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Promiscuous Bioactivty of Phytochemicals

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Authors' contributions

This work was carried out in collaboration among all authors. Author AA conceived the idea. Authors OJU, MAM, MYM, UOC, NUJ and AO wrote the initial draft, Author AA proofread the manuscript. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Phytochemicals are broad, largely studied compounds isolated from plants, generally regarded as a research compound than a nutritive molecule. In recent times, the pharmaceutical industry employs plants in the synthesis of novel drugs and active ingredients. These drugs and ingredients effectively manage neurodegenerative disorders, metabolic diseases, cancer, obesity, and other chronic-degenerative diseases. Although it still remains to be elucidated, the therapeutic strategies in synthesizing novel compounds. In this review, we discuss the major classification of phytochemicals, in addition to its biochemical mechanism of action. Furthermore, this study

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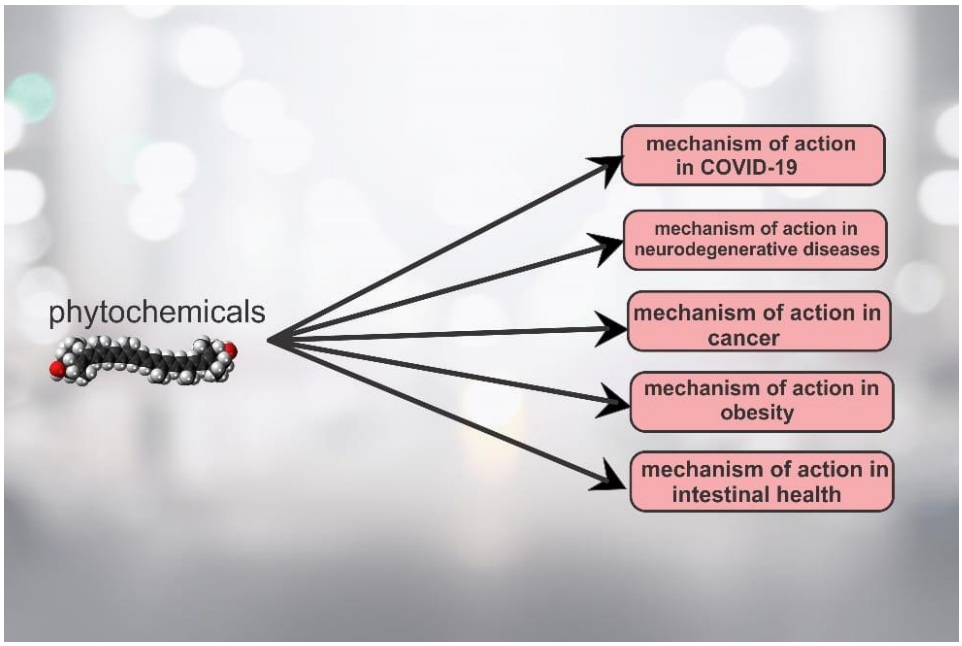
detailed the biosynthetic cascade of various phytochemicals and explained the anti-inflammatory and antioxidant mechanism on various disease processes. Therefore, this review discusses the multifunctional bioactivity of phytochemicals.

GRAPHICAL ABSTRACT



Keywords: Phytochemicals; COVID-19; neurodegenerative disease; cancer; obesity.

ABBREVIATIONS

Reactive oxygen species: ROS, Reactive nitrogen species: RNS, Tumor necrosis factor: TNF-α, Phosphoenolpyruvate: PEP, Erythrose-4-phosphate: E-4P, hydroxyl group: -OH, BRAIN-derived neurotrophic factor: BDNF, nicotinamide adenine dinucleotide phosphate: NADPH, extracellular signal -related kinase: ERK, Electron transport chain: ETC, White Adipose Tissue: WAT, Brown Adipose Tissue: BAT, Transient receptor potential: TRP, Beta adrenergic receptors: β-AR, Cyclic adenosine 3',5'-momophospahte: cAMP, AMP-activated protein kinase: AMPK, Transient receptor potential cation channel subfamily M member 8: TRPM8, Sirtuin1: SIRT1, PPARG coactivator 1: PGC1 α Peroxisome proliferator-activated receptor alpha/gamma: PPAR α /γ, Transient receptor potential ankyrin1: TRPA 1 / TRPV 1, Phosphoinositide 3-kinase: PI3K/Akt , Interleukin 6: 1L- 6, Nitric oxide synthase: iNOS, Monocyte chemotactic protein1: MCP-1

1. INTRODUCTION

Disease is a foremost risk factor that could lead to increase the occurrence of emotional instability and imbalance psychological wellbeing. These diseases include neurodegenerative disorders, aging, obesity, cancer, and the most recent covid-19 infection. This multifactorial disease has not only affected the mental and physical health of geriatrics, but also a major cause of death globally [1]. Medicinal plants have become a highly essential part of the natural environment, containing many of bioactive compounds, secondary metabolites and several other bioactive constituents. Copious studies point that plants contains load of essential phytochemicals and phytonutrients. These phytochemicals exhibit antioxidant, anti-inflammatory, anti-obesity and antivirus potential, thus exhibiting a notable protective role in metabolic diseases [2]. Phytochemicals contain polyphenols and contain terpenoids and glucosinates with different biochemical mechanisms of action as illustrated in Table 1 of this study . Furthermore, in-vitro analysis and in vivo animal studies have extensively affirmed the anti-oxidative, anti-inflammatory and anti-obesity roles of phytochemicals by the termination of free radical species (reactive oxygen species; ROS , and reactive nitrogen species; RNS) from oxidative stress cascades and toll-like receptors; as well as downregulation of nuclear factor kappa light chain enhancer of active β cells NF-k β, inhibition of inflammatory cytokines such as tumor necrosis factor TNF-α, interleukins (IL-6, IL-1 β)and interferon (IFN-γ) [1,3] from proinflammatory immune cascades. Hitherto, dietary supplementation of phytochemicals reduces the damaging effect of free radicals in the brain, enhances the reformation of essential hormones as well as prevents the inflammation of cells. This review explains the biosynthesis and broad classification of phytochemicals, while detailing the structure of several phytochemicals. Furthermore, the role of phytochemicals in the modulation of gut microbes and physiological function, the anti-covid potential of phytochemicals, anticancer and anti-obesity as well as the neuroprotective potential of phytochemicals were all explored. Notable invitro and in vivo contributions are also of notable mention. Thus, despite their extremely varying chemical structures and limited bioavailability, phytochemicals' promiscuous bioactivity is thus appraised.

Table 1. Classification, food source and potential biochemistry effect of phytochemcals

Category		Chemicals	Food/ plant resources	Biochemical effect
TERPENOIDS	1)CAROTENOID TERPENOID	A) LYCOPENE	Tomatoes, water melon, pink guava, wolfberry, sea-buckthorn, papaya, Ker chip	involved in two dissociation of NIF 2 from ARE in the cytoplasm thus leading to the translocation of NIF 2 into the nucleus, a process perquisite to the detoxication and ameliorative process during carcinogenesis. [4]
		B) BETA CAROTENE	Sweet potatoes, carrot, red pepper, chill apricot, sage, paprika, broccoli,	Due to its gene activating potential, carotenoid, terpenoids, are essential in moderating tissue retinoic acid levels inhibits MAPK cascade activities as cell as P53 phosphorylation.
		C) ALPHA CAROTENE	Orange, vegetable, pumpkin, squash, bananas, avocados, and sweet potatoes	Metabolite of lycopene 2,7,11-trimethyltetradeca hexanene-1,14-dial, promotes gap junction communication between cells. [4]
		D) LUMEIN &ZEAXANININ	Green leafy vegetable, egg yolk, kale, green peas, pumpkin, summer squash, broccoli, brussels sprout	Downregulation of Bcl2 & Bcl-XL by (E-E-E)-4-methyl-8-0x0x-2,4,6-nonatrienal, also profess a chemoprotective

Category		Chemicals	Food/ plant resources	Biochemical effect
				effect [4]
		C) ASTA XANININ	Algae, yeast, salmon, trout, krill, shrimp and crayfish	
	2)NON-CAROTENOID TERPENOIDS	A) PERILYL ALCOHOL	Lavender, lemon grass,sage,pepper mint.	Inhibition of pancreatic, skin, liver, colon, prostate (forestomach) carcinoma .
		B) SAPONINS	Beans, peanuts, soy, tomatoes, quimoa, herb giseng, legumes	i) Elimination of scopolamione induced memory impai-rment completely
		C) TERPENOL	Cajuput oil, pineoil, tea, lapsangsoucnong, petitgrain .	Suppression of pro-inflammatory cytokines (TNF-α, IL1β, PGE2), as well as inducible iNOS, COX-2 and TNF-α [4]
		D) TERPENE LIMONOIDS	Lemons, limes, oranges, mandarins, bergamots, grapefruits, pomelos.	
POLYPHENOLS	1) FLAVON OIDS POLYPHENOLS	A) ANTHO CYANINS	Berries, red onions, kidney beans, grapes, pomegranates, acai, violet petals, black rice, tart cherries	Downregulation of mutant p53 protein expression [5]
		B) CATEC HINS	Apples, green tea, chocolate, grape seeds, cocoa, kini,	Alters the synthesis of heat shock proteins in cancers and malignant cell lines. [5]
		C) ISOFLA VONES	Beans, peas, cereals, beer, soybeans, vegetables, meat, milk, fruits, lentins, daidzein, genistein	Oxygen radical inactivation and inhibitor .
		D) HESPE RETIN	Lemons, oranges, citrus fruits and juices, grape fruits	i) Dysregulatio n of RAS protein activator
		E) RUTIN	Buckwheat, grains, asparagus, morusalba, rutagraveolens	Essential in Cell cycle arrest.
		F) QUER CETIN	Onions, coffee, capers, red wine, buckwheat, apples, broccoli, grapes	
		G) SILYM	Milk thistle,	

Category		Chemicals	Food/ plant resources	Biochemical effect
		ARIN	(silybum marianum), artichoke (cyanra scolymus)	
		H) TANGE RETIN & TANINS	Tangerine, citrus peels, apricots, strawberries, cranberries, blueberries, tea, wine, barley, mint, peaches	
	2) PHENO LIC ACID	A) ELLAGI C ACID	Nuts, seeds, berries (raspberries, strawberries), pomegranates	DNA damage repair and scavenging of free radicals
		B) CHLOR OGENIC ACID	Apples, carrots, coffee, beans, grapes, plums, tea, egg plants, tobacco leaves, kiwi fruits, Eucommia, artichoke	Increased activity of prolyl hydroxylase enzyme, thus effectively preventing scurvy.
		C) PARA-COUMARIC ACID	Carrots, tomatoes, cereals, alcoholic beverages, beer	
		D) PHYTI C ACID	Seeds, grains, legumes, brazil nuts, roots, tubers, hazel nut, sesame, almond, tofu, bran, beans	
		E) FERULI C ACID	Rice, wheat , oats, pineapple, grasses, grains, vegetables, flowers , fruits, leaves, beans, seeds of coffee, peanuts and artichoke, popcorn	
		F) VANILL IN	Olive-oil, butter, raspberry, coffee, oatmeal, maple, vinegar.	
		G) CINAM MIC ACID	Cinnamon, stofax, she-butter.	
	3) NON-FLANOID POLYPINENOLS	A) CURCUMIN	Cereals, fruits, ginger, vegetable.	Ameliorate several pathological alterations associated with the development of diabetes such as Nephropathy, cardiopathy or retinopathy.
		B)	Grapes, peanut,	

Category		Chemicals	Food/ plant resources	Biochemical effect
		RESVERATION	vitamin C, blueberries, soy, wine.	
		C) LIGNANS	Beans, berries(tomatoes) wholegrains, variety of plant food.	
GLUCOSINOLATE	1) ISOTHIOCYANATES	A) PHENYL-ISOTHIOCYANATES	Cabbage, mustard, vegetable.	Lowers the risk of cancer. [6]
		B) BENZYL-ISOTHIOCYAANATE	Sugarcane, corn, beetroot.	Induction of phase 2 enzymes such as GST and NADP(H) quinone oxidoreductase1
		C) SULFORAPHANE	Broccoli, kale, cabbage (both white and red varieties), bokchoy, cauliflower.	
	2)INDOLES	A) Indole-3-carbinol(I3C)	Cabbage, savoy, turnip, mustard green.	
ANTHROQUINONES		A) SENNA	Cassia plants	
		B) BARBOLOIN	Chick peas, almonds, peanuts, lentils, tofu, quinoa, mycoprotein, spinilina, tempeh and edamame	
		C) HYPERICIN	Perofratum plants, adenotras, drosocarpium	

2. BIOSYNTHESIS OF PHYTOCHEMICALS

Of mouth-watering significance to plants is the synthesis of phytochemicals, triggered by environmental necessities including but not limited to microbes, presence of herbivores, climate etc. Specific enzymatic reactions control this synthetic biochemical cascade. Several contributing pathways involved in the biosynthesis of phytochemicals include pentose phosphate pathway, shikimic acid pathway, malonyl coA pathway, Nucleotide metabolite pathway, mevalonate pathway, and non-mevalonate pathway as illustrated by Fig. 1.

An essential biochemical cascade exclusively domained in the plastids of plants, highly essential in the synthesis of alkaloids, phenolics, quinones, lignans amidst others is the shikimic acid pathway. The substrate of this pathway is the product of glycolysis and pentose phosphate pathway "Phosphoenolpyruvate (PEP)"and Erythrose-4-phosphate (E-4P). The first reaction involves the condensation od the two sugar moieties, in a reaction catalyzed by Dehydroquinate synthase. This reaction is thus followed by dehydration reaction, in a reaction catalyzed by 3-dehydroquinate dehydratase to form 3-dehydroshikimate [8]. The name of this biochemical cascade is derived in an enzymatic reaction catalyzed by shikimate dehydrogenase, which is immediately phosphorylated via ATP by shikimate kinase; thus, liberating ADP and shikimate-3-phosphate. The free hydroxyl group (-OH) at the 5' carbon reacts with the three carbon sugar moieties PEP to yield the product

5'enol pyruvyl shikimate-3-phosphate, which yields chorismite synthase [8], a substrate necessary in the synthesis of alkaloids, flavonoids, coumarins, lignans, phenolics, alkaloids and cyanogenic glycosides.

2.1 Structure of Phytochemicals

Phytochemicals have been classified into six major categories based on their chemical structures and characteristics. These categories include carbohydrate, lipids, phenolics, terpenoids and alkaloids, and other nitrogen-containing compounds. Several structures of phytochemicals are shown in Figure 3 below.

3. Modulatory Roles of Phytochemicals in Cellular Diseases

Secondary metabolites and several phytoactive constituent represent the functioning ingredient in medicinal plant. Remarkable studies have affirmed that numerous phytochemical and phytonutrient are efficient in several protection against biochemical disorder including neurodegenerative disorders, cancer, obesity, intestinal heath and most recently the present ravaging covid-19 infection [10,11]. These attributed not only to the presence polyphenols or flavonoids or glucosinate compounds but also partly reliant on polyunsaturated fatty acid and Vitamin E [3] . Furthermore, their biochemical protective and remediation efficacy largely depends on their anti-oxidative roles (nullifying and moderating the effect of free radicals), as well as their anti-inflammatory roles (regulating nuclear factor kappa light chain enhancer of activated beta cell [NF -KB], TNF –α [Tumor necrosis factor -α] interleukin [IL-6 , IL -Iβ and IFN -γ [8] in pro – inflammatory immune cascades. Phytochemical employs one of the two strategies enlisted above in counteracting neurodegenerative diseases as well as triggering the release of BRAIN-derived neurotrophic factor [BDNF] in ameliorating brain function. Furthermore, several in vivo studies have indicated dietary phytochemicals in improving the intestinal health as well as the alteration of the gut microbiome. [12,13]. More so, plants extracts containing quercetin, gallic acid, flavonoid, phenols , e.t.c have proven effective in the interaction with major catalytic protease [responsible for cleaving spike responsible for SARS -COV 2 entry into the oropharyngeal tract , while phytochemical such as 5methoxy agenylalkannin, punicalagin are potent in increasing the action of caspase 3 and caspase 9 in human colorectal lymph nodal and small cell lung carcinoma thus inducing apoptosis in cancerous state [14] and inhibition of Bcl -2 by Esculetin during in vivo benzopyrene induce the lung carcinogenesis by Wei et al. Thus, the roles of phytochemicals to the pathological factors of biochemical disorders is detailed.

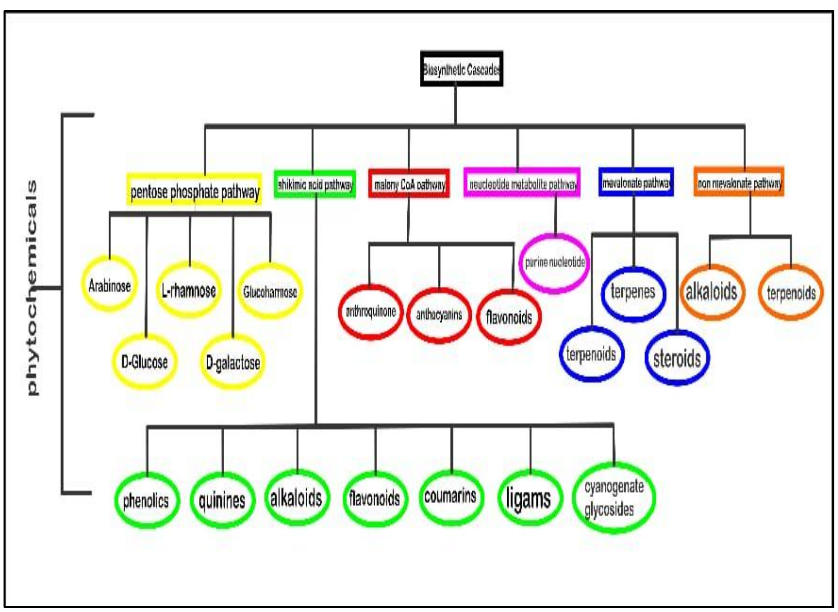


Fig. 1. Illustrating the various biochemical cascades involved in the synthesis of phytochemicals [7]

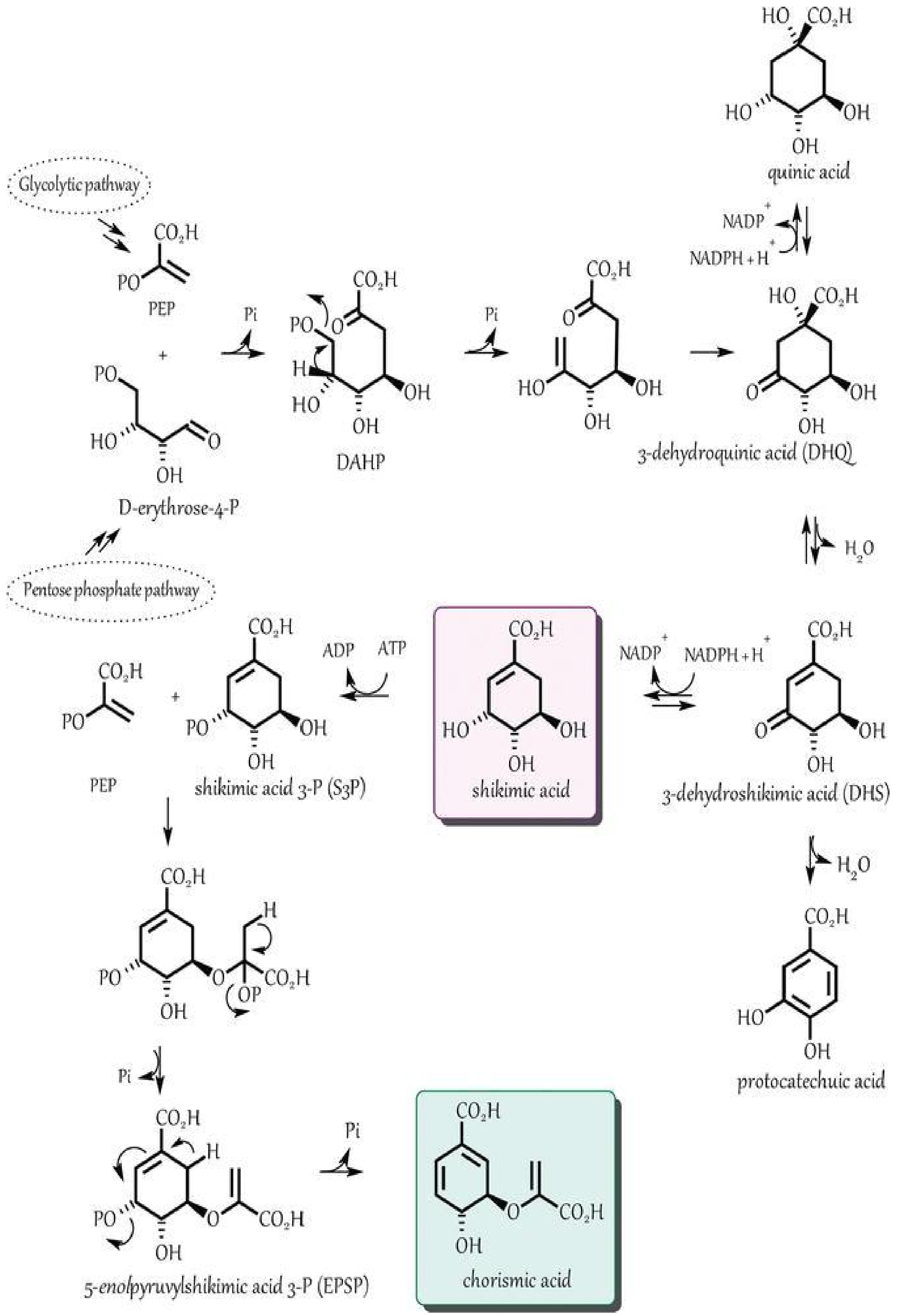


Fig. 2A. Shikimic acid pathway [5]

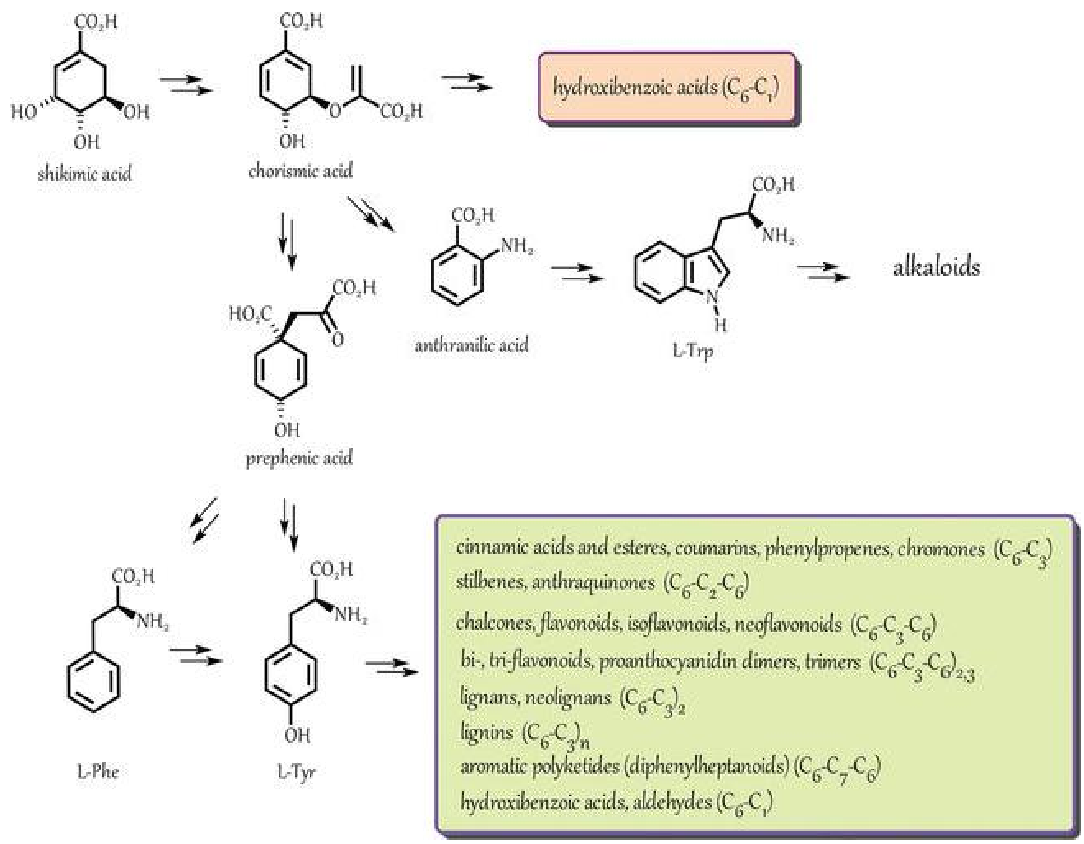
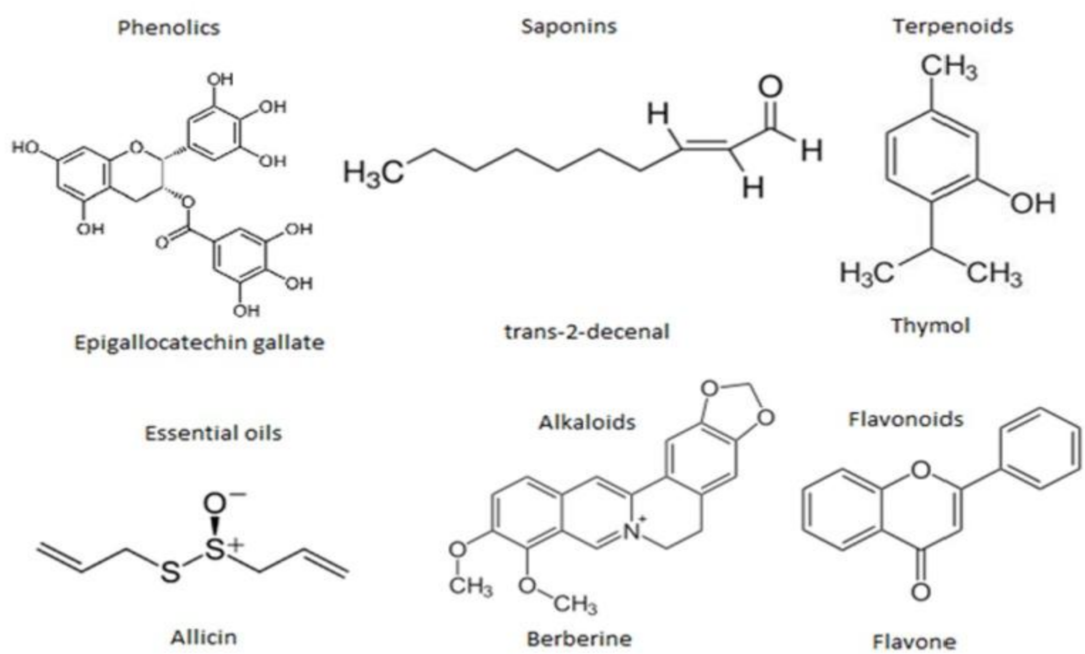


Fig. 2B. Biosynthesis of Alkaloids, L-Phe, Lignans and coumarins from shikimic acid. Source: [9]



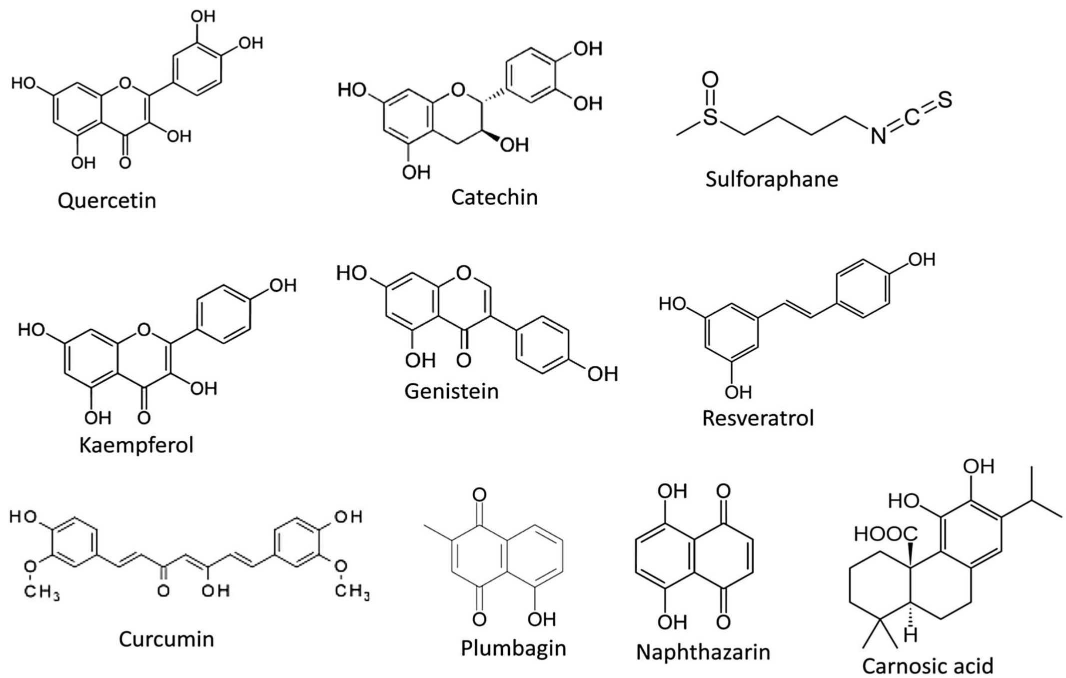
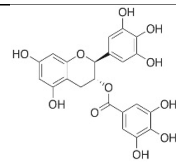
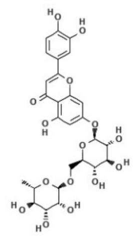
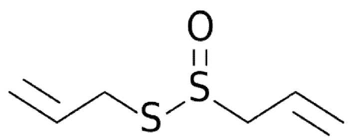
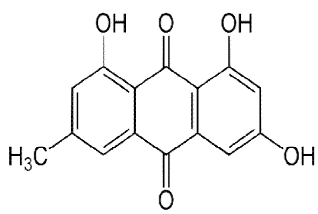
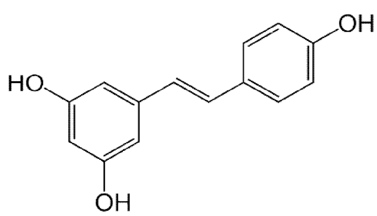


Fig. 3. Structure of Phytochemicals

3.1 Role of Phytochemical in COVID-19 Infection

The alarming pandemic caused by the 2019 Sars-CoV2 virus (covid-19 infection) rapidly escalated, becoming a massive burden on both international and domestic fronts. Computational analysis of these viral strains revealed that the SARS-Cov2 emerged from the β-coronaviruses in a family containing MERS-cov, OC43 and HKU1. After contact with the host cell, the viral spikes bind firmly with the human angiotensin-converting enzyme (ACE2) receptor of the oropharyngeal tract [15]. This virus generates large polyproteins which are proteolytically cleaved by the cysteine protease (3-chymotrypsin-like protease 3CL^pro, otherwise called main protease (MP^pro) and papain-like protease (PL^pro), releasing the replicase enzymes. These replicase enzymes thus produce multiple copies of the viral strain in the host cells. PL^pro post translationally deubiquitinate and deISGylate IRF3 (Interferon Regulatory Factor 3), thus triggering the removal cascade of ISG15 (Interferon Stimulated gene 15) an essential signaling elements of the antiviral innate immunity. Due to the crucial role of the viral polymerase, 3Cl^pro, PL^pro, studies by Alanri 2020, Anan et al., 2003, have targeted them as potential therapeutic targets against the ravaging SARS-coV2 ailment. For years, phytochemicals have been successful managing of several diseases and have led to the synthesis of novel drugs and the development of traditional medicine. An insilico study subjected 1000 phytochemicals from about 60 medicinal plants with potent antiviral activity against the SARS-coV2 polymerase enzymes, 3Cl^pro and PL^pro [16]. This study inferred that luteolin 7-rutinoside is a potent inhibitor of the viral polymerase enzyme, chrysophanol 8-(6-galloyl glucoside) potently inhibits the viral 3Cl^pro protein and withanolide A showed promising signs in the inhibition of PL^pro. Bioactive compounds from acorn, a functional food known for its antimutagenic, anti-inflammatory and antioxidant capability was shown to improve the immune system. These activities were attributed to the presence of polyphenolic compounds, present in the nut . Lectins have shown positive strides as an effective antiviral agent, with clinical trials revealing good tolerability potential of lectin . The overexpression of IL-6, TNF-α, IFN-γ, HGF, VEGF and other inflammatory cytokines have been attributed to lung damage in covid-19 infected patients. However, myo-inositol, certolizumab and fedratinib has been studied to reduce IL-6, downregulates TNF-α and IL-17 levels in SARS-Cov2 infection [17].

Table 2. Bioactive compounds and their mechanism in covid-19 infection

Plants	Active compounds	Structure	Mechanism
Green Tea	Epigallocatechin gallate		Interacts with major protease M^pro [15]
Rumex dentatus	Lueolin-7-rutinoside		Binds to RdRp and thus inhibits the viral replication and their genomic transcription [15]
Allium Sativum	Allicin		Reduces the risk of viral infection and shortens the disease duration. It further relives the severity of the symptoms [16]
Aspergillus spp.	Emodin		Inhibits the interaction of SARS-CoV protein with its receptor ACE2
Vitis vinifera	Resveratrol		Prolong cellular survival after virus infection and inhibits host cell apoptosis [17]

3.2 Role of Phytochemical in Neurodegenerative Diseases

Neurodegenerative diseases is a major cause of scientific concern that affect not only mental health but also physical health a causative factor of infirmity and death. Previous study, have attributed this disease to be a result of neuronal loss and cellular dysfunction due to excessive reactive oxygen species as well as chronic inflammation [18]. The overproduction of ROS in the power house of the cell and nicotinamide adenine dinucleotide phosphate [NADPH] oxidase leads to oxidative damage and reduction in the activity of antioxidant is a central event occurring during neurodegenerative diseases. These oxidative damage causes aberration of biomolecules as well as triggering protein crosslinking [18]. Phytochemicals employs two strategies in ameliorating oxidative damage and pro-inflammatory cytokines [downregulation of cytokines] in counteracting the effect of neurodegenerative disease. These strategies are; i) stimulating the release of brain-derived neurotrophic factor [BDNF], ii) Release antioxidant and phytonutrient [19]. AD and PD is characterized by the release of peroxiredoxin [PRDX 2] and IL-6. However, lycopene and curcumin has been studied to downregulate inflammatory factors [NF-kβ] and activator protein 1 inhibits the release of 1L- 6, TNF-α, iNOS and MCP-1. MAPK signaling cascade, essential in improving cellular and brain functioning has been revealed to be activated by resveratrol, quercetin and amentoflavone. They act by activating pro-survival extracellular signal - related kinase [ERK] this inducing anti- apoptotic factors BCL-2 and BCL-XL and inhibits fas - mediated apoptosis . This action improves cognitive functioning of the brain. Furthermore, epigallocatechin gallate and galangin and tannic acid decreases β -secretase expression end improves behavioral impairment in a neurodegenerative disease animal [20]. Epigallocatechin gallate interacts with the water - fearing moiety of insoluble Aβ, thus inhibits the formation fibril and thus preventing tauopathies. Similarly, luteolin prevents the aggregation of Aβ while the flavin converts toxic aggregated Aβ into non -toxic spherical accumulate. Green tea extracts upregulate BDNF levels while astaxanthin upregulate the induction of BDNF and GDNF, thus exerting neuroprotective activity via ERK /Akt signally cascades during an invitro study. Polyphenols enert their neuroprotective activity through the expression of Tik and neurogenesis as well as displaying an antidepressant effect. These mechanisms are also employed deoxygedum, an extract derived from *Hemerocallis citrine*. Mitochondria dysfunction have been expressed during age-related neurodegenerative disease such as AD, PD and HD. This involves the inhibition of complex-IV and downregulation of complex-1 in the electron transport chain (ETC). Phytoconstituent that exert neuroprotection and regulates the ETC includes myricitrin, hesperidin and hesperetin rutinoside amidst others [21]. Moreover, liquiritigenin, a phytochemical from *Glycyrrhiza spp* has been studied to induce mitochondria fusion and prevents mitochondria dysfunction.

3.3 Role of Phytochemical in Cancer

Cancer; a multi-causative factor disease with over 8.1 million new patients and a fatality record of about 9.6 million globally as at 2018. This disease can be instigated by genetic factors, epigenetic factor, hormonal factor and notably environmental factor, with the prostate, lung, liver and breast cancer being the most prevalent. Cancer is characterized by the inactivation of tumor suppressing gene and activation of

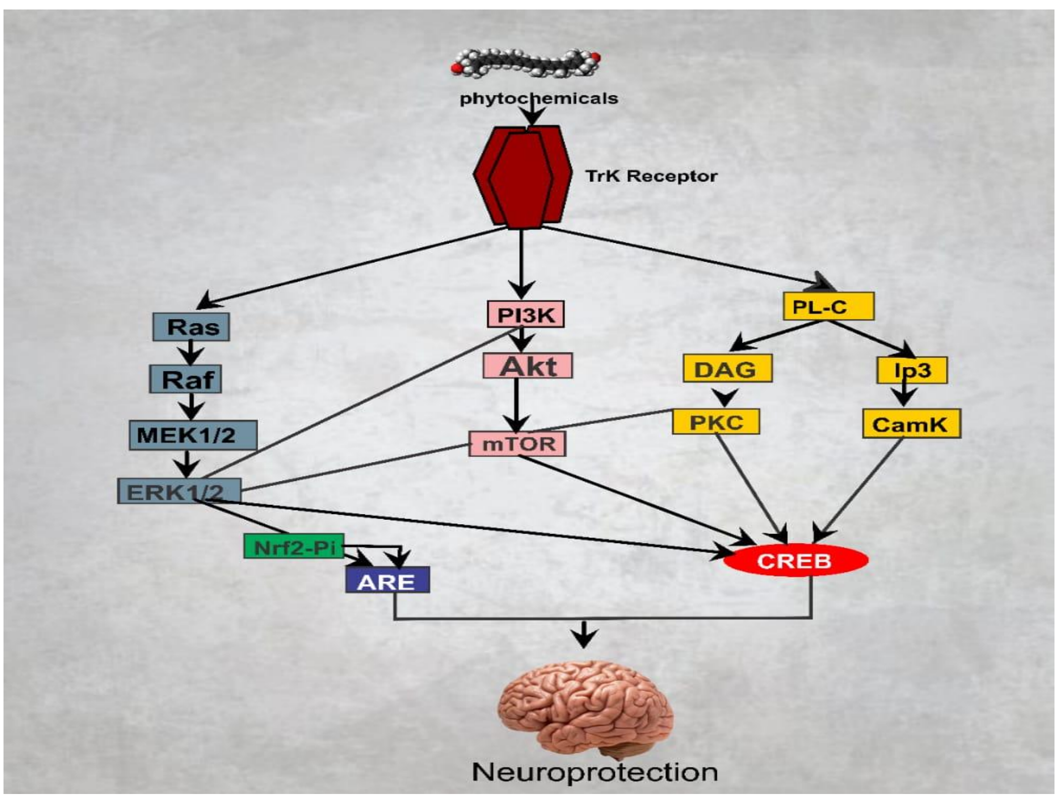


Fig. 4. Neuroprotective effects of phytochemicals by activating PI3K/Akt, PKC, ERK1/2 signaling pathways to promote neuronal survival [6]

proto-oncogenes to oncogenes reaction, which converts normal cell lines to cancerous lines [22]. This reaction is however governed by the release of free radicals, inflammatory cytokines and pancreas hormones, thus causing DNA damage and upregulating apoptotic cascade. More critical is uncontrolled proliferation that occur in cancerous cells as a result of bypassing the G1 phase and the cell cycle check points. Furthermore, cellular signaling cascades such as JAK/STAT, MAPK/ERK, PI3K/Akt/mTOR becomes altered during the repression of tumor suppressing gene [23]. In modulation of cancerous cells by phytochemicals, one or more signaling cascades is/are targeted. Phytochemicals show varying therapeutic potential against cancerous cell lines such as pain relief, suppression of inflammatory cytokines, anticancer and downregulation of free radicals. These anticancer activities may be exhibited via the induction of cell death, modulation of cellular signaling cascades, cell cycle arrest of proliferated cells, prevention of DNA damage and epigenetic changes. A study by Wei et al., 2018, revealed that epigallocatechin-3-gallate resulted in the activation of apoptosis of tumor cells such as breast, prostrate and nasopharyngeal carcinoma cells [24]. This activity was carried out by induction of p53 via the inhibition of tumor suppressive microRNA (miR34a). 5-methoxyangenylalkanin and punicalagin, which are phytochemicals from *Alkanna tinctona* and *Punua granatum* respectively also induce apoptosis by increasing the expression of caspase 3 & 9, in human carcinoma cell. More so, diosgenin extracted from *Trigonella foenum graecum L*. Induced cell death in human colon carcinoma (HT-29) by downregulating Bcl-2 and upregulating caspase 3. Phytochemical from *Berberis lycium royle* arrested cell cycle in promyelocytic human leukemia HL-CO as well as inhibiting the conversion of proto-oncogenes to oncogenes. Moreso, capsaicin from *Calotropis procera* arrested cell cycle at G^{o}-G1 phase and exert a prominent anticancer activity in NB4 (promyelocytic leukemia) and kasumi-1 cells [24-26]. Quercetin and crocetin inhibited the MAPK/ERK cascade expressed by melanoma while gallic acid downregulated PI3K/Akt and Ras/MAPK signaling cascades . The transcription of antioxidant response element that controls the antioxidant defense system is mainly governed by Nrf2 and Keap1 [25,26]. However, phytochemicals such as lycopene, β-carotene and falcarinol analogues inhibited Keap1 and NF-kβ while activating Nrf2. The signaling cascade regulating cell growth and autophagy (mTOR pathway) was inhibited by Apigenin in keratinocytes. While over-expression of prostaglandin synthesis enzyme “Cox-2” is an indicator of tumor proliferation in cancerous cells, several significant studies both invitro & in vivo, showed that phenolics and flavonoids possess great anti-inflammatory potential (inhibition of NF-kβ, reduction of NO, PGE2 and IL-8 levels, repressed TNF-α activities and associated cytokines [27,28].

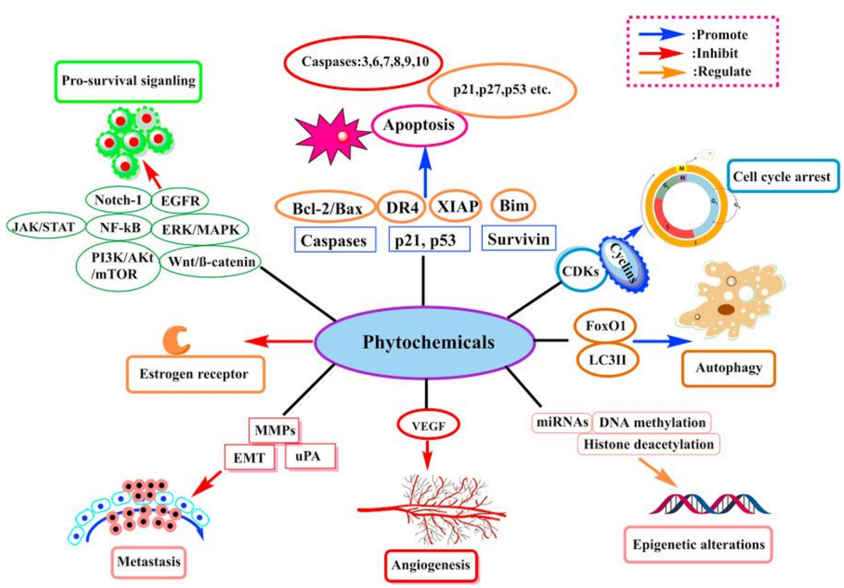


Fig. 5. Illustrating the target of phytochemicals in cancer cells [29]

3.4 Role of Phytochemicals in Obesity

Imbalance between energy produced and energy spent during a prolonged time causes the deposition of energy in form of body fat, a condition known as obesity. These fats are stored in adipose tissue of three types in mammals which are; i) Beige Adipose Tissue, distributed across the waist/abdomen, cervicle muscle and mitochondrial respectively. A study has shown the role of phytochemicals in promoting. UCP+ adipose differentiation thus enhancing energy consumed and curbing obesity [30]. The antioxidant and inflammatory properties of Artepillin C was reported to amplify adipocyte differentiation and enhance the uptake of glucose in 373-L1 cells by acting as a PPAR-γ ligand. Resveratrol, a phytochemical persist in varieties of dietary food has been revealed to enhance sirtuin 1[SIRT 1] expression which deacetylate NF-Kβ , PGC1-α and FOXO L ,thus maintaining body glucose homeostasis [31]. Preclinical studies and clinical investigation carried out on the effect of curcumin on obesity revealed that curcumin causes the browning of fat via the activation of AMPK-mediated cascade and PGC1- α enhances mitochondrial biogenesis thus improving insulin sensitivity and reducing weight [32]. Yoneshire et al in his study explained, catechin employs BAT via the TRPAI / TRPV 1 thus promoting thermogenesis. Continuous treatment with catechins also reduce body weight as well as lowering body cholesterol and LDL levels. Okla et al., in his study also showed catechin to repress catechol-o -methyl transferase, thus inducing the oxidation of excessive fat and heat production. Furthermore quercetin, a common flavanol found in vegetables and fruit decreases body weight fat via the activation of AMPK /SIRT 1/PGCI α cascade. This anti obesogenic activity of quercetin was confirmed by an In vivo study by Kuipers et al. Furthermore, the anti-obesity effect nobiletin from *Citrus reticulata*, chrysin from mushrooms and honey combs, anthocyanin from dietary supplement, and genestein an isoflavone of dietary plant have all been confirmed by literatures. More so several terpenoids, glycosides and phenolic acid have played great release in modulation of obesity and regulating homeostasis. Summarily as presented in this section varying target on which phytochemicals act include TRP, SNS, β-AR, cAMP, AMPK, TRPM8, SIRT1, PGC1 α and PPAR α /γ. Thus, phytochemicals regulate the development, metabolism and functioning of brown and beige fat.

3.5 Role of Phytochemicals in Intestinal Health

Several studies affirmed the effective role of polyphenols on diversity of microbial populations. Thus, attenuating gut dysbiosis and any severe metabolic complication [13,33]. An in vivo study carried out employing concord grape showed improved gut-barrier functioning [33]. This acts by repressing inflammation adiposity and insulin resistance. Similarly, supplementation of mice with resveratrol improved the colon of mucosa and suppressed inflammation. Consumption of red wine increased the availability of bacterial species and thus lowered blood pressure and reduces blood cholesterol and ORP levels [34]. Polyphenols have shown bactericidal and bacteriostatic activity against destructive bacteria by inhibiting quorum sensing, disrupting the integrity of the double lipid membrane, inhibit their replication via the inactivation of DNA polymerase and as well attenuates their growth. Suppression of inflammatory prostaglandin synthesis and reduction of inflammation by hydro caffeic acid in DSS-induced ulcerative colitis was observe. Similarly, Denis et al.,2015 inferred that cranberry metabolites significantly reduce intestinal diseases and signaling of inflammation in Caco-2 cells treated with prooxidants. Attenuation of inflammation in the intestinal by quercetin glycoside, decrease in myeloperoxidase activity by grape seed, increase in goblet cell, decrease in nitric oxide synthase activity, suppression pf intestinal colitis has all been recorded in different in vivo rat studies by Suwannaphet et al., 2010; Paiotti et al., 2013; and Paturi et al., 2014 respectively.

4. CONCLUSION AND FUTURE PROSPECTS

Various phytochemicals have different target sites in different pathogenic elements of obesity, neurodegenerative disorders, covid-19 infection and cancer cells, thus playing a protective role. Substantial studies have revealed the role of fruitful importance of dietary health practices, which enhances cognitive function, suppresses neurodegenerative cascades, improves intestinal health and remediate against dilapidating viruses. Furthermore, phytochemicals have been therapeutically consumed as drugs, although clinical research on favorable effect of phytochemicals still awaits approval. Notably, lipid loving phytochemicals bypasses the blood brain barrier membrane, possessing a good affinity to receptors. Thus, phytochemicals inevitably offer a great hope as a derivative for the synthesis of several therapeutic compounds. Future studies should extensively explore the molecular basis into which phytochemicals can be used to synthesize novel groups of therapeutic compounds.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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