovers in period of six months to a few years.

Long Term Effects: They include cataracts, sterility, prenatal damages, cancer and DNA damage upon internal disposition.

Is ionizing radiation always harmful?

The most perception of radiation that overwhelms mind when handling such topic is

Hiroshima and Nagasaki bombs where many Japanese died and suffered for generations from their harmful destructive consequences. Nevertheless, the key driver for discovering both ionizing and non-ionizing radiations is their beneficial use in peaceful ways in different science applications and industrial fields. Let us demonstrate some of the most remarkable radiation applications that fortunately go in humanity favor [12].

Benefits of radiation

Although irradiation is always associated with carcinogenicity, damaging effects mainly due to the human abuse, but there are other very useful aspects of irradiation, here are some examples.

Food industry

For many years using a dose dependent radiation in food preservation solved the puzzle for fulfilling the increasing needs for a fresh food for decades for many human generations [12]. The process which includes the manipulation of ultrasound treatment (sonication) in the form of gamma rays or electron beams and UV radiation that provides a physical, non-thermal mode (cold-pasteurization) sterilization method [13]. Hence, the major privileges of using radiation are short consuming time, providing a microorganism-free fresh food and reasonable shelf life products. In addition, this process has a minor defect where radiation may affect some nutritional antioxidants constituents [14 , 15] .

Shim *et al.*, 2009[16] stated that irradiation at 10 kGy and above does not produce any toxicological hazards or nutritional or microbiological problems in food. On the contrary, it was proved to decrease the harmful protein contents in some legumes, thereby helping to provide food safety.

Bones and teeth diagnosis by x-ray

It provides an easy and quick examination through the use of a very small dose of ionizing radiation to produce pictures of any tooth or bone in the body especially in cases of fractured joints and bones [17].

Post cancerous radiation therapy

Many researches indicated the powerful results of the application of radiotherapy in a dose dependent manner in enhancement the antitumor immune response. There are two main types of radiation therapy, external and internal procedures. The type of radiation used in treatment protocol depends on many factors, such as type and size of the tumor, how close the tumor is to normal tissues that are sensitive to radiation and many other factors [18].

Treatment of COVID-19 pneumonia using a (LDRT)

Metcalfe, 2020[19] stated that there are multiple supporting studies in the past dating from the 1930s that investigated the effect of administration of a low dose radiation treatment (LDRT); fraction of x-rays (less than 0.5 Gy) against viral and bacterial pneumonia as well as its anti-inflammatory effect. Based on these researches, very recent studies have come to modern aspect to the treatment of COVID-19 secondary pneumonia using a LDRT of external beam x-rays and suggested that COVID-19 patients suffering from persistent pneumonia can have it as an efficient adjuvant treatment that may improve symptoms severity. In a similar supporting study, a small clinical trial, 4 out of 5 patients treated with 1.5 Gy LDRT survived the pneumonia related to corona virus invasion in relatively short time [20, 21].

Relation between radiotherapy treatment, oxidative stress and inflammation process

It is well established that radiotherapy is considered one of the three most approved approaches for cancer treatment besides surgery and chemotherapy. The utility of each treatment strategy or combination between one or more of these trends depends on some limitations e.g. location, size, stage of the tumor, besides patient age and general health conditions [22] .

Radiotherapy treatment works by exposing cancer cells to ionizing waves of energy that kill the cells or stunt their growth. In addition, RT causes cytotoxicity in the target area, and accordingly creating an inflammatory response that gives rise to an elevation in all inflammatory mediators. Whereas RT is destroying or damaging cancer cells, it initiates inflammation cascade through the body organ sand oxidative cellular damage. Thus, the issue that flashes across the mind whether there is a possibility to counteract these harmful effects through phytochemical manipulation for such an essential treatment for enormous suffering cancer patients [23, 24].

Many studies demonstrated that the main healthy tissues being affected by RT are bone marrow, internal GIT organs and skin. Skin damages were eventually recorded by up to 95% of patients who receive RT, this occurs due to the incidence of release of inflammation and oxidative stress indices into the blood stream of patients receiving that kind of treatment [24, 25]. However, various studies handled the destructive effect of RT on healthy cells and even its contribution to an increased risk of infection conditions. A diversity of pathological mechanisms has been proved to play a role in radiation-induced inflammation.

Moreover, the damaging effects of ionizing radiation are moderated by the overproduction of ROS, remarkable decrease in SOD activity associated by a distinct elevation in MDA content. All of these together promote increased lipid peroxidation powered by the oxidative deterioration of cell membranes [7, 25]**.** In addition, other factors that could have an important role in the inflammation process in RT include the inflammatory mediators, TNF-α, and nuclear factor kappa B (NF-κB) which are mainly released due to epithelial cell necrosis, edema, and neutrophile infiltration.

The antioxidative action is one of the variant mechanisms by which fruit and vegetable might exert their beneficial health effects. Thus, the ability of phytochemicals to inhibit free radical generation, by restoring the redox state of the internal tissue organs can possibly provide reasonable explanation for their prophylactic role as well.

On top of all, evidence based researches have indicated that the anti-carcinogenic properties of phytochemicals are due to their anti-oxidative, anti-inflammatory, and anti-proliferative effects. Hence, this reviewemphasizes the protective role, therapeutic benefits of some phytochemicals as antioxidant, anti-inflammatory and radioprotective agents and their structure activity relationship [4, 5, 26]**.**

Plant phytochemicals

Phytochemicals also known as phytoprotectants or nutraceuticals are non-nutritive plant secondary metabolites that belong to different chemicals classeseach class has its own distinctive building nucleus and they possess a variety of biological features against different diseases [1,3]**.** Phytochemicals have no direct contribution in basic processes such as photosynthesis, respiration, and the differentiation or formation of carbohydrates, proteins, and lipids. They exist as a result of chemical conversions and it is believed that their main role in plant life is to the guard against different pathogens, they also affect plant growth, reproduction and adaptation of plant to certain environmental conditions such a variation in temperature, humidity, and drought [27]**.**

Rizeq *et al.*, 2020; Tan *et al.*, 2019 [28,29] and many others clarified the pharmacological actions exerted by the different phytochemicals classes like alkaloids, flavonoids and phenolics, saponins, terpenes and organosulphur compounds **(Fig.2& Table 1).**

Phytochemicals are widely found in edible plants i.e. vegetables (e.g. green leafy vegetables) and fruits (e.g., pomegranates, figs, oranges, and blueberries).They abundantly exist in medicinal plants different organs including herbs, stems, leaves, flowers, fruits, and seeds as well as their existence in considerable and efficient amounts in non-edible parts like peels and seeds. Moreover, they can be found in Marine algae and fresh water algae [29]**.**

Nevertheless, depending on their composition, quantity, their existence in different concentrations is determined. For example, the different chemical classes vary in their concentration among different plant species. Besides, the environmental conditions and seasonal variations are crucial factors that must be taken in consideration [30,31] . Natural occurring pigments are important phytochemicals in plant kingdom and could be classified into three major classes; chlorophylls, carotenoids, anthocyanins and betalains. The first fore mentioned pigments are lipophilicin nature and participate in photosynthesis while anthocyanins and betalains are non-photosynthetic pigments functioning in pollination and absorbing damaging UV radiation. Recent researches proved their antioxidant, anti-mutagenic capacities and many other activities. The mode of action by which they probably possess their antioxidant behavior is by decreasing oxidative stress regulators [29]**.**

Over the past decades, huge number of researches evaluated many effective pharmacological activities reported by phytochemicals e.g. antioxidants, anticancer, cytotoxic agents, antimicrobial, immunity alleviating agents, anti-diabetics, anti-inflammatory in hepatic cirrhosis, kidney dysfunction, skin irritations, anti-hypercholesterolaemics, and in many central nervous system diseases relieving agents, etc. However, many of them have been formulated in the pharmaceutical field [1, 3, 32]**.**

Although systemic corticosteroids e.g. (dexamethasone; glucocorticoids) have been an approved treatment to the harmful effects resulting from RT, but patients receiving corticosteroids have suffered from many health issues as the long term use of such medication led to immunosuppression and consequently may cause some chronic diseases such as diabetes and other heart disorders or serious microorganism invasion[23]**.** Additionally, new research contexts have to be worked on to find safe and yet effective substitute for corticosteroids.

Moreover, countless studies highlighted that the reactive production of oxygen species, inflammatory and tumor mediators is mainly prompted upon and post exposure to the ionizing radiation [43]. Hence, here are some examples showing the handling of some traditionally medicinal plants being used as novel contributes in radioprotective therapy and their mechanism of action **(Fig.3, Fig. 4 & Table2).**

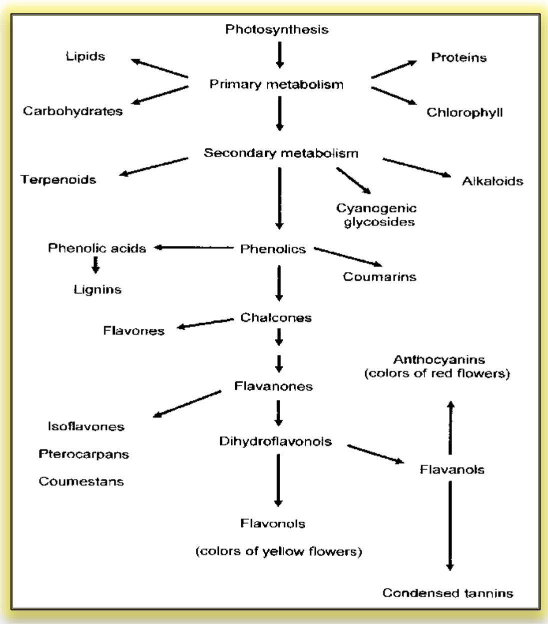


Fig.2: Classification of plant phytochemical classes[29]

The mode of action and structure–activity relationship of plant phytochemicalsasradioprotective, antioxidant and anti-inflammatory agents

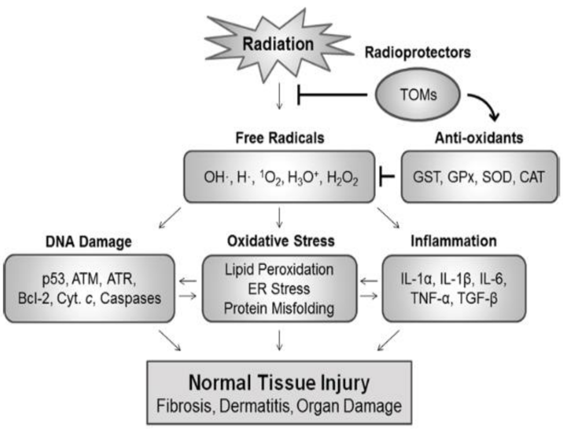


Fig.3: Proposed mechanism for the radioprotective effects of phytochemicals against, oxidative stress response and inflammation[23].

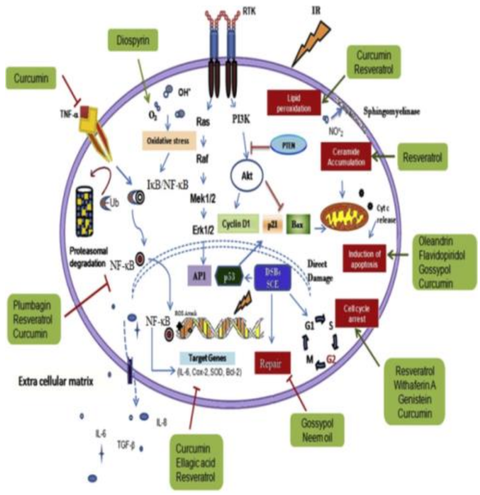


Fig.4: Examples of mode of action of some phytoconstituents on inflammatory mediators[23].

Aged garlic extract contains concentrated radioprotective antioxidants that have more potent antioxidant power comparing to fresh one. An odorless formulation made from aged garlic extract which acted as an efficient immunostimulant and possessed potentiality in normal cell protection against oxidative damage resulting from RT. Furthermore, it acted as prophylactic anti cancer treatment. The major compound to have such activity was proved to be a water-soluble organosulfur compound; S-allylmercaptocysteine, which is exclusively produced in aged garlic and activates apoptosis in different human cancer cell lines e.g. prostate, breast, and colon [44].

Garlic (*Allium sativum* L., Photo1)

Photo1. Aged garlic stages[44].

Curcumin is a naturally occurring phenolic compound from ***Curcuma longa*** L. root which has been traditionally used in many civilizations for its powerful anti-inflammatory effects as demonstrated in Photo 3 [2, 45]. A recent clinical trial study done by [35] evaluated the effect of curcumin formulation, where it possessed a remarkable counteracting cancer-promoting inflammation through modulating inflammatory cancer pathways and mediators (NF-κB, JAK/STAT, and TGF-β). In addition, it blocked (ROS) receptors causing the strong antioxidant and anti-apopototic response. Thus, curcumin plays a crucial role in cancer neurotoxcity, nephrotoxicity, concomitant to the radiotherapy treatment**.**

Turmeric root **(*Curcuma longa*** L., **Photo2**)

Photo2. *Curcuma longa* intact and powdered root L[45].

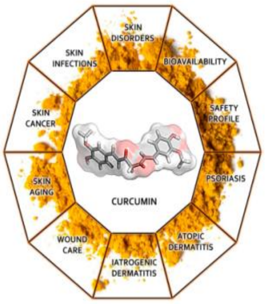


Photo3. Inflammatory effects of curcumin[45].

Pomegranate (*Punicagranatum* L., Photo4)

Photo4.*Punicagranatum* L. ripe fruit[46].

Numerous evidence based studies emphasized the safeguarding impact of the pomegranate fruit, peels and leaves extracts as an extraordinary antioxidant, anti-inflammatory agents besides other pharmacological activities. Moreover, fore mentioned plant extracts acted as anticancer against UVB mediated skin cancer, breast and hepatocellular carcinoma while being safe on normal skin fibroblast cells. Different studies suggested that the mechanism of action is owed to the modulation in transcription necrosis factors and the decrease in the responsible inflammatory mediators **[46].**

Prickly pear (*Opuntiaficus-indica* L. Photo5)

Photo5. *Opuntia ficus-indica* fruits[47].

A novel study acknowledged by **[7]** evaluated the prophylactic effect of the prickly pear fruit peels against irradiation-induced colitis in rats.Results reveled that pretreatment with the petroleum ether extract stopped the elevation in the measured inflammatory, oxidative damages mediatorsas well as tumor necrotic indices (MDA, NO, COX-2, NF-κB, IL-10, ROS, SOD). The results attributed the and anti-inflammatory properties of the extract against irradiation induced colon injury tissues due to the rapid restoring to the redox state of the colonic mucosa that helped their prophylaxis, i.e. the potentiality of the extract to inhibit free radical generation. Nevertheless, the study correlated the preventive effect of inflammation due to the synergistic effect of the isolated terpenoids of which the extract is very prosperous e.g. α-amyrin, betulinic acid, dammaradienone, betulinic acid, β- sitosterol, campsterol and clerosterol.

Marine algae and their secondary metabolites

During recent decades, research investigation of marine algae has unveiled the existence of many radioprotective phytoconstituents mainly polysaccharides, carotenoids and other compounds. Furthermore, marine algae polysaccharides proved to acquire antioxidant, radioprotector, anticancer properties and other pharmacological activities **[47]**. Marine algae are mainly classified into brown, red and green. The brown algae contain mainly sulphated polysaccharides, such as fucoidan, sulfated alginates and sulfated galactans. Their mechanism of action involved interaction with the ROS resulting from ionizing radiation. On the other hand, carrageenan present in red algae undergoes structural changes including desulfation and acidification following γ-ray irradiation, while green type contains free sugars e.g. xylose, glucose, glucuronic acid and alginates that modulate through formation of double bond in pyranose-ring following γ-ray irradiation **[43].**

Table1: Examples of some phytochemical compounds and their mechanism of action as antioxidant and anti-inflammatory agents

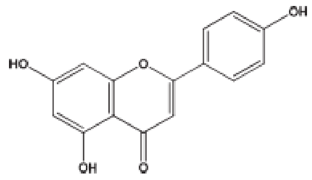
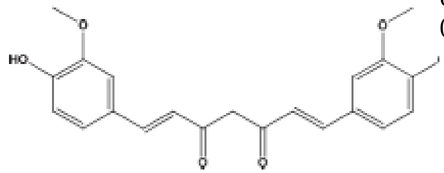
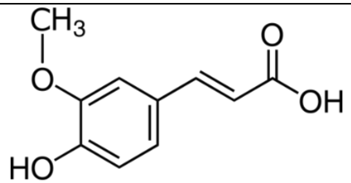
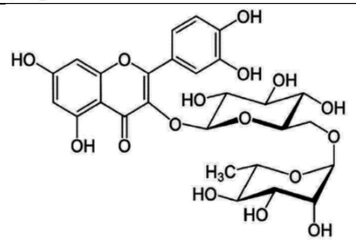
Phytochemical	Structure	Occurrences (e.g.)	Mechanism of action	Reference
Phenolics and flavonoids				
Apigenin		*Lagerstromeia indica*(L.) Pers. leaves, *Pisum sativum* L. fruit peels.	Modulation of vascular endothelial growth factor and hypoxia-inducible factor-1a through activating thrombospodin-1	[33 , 34]
Curcumin		*Curcuma longa* L. root (Turmeric)	Apoptotic effect by blocking the inflammatory pathways(NF-κBJAK/STAT&TGF-β) and Destabilizing ROS.	[35, 36]
Ferulic acid		*Lagerstromeia indica*(L.)Pers.	Inhibition of matrix metalloproteinases.	[33]
Rutin		*Citrus sinensis* L. (sweet orange) and other *Citrus* spp.	Inhibition of COX-2 and IL-10 and SOD prameters.	[33, 34]

Table1: Examples of some phytochemical compounds and their mechanism of action as antioxidant and anti-inflammatory agents (contd.)

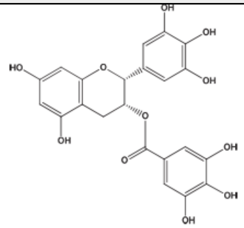
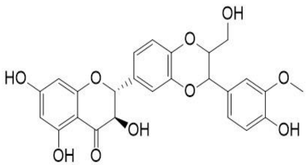
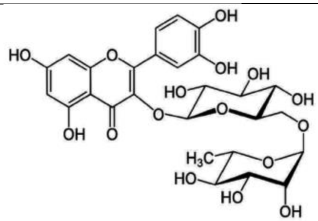
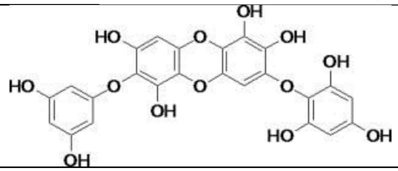
Phytochemical	Structure	Occurrences (e.g.)	Mechanism of action	Reference
Phenolics and flavonoids (cont.)				
Epigallocatechingallate		*Camellia sinensis* L.(Green tea)	Stimulation of cytotoxic T cells and inhibition of angiogenesis in cancer cells.	[37]
Silibinin		*Silybum marianum* L. (Milk sithle or Silymarin)	Inhibition of induced oxidative stress factots (SOD, ROS), induction of apoptosis of tumor cells.	[38]
Quercetin		*Citrus sinensis* L. fruits, *Vicia faba* (L.)	Prevention of UV-induced apoptosis via activation Nrf2, initiating antioxidant response pathway i.e.(acting as anti-fibrotic and anti-aging.	[33]
Diphlorethohydroxycarmalol		brown algae *Ishigeo kamurae*	Radioprotective effect against γ-irradiation-induced damage in (V79-4) cells.	[39]

Table1: Examples of some phytochemical compounds and their mechanism of action as antioxidant and anti-inflammatory agents (contd.)

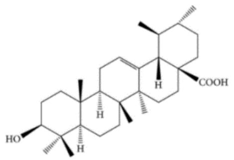
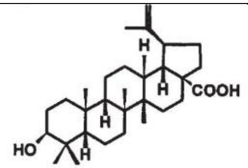
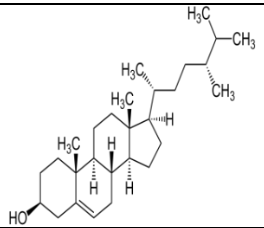
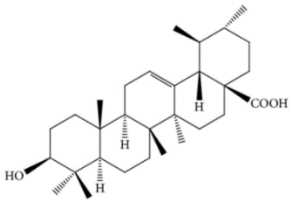
Phytochemical	Structure	Occurrences (e.g.)	Mechanism of action	Reference
Terpenoids and sterols				
Ursolic acid		Apples, basil, bilberries, and many medicinal plants (*Ficus nitida* L.)	Decreases many inflammatory mediators (Cox-2, NF-κB and IL-10).	[4]
Betulinic acid		*Opuntia-ficus indica*	Improve the decrease in SOD, MDAand acts as selective inhibitor of human melanoma cells.	[4]
Campesterol		*Opuntia-ficus indica*(L.) Mill, *Ficus lutea*(Vahl.)	Alleviate some inflammatory indices (NF-κB and IL-10), oxidative stress factors (SOD)	[7, 40]
Ursolic acid		apples, basil, bilberries, and many medicinal plants (*Ficus nitida* L.)	Lowers many inflammatory mediators (Cox-2, NF-κB and IL-10).	[4]

Table 1: Examples of some phytochemical compounds and their mechanism of action as antioxidant and anti-inflammatory agents (contd.)

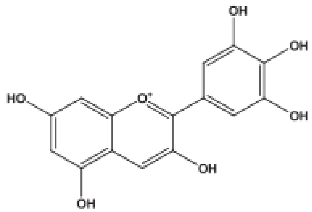
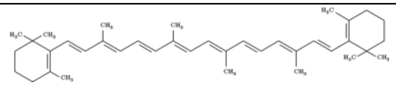
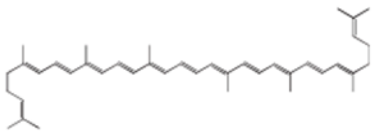
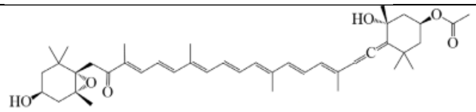
Phytochemical	Structure	Occurrences (e.g.)	Mechanism of action	Reference
Natural occurring pigment				
Delphinidin (anthocyanidin)		Pigmented fruits and vegetables such asstrawberry, pomegranate	Protection of HaCaT cells against solar UVB-mediated radition. Decrease in tumor cell viability, lowers the lipid peroxidation	[27]
β -Carotene		*Daucus carota* L. (carrots) and *Citrus sinensis* L.	Reducing the TNF-*α*- by preserving bioavailability of redox process.	[31, 33]
Lycopene		*Solanum lycopersicum L.*(Tomato)	Lowering the levels of inflammatory factors (IL1, IL6, IL8, and tumor necrosis factor-α (TNF-α)	[41]
Fucoxanthin		*Sargassum Siliquastrum* (brown algae)	Possesses radioprotection in human fibroblasts against UV-B-induced cell damage	[42]

Table 2: Examples of some traditional plants possessing remarkable therapeutic patterns in regard to radioprotection

Plant, Family	Mechanism of action/ Therapeutic effect	Effective Radioprotective Dose	Ref.
Aegle marmelos Corr. ex Roxb. **Rutaceae**	Provided protection against radiation-induced sickness.	15mg/kgb.wt.	[48]
Allium cepa L. **Alliaceae**	Administration of the dried bulb showed efficacy against X-irradiation.	20 mg/kgb.wt	[49]
Curcuma longa L. **Zingiberaceae**	The diferuloyl methane extract has been reported to counteract radiation effect	--	[45]
Ginkgo biloba L. **Cycadaceae**	The dried leaf (30% ethanol extract) has shown potency upon testing a culture exposed to Cf* from plasma of human subjects exposed to irradiation and on rat cerebellar neuronal cell culture against hydroxyl radical-inducedapoptosis.	100µg/ml	[50]
Glycyrrhiza glabra L. **Fabaceae**	Methanol extract (70%)protectedrat microsomal membranes from lipid peroxidation induced by γ-radiation.	100µg/ml	[51]
Mentha arvensis L. **Lamiaceae**	Pretreatment with chloroform extract protected mice against GIT and bone marrow death from radiation.	--	[48]
Moringa oleifera Lam. **Moringaceae**	Administration of Leaf extract post-irradiation remarkably reducedthe percent aberrant cells in metaphase chromosomes to normal range by day 7 in mice.	150 mg/kg i.p.	[52]

*CF is the link between chronic inflammation and carcinogenesis.They were circulating in the blood stream of the irradiated persons even years after the irradiation also called chromosome breakage factors, were first described by radiobiologists in 1968 [53].

Table 2: Examples of some traditional plants possessing remarkable therapeutic patterns in regard to radioprotection (Contd.)

Plant, Family	Mechanism of action/ Therapeutic effect	Effective Radioprotective Dose	Ref.
Opuntia ficus indica (L.) Mill **Cactacea**	Prophylactic action against inflammation upon receiving an oral dose of petroleum ether extract due to blocking the elevation in the measured inflammatory, oxidative stress indices and tumor necrotic indices (MDA, NO, COX-2, NF-κB, IL-10, ROS, SOD).	1g/kg b.wt (oral)	[7]
Panax ginseng L. **Araliaceae**	The water-soluble whole plant extractexerteda potent protection against Co60 gamma radiation in mice.	--	[54]
Piper longum L. **Piperaceae**	The ethanolic extract of fruit exerted radioprotection to WBC and bone marrow cells in mice.	--	[6]
Punica granatum L. **Punicaceae**	Aleviating the level of ROS lead to amelioration in the expression of (NRF2), as well as liver function by inhibiting oxidative stress and inflammation induced by radiation.	---	[6]
Tephrosiapurpurea (L.) Pers. **Fabaceae**	Extract protected albino mice against 5 Gy induced hemopoetic injury.	100μg/ml	[55]

Table 1 Summary of data obtained from least-squares fit of Eq. (20) to k_m vs E_i plots for three selected systems

Redox moiety	Diluent	Method	k_0 (s^{-1})	$E_i^{0'}$ V vs SSCE	γ	fwhm (V)[a]
R1	D1	ILIT	3.4×10^4	0.495	95	-
		CV	3.3×10^4	0.474	100	0.103
R2	D2	ILIT	6.0×10^4	0.340	24	-
		CV	6.1×10^4	0.346	24	0.112
R3	D3	ILIT	3.2×10^6	0.328	12.0	-
		CV	3.2×10^6	0.324	12.1	0.121

[a]Full-width-half-maximum of the cyclic voltammetric peak.

[b]This is the format for table footnotes.Very often you will already have prepared (parts of) your text. If you load that text as a separate document, you can easily insert it into a document based on this template by cutting and pasting between the two documents.

Conclusion and future perspectives

This Review aimed to spot the light on a novel approach in dealing with phytochemicals and their applications in the different pharmacological studies. The target is to understand the correlation between the efficacy of the diversity of plant kingdom phytochemicals, and the potency exerted on the adverse reactions of radiation esp., inflammation, oxidative damage and other related destructive impact on human health.

Since the exposure to radiation has been a critical and serious problem facing nature and humanity in particular, this review may be helpful in refunctioning and making the best use of several valuable reported studies that revealed many promising and encouraging results about the radioprotective, antioxidant and anti-inflammatory effects encountered by a diversity of plants neutraceuticals.

Irradiation has been widely used for the treatment of different cancers, but the side effects reduced the patients' quality of life, due to apoptosis, nephropathy, mutagenesis, gastrointestinal, skin injuries and many other devastating adverse reactions. Since antioxidative pathway is considered one of the most potent mechanism by which phytochemicals could possibly exert their beneficial health miracles, administration of nutraceuticals in a calculated dose dependent manner helped in focusing the attention on them as radioprotectors.

After all, there were many supporting factors for the manipulation of phytochemicals as an adjuvant strategy in inflammation induced radiation treatment, including lack of toxicity to normal cells, abundance and being extremely economical.

Hence many future studies and clinical trials should be performed to unveil more about the otherunknown pharmacological aspects of the phytochemical compounds.

2. Conflicts of interest

There are no conflicts to declare.

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