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Phytowaste as nutraceuticals in boosting public health

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Abstract

The utilization of bioactive constituent of peels and seeds provide an effective, environment friendly and inexpensive therapy for different forms of human disease, and the production, improvement and documentation of novel nutraceuticals. This review systematically presents findings and further understanding of the reported benefits and therapeutic applications of peel and seed extracts on innovative cell culture and animal studies, as well as phased clinical human trial research. The extracts of seed and peels were reported to possess high quantities of bioactive substances with antioxidative, antidiabetic, hepatorenal protective, antithyroidal, anti-inflammatory, antibacterial, cardiovascular protective, neuro-protective effects, anticancer and wound healing activities. Therapeutic activities of the bioactive substances of peel and seed extracts include elevation of Superoxide dismutase (SOD), GSH-Px, t-GPx, Catalase and GST activities, with the suppression of MDA levels, hydroperoxide generation and lipid peroxidized products, the extracts also regulate inflammatory mediators and cytokines as they are reported to suppress the secretion of inflammatory cytokines, which include; IL-1β, PGE2, TGF-β and TNF-α and induces apoptosis and cell differentiation. This review revealed the therapeutic importance and best utilization of peels and seed extracts of fruits and vegetables.

Introduction

Living creature's interdependence and interrelatedness is well documented, and reported to be due to parallel evolutionary trends [1] Plants use as food and medicines has led to its traditional uses in ethnomedicine; the treatment and remedy of various kinds of ailments, diseases and poisoning in which they can reverse or reduce its toxicity.

In the use of these plant produce, the outer skins are often peeled off and discarded, as they are most times nonedible and are considered not useful. Often the hitherto non-edible hard seeds and peels are regarded as phytowastes and discarded as such. Fruit vendors in streets and markets, and fruit processing industries as such generate so much waste, which may pose an environmental hazard, and a source of ill-health if not managed and properly utilized. Hence, re-using them as alternative source of antioxidant could bring cost effective new generational therapeutics and measurable economical profits to the Pharmaceutical and nutraceutical industry and contribute to reduction of pollution [2].

The peel wastes from fruit may contain the same valuable components generally found in fruit. These valuable substances may be used to formulate preparations with pharmacologic/ medicinal, nutritive, and energy values. Recycling of fruit peel wastes has not only help lessen solid waste problems but also helped to discover important substances that have been proven to have vital use. Phytochemicals of interests can also be extracted through a proper distillation, industrial extraction, scientific incorporation and management of these fruit peels [3].

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Fruit peels extracts are now serving as one of the primary sources for isolation and extraction of secondary metabolites [4–6]. Apart from their therapeutic and beneficial effects, which has been scientifically proven and documented through various in vitro, in vivo and clinical phase trials across different cultures and civilizations, on a myriad of ailments that include; osteoarthritis, cardiovascular diseases, diabetes and cancer. This is because of the very rich in bioactive components such as mangiferin, phenolic acids, gallic acid flavonoids, catechin and gallic acid derivatives etc.

Oxidative stress is often aligned as the root cause of several diseases and tissue damage [7], this has informed the reason for the maintenance of a healthy homeostasis between oxidants and antioxidants in modern medicine. However, there are concerns over the use of plants or herbal preparation because of the lack of prescribed dosage, counteractive effective when more than one plant is involved, how safe is the method of preparation and the antagonist effects in combination with other medications. Venables et al., (2008) [8] reported concerns of unidentified toxicity, precise mechanism of action, exact dose to cure a particular ailment, its availability and exact composition, however, the renewed research focus, newer techniques and methodologies available, coupled with newer discoveries of potent antioxidants in peels points to a reduced likelihood of potential drug toxicity or adverse drug reactions to usage. However, Parmar et al., (2010) [9] observed that such renewed research focus could provide better insight of molecular pathways and understanding of the biological effects. This review explored the beneficial and therapeutic applications of peels and seeds extract in several cell lines, animal studies and clinical human research.

Methodology

Several online databases such as Google scholar, Springer, PubMed, Research gate, and Scopus were searched independently for relevant research articles, using different search terms such as fruit peels therapy, fruit peels and seed used as antidotes, fruit peels and its therapeutic effects, health benefits of fruit peels, therapeutic effects of peels and seeds, health benefits of seed and peels, seed peels therapy, hepatorenal protective effect of seeds and fruits, peel and seed therapy in non-communicable diseases. The full texts of all collated articles were screened for the inclusion and exclusion criteria by evaluating and appraising the tittle and abstract of each article, research articles that reported the therapeutic roles of peels and seeds extract and articles where peels and seeds extract ameliorate a particular ailment or disease were used. Excluded articles include duplicates as a result of search from different database, foreign language articles, studies on peels used for bioremediation.

Search results

A total of 198 articles were found during the initial search, 38 articles were removed because they appeared as duplicates, in the course of title and abstract screening 30 articles were removed as they were not very relevant to the focus of the review leaving a total of 130 for further review, 2 more articles were not available in English. Further review of the full text of the remaining articles to ascertain the suitability of the article for relevant data extraction. The appraisal and use of the inclusion and exclusion criteria resulted in the exclusion of 32 more articles. At the end 96 articles were left and used in this systematic review. The articles provide the therapeutic effects of several peels and fruits. Figure 1 shows the study selection flow diagram.

Mechanism of actions

Peel extracts have several mechanisms of action by which they act, most peel extracts act as antioxidant mainly by scavenging radicals directly in a dose-dependent manner [10]. Flavonoids act as chain-breaking antioxidants in their scavenging mechanism or recycle other chain-breaking antioxidants such as α-tocopherol by donating a hydrogen atom to the tocopheryl radical while some flavonoids prevent the formation of free radical by chelating divalent metal ions [9]. A study by Kim et al., (2005) [11] revealed that *Citrus reticulate* peels extract displayed potent tumor-suppressing activity in SNU-C4 human colon cancer cells, such extracts include quercetin and quercetin-3-*O*-beta-D-glucopyranoside, with its anticancer effect is believed to be through the up-regulation of the proapoptotic gene *Bax* and apoptotic gene *caspase-3* or downregulation of the antiapoptotic gene *bcl-2.* According to Narayana et al., (2001) [12] these extracts also possess lipid-lowering and anti-atherosclerotic properties, which act as effective cardiovascular protection through its ability to oxidatively modify low-density lipoproteins (LDL) via a scavenger receptor in atherosclerosis pathogenicity, which then leads to the formation of foam cells. These antioxidant activities can be enhanced by transition metals and important pro-oxidants like iron and copper. Hesperidin and naringin (bioflavonoids) present in peels play an antidiabetic role by increasing serum insulin, hepatic glycogen content and hepatic glucokinase activity, while decreasing serum glucose concentrations, glucose-6-phosphatase and phospho-enol pyruvate activity in mice [13].

The biomolecules of the peel extracts play major role in thyroid stimulatory activity by influencing thyroid hormone metabolism. A study by Divi and Doerge (1996) [14] showed the antithyroidal role of the phenolic

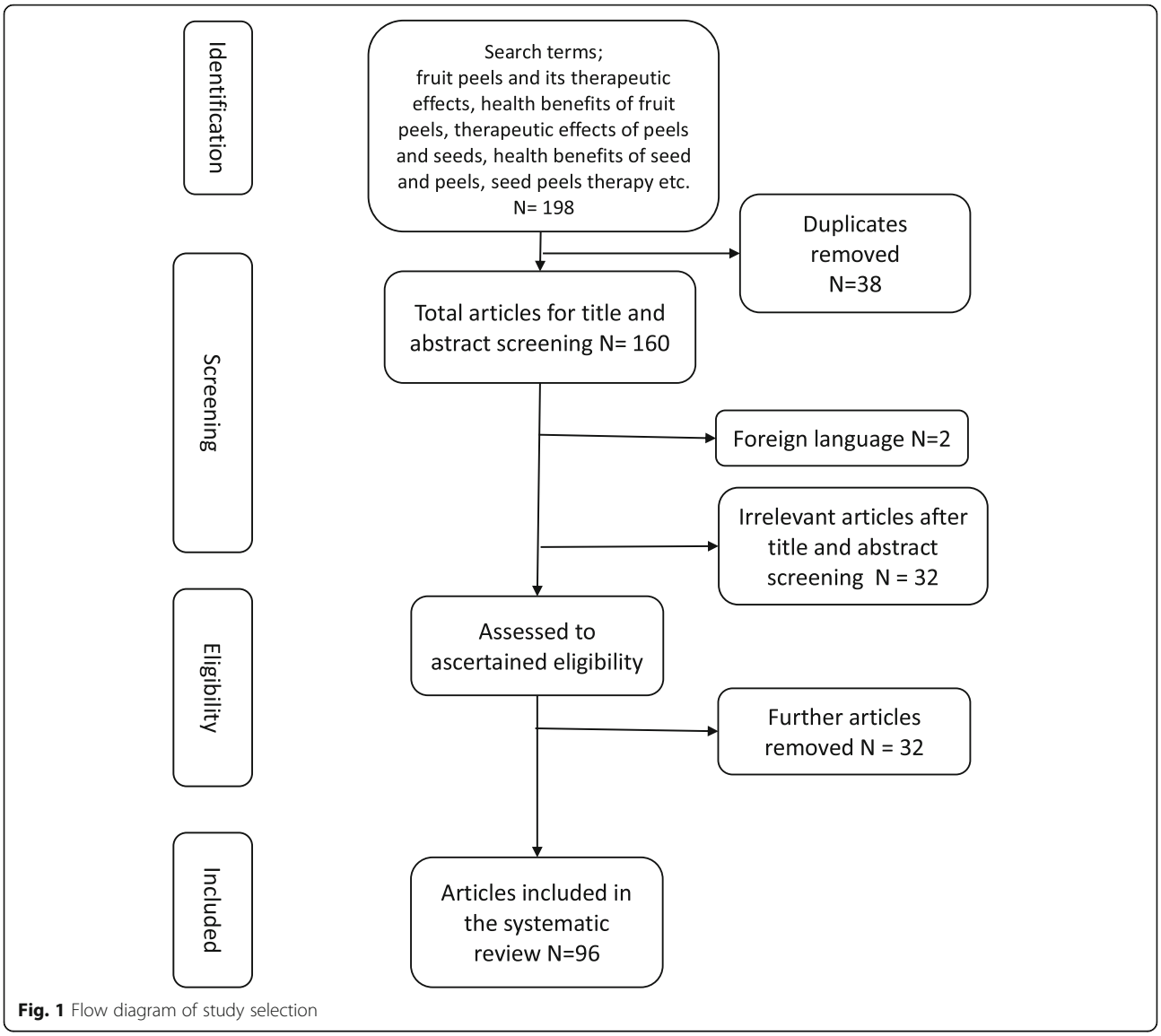

Fig. 1 Flow diagram of study selection

compound naringin which is mediated through thyroid peroxidase (TPO) inhibition, a key enzyme in the biosynthesis of thyroid hormone. Similarly, the high dopamine content of *Musa paradisiaca* peel extract inhibits TPO [15, 16] Auraptene in citrus peel elicit anti-inflammatory effects via reducing the expression of NF-κB, tumor necrosis factor alpha (TNF-α) and IL-1β [17]. These extracts also inhibited the activation of hepatic stellate cells (HSCs) by down-regulating the expression of TGF-β1 and α-SMA. Auraptene treatment increased the bile flow and biliary bile acid output while decreasing hepatic uptake of bile acids, consequently alleviate 17α-ethinylestradiol (EE)-induced cholestasis, associated with induction of efflux transporters (Bsep and Mrp2) and downregulation of Ntcp. Hence, auraptene reduce bile acid synthesis through repressing Cyp7a1 and Cyp8b1 but increase bile acid metabolism through an induction in the gene expression of Sult2a1 [18].

The precipitation of membrane proteins resulting in microbial cell lysis is the reported mechanism of antimicrobial activity of pomegranate peel phenolics [19]. Therapeutic interventions with extract of passion fruit peel as adjunctive therapy in asthmatic patients is reported to be via the antioxidant flavonoids properties [20]. Figure 2 described the mechanism of actions of the peel and it resultant therapeutic effects.

Antioxidant activities of Peel and seed extract

Banana peel extracts (*M. paradisiaca* L.) increase superoxide dismutase (SOD) and glutathione levels but reduce hydroperoxides, peroxidation products (MDA), conjugated dienes and the enzymatic activities of catalase

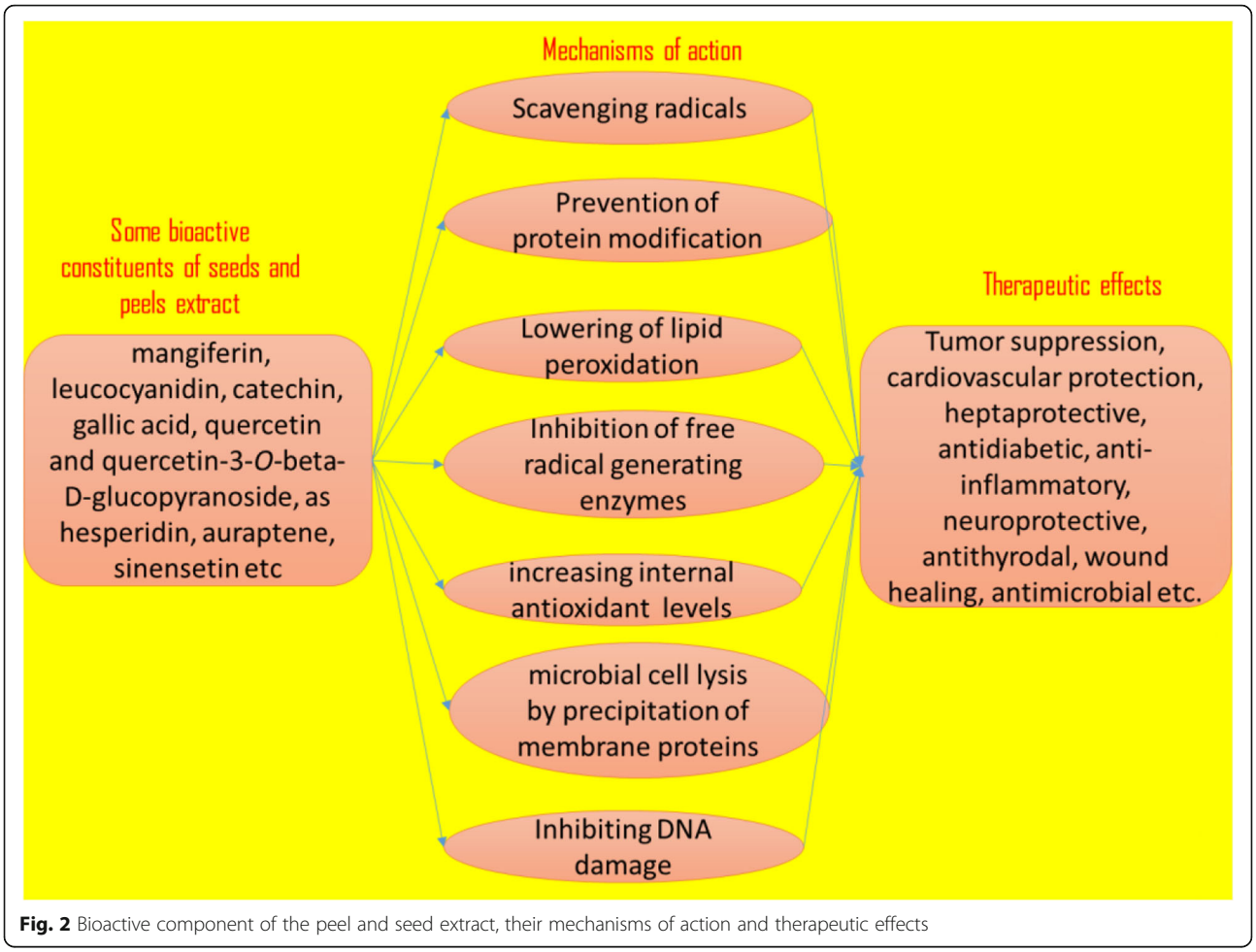

Fig. 2 Bioactive component of the peel and seed extract, their mechanisms of action and therapeutic effects

(CAT) in fatty acids rich diet fed experimental rats [21]. Duda-Chodak and Tarko [2] reported essential diversities of bioactive compound among the peels and seeds of domestic and imported fruits. The peels had higher ability to scavenge free radicals and higher polyphenols concentration than the seeds [2]. Fresh and dried peels of *Satsuma mandarin* have potent protective activity against *Musa cavendishii* the generation of linoleic acid hydroperoxide, which were often due to their high tannin contents [22]. *S. mandarin* peels contain considerable ascorbic acid and have a beneficial effect on blood circulation, as well as bronchial and asthmatic conditions.

Someya et al., [23] identified the abundance of gallocatechin in the banana peel *M. cavendishii* peel and the major component responsible for the antioxidant activity against lipid auto-oxidation. Dietary supplementation of feed with 5% banana peel improved the antioxidant capacity, regulated the expressions of certain cytokine-related genes and enhanced GPx [24]. Rutin, quercetin, catechin, quercitrin, kaempferol, chlorogenic and ellagic acids are phenolic compounds extracted from unripe plantain peels, these are reported to inhibit Fe^{2+}-induced lipid peroxidation linked with erectile dysfunction [25]. Such chelating and antioxidant properties were also reported by [26] for melon peel in different concentrations (0.5 to 2.5 mg/mL) with 46% hydromethanolic, 49% hydroethanolic and 61% for the aqueous extract efficacy.

Rambutan peel phenolic extract has high antioxidant and antiglycation activities in vitro and in vivo [27]. Pomegranate (*P. granatum*) peel is a rich source of flavonoids, phenolic compounds, glycosides, saponins, alkaloids and tannins. Others include nutrients like; proteins, carbohydrates and minerals like sodium, calcium, magnesium, potassium, phosphorus iron and vitamin C [28]. These are potential resources that confer on Pomegranate blood thinning, cardiovascular protective, anti-artherosclerotic, antilipidemic, antimutagenic and antioxidant properties [6].

The phytochemical, antioxidant activity and mineral composition of soursop (*Annona muricata*) peel and seed have been investigated [29, 30]. The peel and seed extract showed the scavenging abilities of soursop, in the peel, tannins, glycosides, steroids, alkaloids, phenols,

resins, flavonoids, phlobatanins, carbohydrates and balsams were present while saponins, steroids, flavonoids, terpenoids, volatile oils, phlobatannins, carbohydrates and balsams were present in the seed. These constituents contribute to their cardiovascular protective effects [31]. Burčová et al., [32] reported that Sea buckthorn contains antioxidants like α-, β-, γ- and δ-tocopherols with higher amounts of α-tocopherols and palmitoleic acid (also present in human skin) in peels. While the seed contains β-tocopherol and unsaturated biologically active fatty acids. α-, β-, or γ-tocopherols that are less effective when compared with the delta component.

Mango peel is rich in Vitamin C and Vitamin E, peroxidase, protease, oxidase, xylanase, polyphenol and amylase activities. Ripe peel extract has more lipid peroxidation potentials compared with unripe mango peel, which has a higher lipoxygenase inhibitory activity [33]. Pineapple (*Ananas comosus*) peel contains antioxidants in threonine, 3-methylglutaric acid, valine, and α-linolenic acid, whereas epicatechin was responsible for the α-glucosidase inhibitory activity [34]. Two varieties of Avocado (*Persea americana* Mill.) 'Hass' and 'Fuerte', peels and seeds have been shown to possess phenolic composition and in vitro antioxidant activity [35] (Table 1).

Wound healing

Wound healing involves processes like inflammation, proliferation, migration of different cell types, especially fibroblasts and restoration of a functional barrier in nearly all types of tissue damage in a complex but dynamic way, resulting in the contraction and closure of the wound [40]. These Fibroblasts produce collagens, elastin, and proteoglycans, which are very important in wound healing. These process involves the formation or triggering of Reactive oxygen species (ROS), which are essential in cell signaling and immune responses leading to the complete healing [41, 42].

Banana skin is often used as a temporary barrier to skin breakage, and its powder added to chitosan results in a decrease in swelling, which is a process involved with the inflammatory process of pain perception and wound healing. These banana peels are also thought to increase water resistance, a functional attribute of normal skin, due to interaction between negatively charged compounds in banana peel powder such as carboxylic acids and positively charged groups on the chitosan backbone chain. Addition of banana peel constituents such as lignin decreases the level of swelling in wound dressing [43], while also acting as an antiseptic in its modulation of immune system [44]. A study by Padilla-Camberos et al [45] showed that *M. paradisiaca* peel extract has the capacity of wound healing due to the presence of tannins, alkaloids, saponins and phenols as principal constituents conferring antioxidant capacity, these wound healing efficacies are often dependent on the extraction process.

Atzingen et al. [46] reported an increase in the number of polymorphonuclear cells and concentration of collagen fibers, a reduced wound contraction and vascular proliferation, following the use of 4% *M. sapientum* L. peel gel for the treatment of the lesions by excision model. *M. sapientum Linn. Var. Compressa* peel extract exhibits an anti-hemmorrhagic effect on Sparague rats tested using modified bleeding time [47]. It exhibits significant anti-hemmorhagic effect at different level of concentrations. The 50% concentration of *M. sapientum Linn. Var. Compressa* exhibits the shortest mean bleeding time results and it was also the most statistically significant.

Phenol-rich methanolic extract of dried pomegranate peel caused a complete wound healing on the skin of Wistar rats [48]. This effect is further supported by histopathological and biochemical observations following orally infusions of pomegranate seed extract in rabbits [49, 50].

Pomegranate peel extract promotes wound healing by increasing the migration of fibroblast, accelerating the second stage of the healing, and decreasing the number of immune cells in the vicinity of the wound and injury, and its effects are attributed to its phytochemical constituents, which include; saponins, sterols, triterpenes, alkaloids, flavonoids, tannins and cardiac glycosides [51].

The fruit peel extract of *Cucurbita moschata* Duchesne, due to its high content of mucilage, antioxidant and moisturizing effect could act as a burn healing agent [52]. Other pumpkin peel effects on wound healing include its immunomodulatory effects, natural killer cells activity, proliferation of lymphocytes and promotion of CD4+ and CD8+ cells [53].

Other flavonoid rich fruits like Grape seed extract GSE proanthocyanidins, a procyanidolic oligomer according to play an important part in accelerating skin wound healing process [54–56] (Table 2).

Antidiabetic

Bioactive components of peel and seed extracts have great medical potentials in the treatment and management of diabetes. Attenuating the antagonizing the damaging effects of ROS through antioxidant functions is a generally agreeable mechanism. Such a mechanism may occur directly or indirectly by increasing the activity of certain antioxidant enzymes, such as Paraoxonase (PON1), Superoxide dismutase (SOD), and catalase (CAT) [58]. As far back as 1998 avocado was used in the treatments of diabetes in adult male rabbits [59]. observed aqueous seed extract of avocado reduced hyperglycemia after an oral glucose overdose. Aqueous

Table 1 Antioxidative properties of some peels and seed extracts

Plants	Bioactive compounds	Test organism	Conc/ body weight	Therapeutic activities	Mechanism of action	References
Hippophae rhamnoides (Sea buckthorn) Seeds and peels	α-linolenic acid, Linoleic acid, and vaccenic acid tocopherols	–	–	Antioxidant	Free radical scavengers	[32]
P. granatum (Pomegranate) Seeds and peels	Alkaloids, flavonoids, phenolic compounds, glycosides, saponins, carbohydrates and protein	–	–	Antioxidant function	Free radical scavengers.	[6]
Cucumis melo L. var. reticulatus (melon) Seeds and peels	salicylic acid, gallic acid, ellagic acid, quercetin, catechin, eugenol, vanillin, and vanillic acid	Cell lines	0.1–1.0 mg/mL	antioxidants and antiproliferative activities	hydroxyl radicals scavenging, chelating activity and cell growth inhibition	[26]
A. muricata L. (Soursop) peel and seeds	Flavonoids, β-carotene-linoleic acid	–	–	Antioxidant	Free radical scavenging	[29, 30]
S. mandarin Citrus unshiu Marcorv.) peel	ascorbic acid	–	–	linoleic acid hydroperoxide inhibition and antioxidative activities	suppressive activity against hydroperoxide generation	[22]
Mangifera indica (Mango) peel	Polyphenol, anthocyanin and carotenoid	–	–	Antioxidative activites	ROS scavenging, Redox reactions	[33]
Mangifera indica (Mango) peel	vitamin C, polyphenols, vitamin E, carotenoids,	HeLa cells line	0, 50, 100, or 200 μg/ mL	antioxidant and antiproliferative activities	HeLa human cervical carcinoma cells proliferation inhibition characterized by down regulation of Bcl-2 and increased Bax/Bcl-2 ratio. The extract triggered the degradation of poly ADP-ribose polymerase in HeLa cells and proteolytic activation of caspases-3, −8, and −9 and the	[36]
Musa acuminata (banana) peels	phlobatannins, flavonoids, alkaloids, tannins, anthocyanins, glycosides and terpenoids	fish	1–7%	Antioxidant Status, reduced cytokine responses and disease susceptibility	Suppressed the upregulated expressions of *IL-1* and *TNF-* in examined tissues of the fish	[24]
M. cavendishii peels	Gallocatechin			Antioxidant	Inhibits lipid auto-oxidation	[23]
Unripe *Carica papaya* peel and seed	Apigenin, Syringic acid, Vanillic acid, Luteolin, Genistein, o-Coumaric acid, p-Coumaric acid, Ferulic acid, Sinapinic acid etc.	rats	(0–25 mL	Inhibit Fe^{2+}-induced oxidative stress	Significant decrease in the malondialdehyde pancreatic contents and inhibitory effect on Fe^{2+}-induced lipid peroxidation.	[37]
A. comosus (Pineapple) peel	epicatechin, catechin, ferulic acid and gallic acid			Antioxidant and α-Glucosidase inhibitory activities	nitric oxide scavenging, Free radical scavenging, and α-glucosidase inhibitory activities.	[34]
Musa paradisica (Banana)	polyphenols, carotenoids, L-dopa and dopamine	Human blood	1 ml	antioxidant potency		[38, 39]

extracts of avocado seeds (300 or 600 mg/kg body weight) administered for 21 days to Alloxan-induced diabetic rats, it revealed reduction in blood glucose by about 78–73%. Hence, the drug-induced pancreatic islet cells deterioration was inhibited by the extract.

Passion fruit (*Passiflora edulis* f. flavicarpa Deg.) peel flour has pectin as one of its components, and is rich in soluble fiber [60, 61]. used yellow passion fruit peel flour supplement as adjuvant therapy decreased blood glucose and insulin resistance in type 2 diabetic animals and patients. The study further reported that the extracts protected the end organs by restoring the anti-oxidants enzyme, increasing superoxide dismutase level (SOD) and decreasing catalase (CAT) and Thiobarbituric Acid

Table 2 Wound healing properties of some peels and seed extracts

Plants	Bioactive compounds	Test organism	Conc/ body weight	Therapeutic activities	Mechanism of action	References
M. paradisiaca peel	alkaloids and tannins, saponins and phenols	Rats	100 mg/kg	Wound healing	Complete epithelialization through elevation of collagen fibers and fibroblast cellular infiltration, the extract showed more proliferating blood capillaries	Padilla-Camberos et al [45]
Pomegranate seed	gallic acid, catechin and saponins	Rabbit	100 mg/kg	Wound healing	Elevated CAT activity and GSH concentrations	[49]
C. moschata Duchesne fruit. Pumpkin peel	gallic acid	Wistar rats	10% and 20%	burn wound healing activity	immunomodulatory activity through increase in natural killer cells and splenic lymphocyte proliferation	[52]
(*Musa sapientum Linn. Var. compressa*) Saba Banana peel	Leucocyanidin	Sparague Dawley Rats	50–100% extract	Skin wound healing, anti-hemorrhagic	increased concentration of collagen fibers, reduced vascular proliferation and Reduced wound contraction,	[46, 47]
P. granatum peel	gallic acid, catechin, saponins, triterpenes, sterols, tannins, alkaloids, flavonoids and cardiac glycosides	Rats	10% (wt/wt) 100 mg/kg/ day for 15 days	wound healing activity	fasten the process of healing improved histopathological parameters through the precipitation of proteins from animal hide. Reduced the number of immune cells, accelerating the second stage of the healing, and the migration of fibroblast to the wounded tissue.	[48, 50, 51]
Grape seed and peel	proanthocyanidins		2%	wound healing	shortening the healing by enhancing the process of contraction and closure of wounds, time	[54–57]
M. acuminata Colla AAA) peel	biogenic amines, L-dopa and dopamine		5 mg	Antihemolytic Activity		

Reactive Substances (TBARS) level in visceral organs. Induced hyperglycemic condition was also ameliorated by *M. indica* and *Citrullus vulgaris* peel extracts was reported to decrease serum glucose and increase in insulin concentrations in induced hyperglycemic conditions, through mechanisms involving the reduction in the oxidative stress, and directly related to insulin secretion and β-cell apoptosis [62].

Peel extracts from *Citrus sinensis* and *P. granatum* with high total polyphenols content have been associated with antidiabetic and antiperoxidative effects [63]. reported maximum glucose lowering and antiperoxidative activities at 25 mg/kg for *C. sinensis* and 200 mg/kg for *P. granatum* peel extracts, this doses also resulted in higher insulin levels [64]. The methanolic seed extract of pomegranate significantly decreased the level of blood glucose by 47% and 42% respectively, after 12 h on streptozotocin-induced diabetes rats [64, 65]. Mcfarlin et al., [66] reported that consumption of pomegranate seed oil (PSO) decreased weight gain and reduced the risk for type 2 diabetes in wild type CD-1 mice by improving insulin sensitivity in a period of high-fat feeding. PSO is rich in linolenic acid and leptin an adipose tissue-derived hormone, important for the regulation of both energy intake and energy expenditure and lower levels of adiponectin, it is also involved in fatty acid catabolism and glucose regulation.

The pharmacological evaluation of rambutan peel phenolic extract has confirmed the high antioxidant and antiglycation activities with amelioration in fasting blood glucose level of the diabetic mice [27]. Rambutan peel phenolic extract reduced in a dose-dependent manner, the total cholesterol, triglyceride, creatinine and lipid peroxidation in diabetic mice. It also increased superoxide dismutase and glutathione peroxidase in diabetic mice (Table 3).

Antimicrobial/anti parasitic/ antiprotozoal activities

The antimicrobial mechanisms of phenolic compounds involve the inhibition of enzymes such as glycosyltransferases leading to bacterial death due to membrane protein precipitation [68]. Malvidin, petunidin and cyanidin are anthocyanin compounds with strong antimicrobial activities and potentials found in *Syzygium cumini* (black plum) fruit peel [69]. *S. cumini* fruit peel extract was observed to have equal potency against both Gram-negative and Gram-positive bacteria, and are comparable with antibiotics like methacillin and penicillin. Lemon peel (*Citrus limon*) oil exhibited high antibacterial activity against Gram positive bacteria (*Staphylococcus aureus*, *Mycobacterium smegmatis*, *Bacillus cereus*, *Micrococcus luteus, Listeria monocytogenes*) and Gram-negative bacteria (*Proteus vulgaris, Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella*

Table 3 Anti-diabetic properties of some peels and seed extracts

Plants	Bioactive compounds	Test organism	Conc/body weight	Therapeutic activities	Mechanism of action	References
M. indica, C. melo and *C. vulgaris* peel	polyphenols and ascorbic acid	Rats	50–300 mg/kg	Ameliorate thyroid dysfunctions and hyperglycemia/diabetes mellitus.	Decreased the levels of tissue glucose, LPO, creatinine kinase-MB, serum lipids, and increased the levels of insulin and thyroid hormones.	[62]
(*P.edulis)* (Passion fruit) peel and seed	soluble fiber and pectin	Human	30 g/day 250 and 500 mg·kg – 1	hypoglycemic action	Decreased triglycerides levels, insulin resistance, reduce glucose intolerance in type 2 diabetic patients and serum cholesterol	[60, 61]
(*Nephelium lappaceum*) Rambutan peel	Phenol	Mice	50–200 mg/kg bw	Anti-Diabetic	Recovered glycogen content, increased the activity of superoxide dismutase and glutathione peroxidase. It also atenuated lipid peroxidation in diabetic mice, the mesangial index and the expression of TGF-β in the kidney of diabetic mice.	[27]
Avocado seed	–	Male rabbits		Reduced the hyperglycemia.	Restored pancreatic tissue function and inhibits intestinal glucose absorption	[59]
C. sinensis or *P. granatum* peel	flavonon glycosides, hespiridin and naringin	male mice	25 mg/kg of CS and 200 mg/kg of PG.	glucose lowering and antiperoxidative activities	Decrease in LPO and an increase in GSH content in hepatic, cardiac and renal tissues, activation of non-enzymatic antioxidant defense machinery.	[65]
Pomegranate peel and seed oil	linolenic acid,	Mice, rats	2 ml/kg/day, 200, 300 and 600 mg/kg	hypoglycemic activity improved insulin sensitivity anti-inflammatory properties	Reduced glucose and the pro-inflammatory cytokines IL-6 and TNF-α plasma levels and increased the level of the anti-inflammatory cytokine IL-10.	[63, 64, 66, 67]

pneumoniae) and antifungal activity against *Kluyveromyces fragilis*, *Candida albicans*, *Rhodotorula rubra*, *Hanseniaspora guilliermondii* and *Debaryomyces hansenii* yeasts [70]. Essential oil obtained from citrus peel showed remarkable antibacterial activities against *Cutibacterium acnes* which provides a potential therapy for treatment of acne [71]. The antimicrobial activities of essential oil of lemon peel showed high antimicrobial activities with all microorganisms such as *Bacillus subtilis, S. aureus, Bacillus pumilus, C. albicans* and *E. coli* species except *P. aeruginosa* [72].

The antimicrobial activity of various extracts from pomegranate fruit peels against some food-borne pathogens using both in vitro (agar diffusion) and in situ (food) methods have been studied[73]. Phytochemical analysis revealed the presence of active inhibitors in peels, including phenolics and flavonoids. The 80% methanolic extract of peels (water–methanol extract) was a potent inhibitor for *S. aureus, Listeria monocytogenes, E. coli and Yersinia enterocolitica*. The minimum inhibitory concentration (MIC) of water–methanol extract of pomegranate fruit peel against *Salmonella enteritidis* was the highest (4 mg/ml) [73].

A combination of chitosan with banana peel fillers has a synergistic interaction with a broad antimicrobial spectrum against Gram-positive and Gram-negative bacteria even against strains of yeast culture that show the ability of biofilm formation [43]. The results show that the chitosan sanitary membrane as a banana peel has a synergistic action with the highest activity of 10% wt.

The in vitro and in vivo anthelmintic activity of citrus peels against *Ascaridia galli,* has been investigated [74]. Oil emulsions from orange was recently patented for the treatment of gastrointestinal nematodes in ruminants [75]. Limonene an active principle in citrus peels with anthelmintic activity in ruminants is reported to provide effective control against *Haemonchus contortus* in sheep [76].

The chloroformic and ethanolic seed extracts from *P. americana* seeds showed giardicidal and amoebicidal activities. The chloroformic extract inhibited the growth of *M. tuberculosis* multidrug resistance (MDR) SIN 4 isolate and three out of four mono resistant reference strains of *Mycobacterium tuberculosis* H37Rv, showed MIC = 50 μg/ml. The extract was also active *at* MIC values < 50 μg/ml against *M. fortuitum M. smegmatis M. avium, and M. abscessus* non-tuberculosis *Mycobacterium s*trains [77].

Friedman and co-workers demonstrated that multiple potato peels prepared from commercial potatoes contain potato phenolic compounds; chlorogenic acid, caffeic acid, glycoalkaloids α-chaconine and α-solanine and quercetin [78]. They are also used for their antiprotozoal activity against pathogenic trichomonad strains that infect humans, farm animals, and felines. These activities varied by both potato variety and trichomonad organism.

Russet potato peel samples had the highest activity against all strains of the evaluated peels (Table 4).

Cardiovascular protection

Oxidation of Low-density lipoproteins (LDL) generates harmful species, and contribute to the atherosclerotic process [80]. Aqueous seed extract of *P. americana* reduced the blood pressure in hypertensive rats at a dose of 500 mg/kg body weight with by reduction in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and triglycerides (TG) levels in the plasma, kidney, liver and heart [81]. Similarly, there was significant reduction in the levels of total cholesterol and LDL-C in CD-1 adult male mice using Avocado seed flour of *P. americana* mill supplementation [82]. The cardioprotective effects of Pomegranate peel (100 mg/kg) in a rat model is via a reduction in creatine kinase-MB, lactate dehydrogenase, lipid peroxidation levels and glutathione, suggesting its usefulness against cardiac attack or arrest [83, 84]. Pomegranate peel powder has also been used as a dietary fiber source for the treatment of hypercholesterolemia and atherosclerosis.

Hepato-renal protection

P. *granatum* (Pomegranate) peel extract decreased lipid peroxidation in cardiac, hepatic and renal tissues, it also facilitated the scavenging ability of superoxide anion and hydrogen peroxide [63]. Wei et al., investigated the preventive efficacy of extracts of pomegranate peels and seeds on liver fibrosis induced by carbon tetrachloride (CCl_4) in rats [85]. The extract treatment attenuated CCl_4–induced increase in the levels of TGF-β1, hyaluronic acid laminin, hydroxyproline and procollagen type III. They also restored the decreased superoxide dismutase (SOD), glutathione peroxidase (GSH-Px) activities and inhibited the formation of lipid peroxidized products in the rats exposed to CCl_4. Pomegranate peel extract has been shown to have mild antihepatotoxic effect against paracetamol induced hepatotoxicity but greatly potentiated the protective of N-acetyl cysteine NAC on paracetamol induced liver toxicity [86]. Treatment with *P. granatum* (pomegranate) peel and seed oil extracts pre, during and post diethylnitrosamine administration improved liver functions, decreased the levels of DNA fragmentation, MDA, caspase-3 and GSR activities, with elevation in levels of GSH, SOD, GST and t-GPx activities. This indicates that these extracts reduced the oxidative stress and apoptosis induced by diethylnitrosamine. Some workers have reported the antioxidant functions of *P. granatum* peel and *Vitis vinifera* seeds extracts against diethylnitrosamine (DEN)-induced oxidative stress and hepatocellular damage in Wistar rats [87, 88]. In HepG2 cell lines, the extracts possess antioxidant potential. Both

Table 4 Antimicrobial/antiparasitic properties of some peels and seed extracts

Plants	Bioactive compounds	Test organism	Conc/body weight	Therapeutic activities	Mechanism of action	References
P. americana seed	Catechin, lignans and epicatechin	Microorganism	≤50 μg/ml	Antiprotozoal and Antimycobacterial activities	Causes the precipitation of membrane proteins, inducing membrane lysis and antimicrobial activity	[77]
S. cumini peels	malvidin, petunidin and cyaniding	Microorganism	5-10 mg	Antimicrobial activities	Inhibits microbial activities	[69]
C. reticulata peel	Terpenes, d-limonene		5 Ml	Antibacterial acne therapy	Inhibit microbial activity,	[71]
P. granatum L. (Pomegranate) peel	phenolics and flavonoids		4 mg/ml	Antimicrobial activities	Protein precipitation and enzyme inhibition of microorganisms,	[19, 73, 79]
C.s limon L.(citron) peel	Phellandrene, Pinene, D-Limonene, Terpinene and Citral D-Limonene		200 μg/mL, 100 μg/mL, 50 μg/mL, 25 μg/ mL and 12.5 μg/ mL	Antimicrobial Activity, Antioxidant Activity	Exhibited free radical scavenging and inhibit microbial activities	[70, 72]
Potatoes peel	Glycoalkaloid α-chaconine, caffeic acid, α-solanine, chlorogenic acid,			antitrichomonad activity	Active against bovine and mostly inactive against feline trichomonads	[78]
orange, lemon, and mandarin peel	Limonene, β_-Pinene, α-Pinene and Sabinene	Chicken	600 and 1200 mg kg − 1	Anthelmintic effects	Decreased worm motility and notable reduction in worm burden	[74, 76]
Banana peel			10% wt	Antimicrobial	Exhibited free radical scavenging and inhibit microbial activities	[43]

extracts contain alpha-tocopherol-beta-D-mannoside, a vitamin E derivative which might play a major role in its antioxidant potential and increased level of vitamin E [87, 88].

Auraptene (coumarin present in the peels of citrus fruits, such as grapefruit) treatment is known to alleviate 17α-ethinylestradiol (EE) -induced cholestasis by increasing the bile flow and biliary bile acid output [18]. Similar hepatoprotection by auraptene against thioacetamide (TAA)-induced hepatic fibrosis in mice have been reported [17]. Auraptene was found to be remarkably protective against liver injury induced by TAA in mice and maintained the homeostasis of bile acid via regulation of farnesoid X receptor (FXR) target genes including Bsep, Mrp2, Ntcp, Cyp7a1 and Cyp8b1 [17].

Parmar and Kar reported a dose specific antiperoxidative property of the *M. indica, C. melo* and *C. vulgaris* fruit peels in rat's liver, the major target organ of a drug, the maximum antiperoxidative effect was observed with 200 mg /kg of *M. indica*, while for *C. melo* and *C. vulgaris* was at 100 mg/kg, which suggested that these doses are not only safe but might have high therapeutic potential [62]. Dried Citrus unshiu peel, also known as Chinpi, is used as an alternative remedy to improve allergy, inflammation and hepatopathy [89]. Supplementation with 2 g Grape seed extract/day for 6 months improved glomerular filtration rate (GFR) and proteinuria, enhanced the anti-oxidant status while attenuating the lipoperoxidation and carbonylation. Grape seed extract GSE reduced inflammation by decreasing C-reactive protein, triglyceridemia and counteracted anemia and thrombocytopenia [90].

Farrag et al. Reported the protective effect of *Nigella sativa* seeds against Lead-induced hepatorenal damage in rats [91]. The lead caused significant elevation in aspartate aminotransferase (AST), Urea, creatine, total cholesterol and triglycerides in serum, decrease in serum total protein and albumin, histopathological observation showed an indication of severe damage to the liver and kidney, *N. sativa* extract remarkably improved both the biochemical and histopathological conditions of the rats by decreasing AST, Urea, creatine, total cholesterol and triglycerides levels in serum, *as such* averting the progression of disease in stage 3 and 4 patients of chronic kidney disease [92]. Treatment of induced bromobenzene hepatorenal injury with black seed oil could attenuate hepatorenal injury, alleviate the increase of GSH, SDH, LDH, G-6- Pase, serum protein, NO, Na + –K + -ATPase, phospholipids levels and attenuate MDA, SOD, AST, ALT and ALP [93]. Pre-administration of Apple peel polyphenolic extract at 250 and 500 mg/kg·bw in mice before of CCl_4 injection show strong in vivo protective effects, decrease in serum alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase activities, hepatic malondialdehyde level, and enhance antioxidant superoxide dismutase and glutathione peroxidase activities [94].

Urtica dioica seeds show great ameliorative potential and antioxidant capacity in aflatoxin induced hepatorenal injury, and alleviated organ induced degenerative changes in broilers affected by aflatoxicosis [95]. This antihepatotoxicity marked by decreased AST, ALT and gamma glutamil transpeptidase (GGT) levels and hepatic lipid peroxidation and elevated the antioxidants levels as evident by histological observation [96].

Date seed *Phoenix dactylifera* L. var. Khalas extract displayed marked protective potential against CCl_4-induced liver and kidney injury at 100 mg/kg/rat. The extract reduced the elevated alkaline phosphatase (ALP), c-glutamyl transferase (GGT), serum levels of alanine aminotransferase and aspartate aminotransferase (ALT and AST), malondialdehyde (MDA) formation, total cholesterol (TC), bilirubin, creatinine, low-density lipoprotein cholesterol (LDL-C) and calcium, while increasing the attenuated serum levels of high-density lipoprotein cholesterol (HDL-C) and total protein (TP) in a dose dependent manner [97].

Kolaviron, a biflavonoid from *Garcinia kola* seeds, reversed the anti-TB drugs-induced oxidative stress in the liver and kidney of rats. Kolaviron significantly reduced the biochemical indices and oxidative stress markers [98]. Kolaviron suppressed superoxide anion radical production, exerts potent anti-inflammatory action that inhibits production of tumor necrosis factor alpha (TNF-a), and activation of NF-kB (Table 5).

Anticancer

Cancer is one of the most leading cause of death in developed and developing countries. Early detection and implementation of appropriate preventive measures to reduce the cancer burden remain the mainstay in cancer management. The hallmark of a promising anticancer therapeutic agent is its ability to inhibit selectively proliferation of malignant but not normal cells. Lemon peel possess the strong antioxidant activity, mandarin peel exhibited moderate cytotoxic activity against HL-60 cells, whereas grapefruit and lemon peels were ineffective anti-leukemia in his study of fruits' phytochemical content, antioxidant, anticancer, antiproliferation, and antigenotoxic activities [100]. Citrus peels possessed immunostimulation activity via augmentation of proliferation of mouse splenocytes (T-lymphocytes) and exerted non-cytotoxic, and antigenotoxic activities through remarkable reduction of chromosomal aberrations induced by cisplatin in mouse splenocytes. Diab, showed a weak to moderate antitumor activity of the tested citrus peels in HL-60 cells, the extracts increased the cell viability and stimulation index of mouse splenocytes [100].

Table 5 Hepatorenal protection properties of some peels and seed extracts

Plants	Bioactive compounds	Test organism	Conc/body weight	Therapeutic activities	Mechanism of action	References
N. sativa seed	Oil	Humans	2.5 mL,	Prevents chronic kidney disease	Improved the biochemical parameters as well as clinical features	[92]
N. sativa seed	Oil	Rats	5% / 90-130 g	Hepatorenal protection	Extract showed improvement in biochemical and histopathogical findings show increase in GSH, SDH, LDH, G-6-Pase, serum protein, NO, Na + −K + -ATPase, phospholipids levels and decrease in MDA, SOD, AST, ALT and ALP	[91, 93]
P. dactylifera L. var. (Date) seed	Proanthocyanidin	Wistar rat	200–300 μg/mL	Hepatorenal protection	Attenuated the elevated serum levels of ALT and AST, ALP, GGT, TC, LDL-C, bilirubin, creatinine, and calcium, increased the diminished serum levels of HDL-C and TP.	[97]
G. kola seed	Kolaviron,	Wistar rats	200 mg/kg	Hepato-renal protection	Restored the antioxidant parameters and biochemical indices to near normal. Suppress production of SOD, exerts potent anti-inflammatory action that inhibits production of TNF-a and activation of NF-κB	[98]
Grape seed	flavonoïds, non flavonoïds, proanthocyanidins	humans	35 mg/kg,	Improves Renal functions	Improved GFR and proteinuria, increased the anti-oxidant status as assessed by high plasma CAT and SOD and also lowered LPO and carbonylation. It ameliorated inflammation by decreasing CRP, triglyceridemia and counteracted anemia and thrombocytopenia.	[90]
Citrus grape peel	Auraptene	Mice	7.5, 15, 30 mg/kg	hepatic fibrosis inhibitor	Inhibited the activation of HSCs by down-regulating the expression of TGF-β1 and α-SMA and expressed anti-inflammatory effects via reducing the expression of NF-κB, TNF-α and IL-1β	[17]
Grape fruit peel	Auraptene	Mice primary hepatocytes	5, 10 or 20 mg kg − 1	Cholestatic liver injury inhibitor	Reduced the bile acid synthesis through repressing Cyp7a1 and Cyp8b1, and increased the bile acid metabolism through an induction in the gene expression of Sult2a1.	[18]
Pomegranate peel	Catechols, Flavanones, Flavone glycosides, Phenolic acids, Phenylpropanoids	Male albino rats	430 mg/ kg b.w	hepatoprotective	Decreased LPO in hepatic, cardiac, and renal tissues and had a facilitatory effect on the scavenging ability of SOD and hydrogen peroxide	[63, 86]
Pomegranate peel and seed	punicic acid, iso-flavone genistein, phytoestrogen coumestrol, sex steroid hormones and polysacchaides	Rat	Peels: 150 mg/kg body weight Seed: 100 mg/kg body weight, 0.2 ml/kg	liver fibrosis inhibition	Decrease the level of TGF-β1 and inhibition of collagen synthesis, restored the decreased SOD, GSH-Px, GST and t-GPx activities and inhibited the formation of lipid peroxidized products. It also decreased the levels of MDA, DNA fragmentation, caspase-3 and GSR activities	[85, 87]
(*P. granatum* L.) Pomegranate peel	phenolics, flavonoids, ellagitannins and proanthocyanins	Cell lines	2, 5, 10 and 100 mg/kg)	Urinary Bladder Urothelial Carcinoma inhibition	Decrease the volume and weight of T24 tumors and caused the apoptosis in the xenografted tumors	[99]
P. granatum peel and *V. vinifera* seeds	phenols, flavonoids, and tannins	rats	400 mg/kg	Hepatocellular protection	Increased superoxide radical levels in tumor cells	[88]
U.dioica (Stinging nettle)seed	unsaturated fatty acids, palmitic, and omega-3	Rats	2 mL	Hepatoprotective	hydropic degeneration, dysplastic hepatocytes, bile-duct proliferation and periportal fibrosis and prevent	[96]

Table 5 Hepatorenal protection properties of some peels and seed extracts *(Continued)*

Plants	Bioactive compounds	Test organism	Conc/body weight	Therapeutic activities	Mechanism of action	References
					the formation of the ROS or scavenges	
U. dioica seed	palmitic, and omega-3	broiler	30 ml	Hepatorenal protection against aflatoxicosis	Decrease MDA and increased the antioxidant system towards normality, particularly in the liver, brain, kidney and heart.	[95]
Apple peel	Polyphenols	mice	250 mg/kg·bw	Hepatoprotective	Relieve lipid peroxidation, enhancement of the antioxidative defense system and suppression of the inflammatory response	[94]
Ripe and unripe Plantain peel	Gallic, caffeic acids, rutin, quercitrin, quercetin, catechin, kaempferol, chlorogenic and ellagic acids	Wistar rat		Erectile dysfunction modulation	Inhibition of enzymes associated with erectile dysfunction and lipid peroxidation	[25]

Citrus peels have non-volatiles (mainly polymethoxy flavones) and volatiles (essential oils, limonoids) as their bioactive/anticancer constituents. Other workers have explored the anti-tumor effects of gold lotion an extract of multiple varieties of citrus peels containing abundant flavonoids and a large percentage of polymethoxyflavones in a human prostate tumor xenograft mouse model [101]. Intraperitoneal injection and oral administration of gold lotion reduced both the volumes (78%–94% inhibition) and weights (57%–100% inhibition) of the tumors without any observed toxicity. The extract caused an induction of apoptosis in prostate tumors, down-regulation of metastasis (matrix metallopeptidase-2, MMP-2 and MMP-9), the protein levels of inflammatory enzymes (inducible nitric oxide synthase, iNOS and cyclooxygenase-2, COX-2), angiogenesis (vascular endothelial growth factor, VEGF) and proliferative molecules.

C. reticulata peels extract and oil showed significant activity against Dalton's Lymphoma Ascites (DLA) cell line. *C. reticulata* peel water extracts induced cell cycle arrest of DLA in G0/G1 phase followed by nuclear condensation, formation of apoptotic bodies membrane blebbing and DNA damage leading to apoptosis. In in vivo experiments, *C. reticulata* peel extract pretreated mice were significantly (50%) protected from DLA compared to post-treated mice (33%). Some citrus peels such as grapefruit (*Citrus paradisii*), orange (*C. sinensis*) and shaddock (*Citrus maxima)* are rich in phenolic compounds such as quercetin, caffeic acid, kaempferol, catechin and naringin [102, 103]. Orange peel extracts had the strongest inhibition of metalloproteinase and proteasome activities MMP in primary human colonic tumor Caco-2 and the metastatic cell lines LoVo cells, while shaddock had the least. Shaddock peel extracts also had the least MMP inhibition in LoVo/ADR lysates. Grapefruit had the least proteasome inhibition in Caco-2 and LoVo lysates.

Mango peel extract was found to have an antioxidant activity and, in a dose,-dependent manner significantly inhibit the proliferation of HeLa human cervical carcinoma cells. Ali et al. confirmed apoptotic signaling induced by mango peel extract was characterized by down-regulation of Bcl-2 and increased Bax/Bcl-2 ratio [36]. Mango peel extract treatment triggered the proteolytic activation of caspases-3, – 8, and – 9 and the degradation of poly Adenosine Diphosphate (ADP) ribose polymerase in HeLa cells [36].

Pomegranate peel is an affordable promising chemopreventive product and a promising herbal drug remedy used in the treatment of prostate cancer by inducing prostate cancer apoptosis mediated by mitochondrial intrinsic pathways [104, 105]. Pomegranate peel inhibit nuclear factor kappa B (NF-kB)-dependent reporter gene expression associated with proliferation, invasion, and motility in aggressive breast cancer phenotypes [106, 107]. Further investigation indicated that Pomegranate (*P. granatum*) peel increased the expression ratio of Bax/Bcl2 and activation of apoptosis executor caspase 3 and has the potential to inhibit migration and invasion, two critical steps in prostate cancer metastasis, downregulation of MMP2/MMP9 and upregulation of Tissue inhibitor of metalloproteinases 2 (TIMP2). Pomegranate peel exhibited inhibitory activity in human urinary bladder urothelial carcinoma T24 and J82 cells [99]. The study observed that the oral consumption of ethylacetate layer (2, 5, 10 and 100 mg/kg) of pomegranate peel could decrease the volume and weight of T24 tumors and caused the apoptosis in the xenografted tumors [99, 108]. established the chemopreventive activity of pomegranate seed oil against both tumor incidence and multiplicity. The evaluation of the potency of *P. granatum* L. Fruit Peel on breast cancer cells, has shown that *P. granatum* peel reduces cell proliferation and induces apoptosis on MCF-7 breast Cancer cells, with significant

increases in the apoptotic cell numbers at 100, 200, and 300 lg/mL *P. granatum* peel concentrations [109]. In addition, expression of the pro-apoptotic gene Bax was increased, and that of the anti-apoptotic gene Bcl-2 was decreased after 200 and 300 lg/mL [109].

P. guajava peel and seed extracts exert anti-cancer control on both haematological and solid neoplasias [110]. *P. guajava* extract's antitumour properties are tightly bound to induction of differentiation [110]. The peel causes cell differentiation as the use of ex vivo myeloid leukaemia blasts corroborated that *P. guajava* was able to induce cell death but did not exhibit anti-cancer effects on all malignant cells investigated, indicating selective activity against certain types of tumour.

Melon peels and seeds extract could be promising antitumor agents and exhibit several activities against different tumor cell lines [26]. Nirmala and Narendhirakannan investigated the efficacy of *V. vinifera* peel and seed aqueous extracts, the peel and seed demonstrated chemopreventive potential by attenuating the cumulative number of tumors while enhancing the antioxidant enzyme activities in the gold nanoparticles treated mice [111]. The down-regulated expression of mutant p53, Bcl-2 and the levels of pan-cytokeratins could have enhanced the process of apoptosis in the chemical carcinogenesis process.

A natural product isolated from the peel of *M. sapientum* L. (±)-19b induced cell apoptosis and exhibited potent in vitro antivascular and in vivo antitumor activities through the disruption of intracellular microtubule network, causing G2/M phase arrest and depolarization of K562 cells mitochondria [112] (Table 6).

Anti-inflammatory

Inflammation is a cellular reaction to injury or insult, and has been linked to the development or worsening of several non-infectious diseases. Inflammatory cells include neutrophils, macrophages and monocytes, and may inflict damage to nearby tissues in the various diseases presentations and sequel, such as emphysema, acute respiratory distress syndrome, athero- sclerosis, reperfusion injury, malignancy and rheumatoid arthritis [115].

Extracts and essential oils derived from citrus fruits exhibit in-vitro anti-inflammatory activities by inhibiting the production of pro-inflammatory cytokines [116] through blocking c-Jun NH_2-terminal kinase (JNK), extracellular signal regulated kinase (ERK) and NF-κB signaling pathways in lipopolysaccharide-activated macrophages [117] *C. melo* var. *reticulatus* peels at 50 mg/kg caused a significant reduction in both TNF-α and IL-1β levels, while *C. melo* var. *cantalupensis* peels caused the most significant reductions in PGE-2 and *interleukin-6* (IL-6) levels [118]. Same was observed with essential oil from the peels of *Citrus limetta* as reported by Maurya and co-workers to decrease the production of pro-inflammatory cytokines (TNF-α, IL-6 and IL-1β) in lipopolysaccharide-induced inflammation in macrophages in a dose-dependent manner without any cytotoxic effect [119]. In the *in - vivo system* primary skin irritation study in rabbits revealed that *Citrus limetta* fruit peels essential oil is safe for topical application on skin.

Lin et al. evaluated the effect of gold lotion a formulated product extracted from the peels of six citrus fruits (*C. hassaku, C. limon, C. natsudaidai, C. miyauchi Iyo* and *Satsuma)*, on imiquimod (IMQ)-induced psoriasis-like inflammation in mice, the study indicated that oral administration of gold lotion reversed IMQ-induced psoriasis-like inflammation in BALB/c mice [113]. It also attenuated the infiltration of T cells and neutrophils and the expression of pro-inflammatory cytokines in skin lesions, and lowered the percentages of Th17 populations in the lymph nodes, impaired the IMQ-induced type I interferons mainly IFN- - *α*/*β*. Peels of *C. grandis* showed an anti-inflammatory effect in xylene-induced ear edema and carrageenan-induced paw edema in mice. These coumarins were responsible for the regulation and inhibition of inflammatory mediators and cytokines in lipopolysaccharide induced RAW 264.7 cells [120]. *H. rhamnoides* peel extract exhibited maximum edema-reducing effect and suggest that the activity is most probably based on a membrane stabilizing effect caused by the inhibition of degranulation of mast cells [121].

Ouachrif et al., explored and compared the analgesic and anti-inflammatory activities of the methanol extract obtained from fruit peels of two varieties of pomegranate Amrouz and Sefri [122]. *P. granatum* contains active constituents such as punicalagin, strictinin A, punicalin and granatin B which possess antinociceptive and anti-inflammatory activities [122].

In a study using pear peel extract, Carrageenan-induced mice hind paw edema and xylene-induced mice ear edema models were used to determine the anti-inflammatory activity of the peel. The methanol extract of pear peels showed an appreciable reduction in mice paw edema in a dose-dependent manner [123]. The anti-inflammatory and antinociceptive activities of essential oils from peel and seed of *Campomanesia adamantium* fruits in rat have been evaluated confirming that 100 mg/kg seed and peel essential oils from *C. adamantium* fruit inhibited inflammation, leukocyte migration and neurogenic pain and oedema [124].

To confirm the anti-inflammatory effects of Ursolic acid (UA), a pentacyclic triterpene acid found in apple peels (*Malus domestica*, Borkh, Rosaceae) was used in zymosan-induced paw edema, the injection of zymosan in the pleural cavity of mice induced a leukocyte influx

Table 6 Anticancer activities of some peels and seed extracts

Plants	Bioactive compounds	Test organism	Conc/ body weight	Therapeutic activities	Mechanism of action	References
Lemon, Grapefruit, and Mandarin Citrus peel	Flavonoids Phenol	Human leukemia HL-60 cells and mouse splenocytes	20-500 µg/mL	anticancer, immunostimulation and antigenotoxic potential	Citrus extracts exerted non-cytotoxic, and antigenotoxic activities through remarkable reduction of chromosomal aberrations induced by cisplatin in mouse splenocytes for 24 h	[100]
citrus peel	Gold lotion	human prostate tumor/ xenograft mouse model, mice	1 or 2 mg kg_ 2 or 4 mg kg_	anti-cancer effects and ameliorates Psoriasis-Like Dermatitis	Down-regulation of proliferative molecules and the inflammatory enzymes (inducible nitric oxide synthase, iNOS and cyclooxygenase-2, COX-2), metastasis (matrix metallopeptidase-2, MMP-2 and MMP-9), angiogenesis (vascular endothelial growth factor, VEGF). Induced cell cycle arrest of DLA in G0/G1 phase, nuclear condensation, formation of apoptotic bodies, membrane blebbing and DNA damage leading to apoptosis in prostrate tumors.	[101, 113]
C. reticulata peel	Flavonoids, Terpenes compounds	Mice, cell lines	25 mg/kg,	anti-tumor activity;		[102]
C. paradisii (Grape fruit), *C. sinensis* (orange) and *C. maxima* (shaddock) peel	naringin, quercetin, kaempferol, glycoside rutin epicathecin, isoquercetrin and kaempferol, catechin, caffeic acid	colon cancer cell lines	10–100 µg/L	Anticancer activities	Inhibited proteasome activity in extract-treated cells	[103]
P. granatum L peel	ellagic acid, Gallic acid, p-Hydroxybenzoic acid, Caffeic acid, Chlorogenic acid, p-Coumaric acid and Ferulic acid	Cell lines	100, 200, and 300 lg/mL	Reduces Cell Proliferation and Induces Apoptosis on Breast Cancer	Enhanced Expression of the Bax pro-apoptotic gene, and decrease of the anti-apoptotic gene Bcl-2	[109]
P. granatum L peel and seed	Polyphenols, seed oil, γ – tocopherol, β-sitosterol, stigmasterol, campesterol, rutin, ellagic acid	DU 145 human prostate carcinoma cells	0 to 100 µg/ml	prostate cancer suppression	mitochondrial mediated intrinsic pathway apoptosis in prostate cancer cells. Exposure to PoPx led to loss of mitochondrial transmembrane potential (Dym), increase the expression ratio of Bax/Bcl2 and activation of apoptosis executor caspase 3, increase and accumulation of reactive oxygen species (ROS).	[104, 105]
Psidium guajava L. (Myrtaceae) peel	Quercetin, oleanolic acid, arjunolic acid, gallic and ferulic acids	NB4 cells	0–3 mg / ml.	anti-neoplastic effects	induction of apoptosis and cell differentiation	[110]
Sucrier banana peel	catechin, procyanidin, ferullic acid, gallic acid	B16F10 mouse melanoma cells		Inhibition of Melanogenesis	decreased expression of melanogenesis relate protein as microphthalmia-associated transcription factor (MITF) and tyrosinase protein following 24 h incubation with α-melanocyte stimulating hormones (MSH) stimulating.	[114]
V. vinifera (Grapes) peel and seed	esveratrol, flavanols, phenolic acids, flavonols, proanthocyanidins and anthocyanins	Mice	2 mg	antioxidant activity and apoptosis induction	Down-regulation of mutant p53 expression, Bcl-2 and the levels of pan-cytokeratins might have facilitated the process of apoptosis in the chemical carcinogenesis process.	[111]
M. sapientum L.(Banana) peel	(±)-19b	Cancer Cell Lines, Human Normal Hepatocyte LO2 Cells	0, 5, 10, and 20 nM	Anticancer	Disrupted the intracellular microtubule network, caused G2/M phase arrest, induced cell apoptosis, and depolarized mitochondria of K562 cells.	[112]

and exudation 4 h after stimulation. When treated with Ursolic acid, it attenuated protein extravasation into the thoracic cavity; paw edema was reduced by 46%; tibiofemoral edema by 40%; and leukocyte influx into the synovial cavity reduced the levels of mediators related to synovial inflammation, such as KC/CXCL-1 levels by 95%, TNF-a levels by 76% and IL-1b levels by 57% [125] Ursolic acid inhibited the increased vascular permeability in these models of inflammation.

A piece of banana peel when placed on a wart, with the yellow side out, can be a natural alternative to kill off a wart and to reduce swelling and irritation after a mosquito bite by rubbing the affected area with the inside of a banana skin [126] (Table 7).

Neuroprotection

The role of *G. kola* seed extract as an antidote in restoring the activity of reduced acetylcholinesterase by stimulating *Clarias gariepinus* with the enzyme inhibitor glyphosate pesticide formulation [127]. The seed extracts normalize the secretion of acetylcholinesterase by stabilizing the concentrations of the neurotransmitter acetylcholine.

Treatment with Citrus unshiu peel extract enhanced dexamethasone-induced depressive-like behaviors and attenuated neurotoxicity effects in a concentration dependent manner in SH-SY5Y cells [89]. Repeated dexamethasone injection markedly reduced brain derived neurotrophic factor (BDNF) level, tropomyosin receptor kinase B (TrkB), and cyclic AMP-response element-binding protein (CREB), while Citrus unshiu peel extract treatment enhanced these levels in the hippocampus and cerebral cortex regions. It has also been reported that extracts of four batches of nobiletin-rich *C. reticulata* peels, facilitated cAMP-response element (CRE)-mediated transcription in cultured hippocampal neurons [128]. It was found that tangeretin, 6-demethoxynobiletin, 6-demethoxytangeretin, and sinensetin, contained in the extract, contributed to the CRE-mediated transcription-enhancing activity of the extract toward hippocampal neurons and facilitated PKA/ERK/CREB signaling in the culture [128]. Additionally, the extract restored MK-801-induced learning and memory impairment through the activation of ERK signaling in animal. Naringenin abundant in the peels of citrus fruits reduced anxiogenic-like behaviour impairment induced by the exposure to 50 mg of Fe-dextran/kg/day intraperitoneally for 28 days in rats. Naringenin attenuated iron-induced reactive oxygen species formation and restored the iron-induced decrease of the acetylcholinesterase expression level, mitochondrial membrane potential and mitochondrial complexes activities in the hippocampus of rats. It also restored the alteration on the activity and expression of

Table 7 Anti-Inflammatory Properties of Some Peels and Seed Extracts

Plants	Bioactive compounds	Test organism	Conc/ body weight	Therapeutic activities	Mechanism of action	References
C. grandis (Pomelo) peel	Coumarins	Mice	10 mL/ kg.	anti-inflammatory effect	Regulates inflammatory mediators and cytokines by suppressing the secretion of inflammatory cytokines such as IL-1β, PGE2 and TNF-α induced by LPS in RAW 264.7 cells	[120]
P. granatum Linn. (Lythraceae) (Pomegranate) peel	Flavonoids, tannins Ellagic acid, punicalagin, punicalin, strictinin A and granatin B	Rats and mice	50, 100 and 150 mg/kg	anti-inflammatory and antinociceptive effects	Antagonize the release of endogenous inflammatory mediators	[122]
C. melo var. *cantalupensis* and *C. melo* var. *reticulatus* (Muskmelon or cantaloupe) peel	β-carotenes, rosmarinic acid, feruloyl quinic acid and coumaroyl quinic acid	Sprague Dawley rats	25 and 50 mg/ kg	anti-inflammatory activity	Significant reductions in both TNF-α ($P < 0.05$) and IL-1β ($P < 0.001$) levels. Suppressed NF-κB activation and iNOS promoter activity in RAW264.7 cells stimulated with LPS	[118]
Pyrus spp.(Pear) peel	arbutin, oleanolic acid, ursolic acid, chlorogenic acid, epicatechin, and rutin	Mice	1 g/kg and 2 g/kg,	Anti-inflammatory capacity	–	[123]
H. rhamnoides (Sea buckthorn) peel and seed	Ursolic acid and oleanolic acid	Rats	500 mg/kg	Anti-Inflammatory Activity	Result suggest that the activity is most probably based on a membrane stabilizing effect caused by the inhibition of degranulation of mast cells	[121]
C. adamantium (Myrtaceae) (Gabiroba) seed and peel	flavonoids and chalcones	Rat	100 and 300 mg/kg	Anti-inflammation and pain relief	Inhibited leukocyte migration, inflammatory and neurogenic pain and oedema	[124]

ectonucleotidases such as adenosine triphosphate diphosphohydrolase and 5′-nucleotidase, enzymes which hydrolyze and therefore control extracellular ATP and adenosine concentrations in the synaptic cleft and iron induced cholinergic deficits in the cerebral cortex in rats [129]. Naringenin exerts protective effect against cerebral ischemic injury, attenuates bamyloid toxicity [130] induces the activation of MAP kinases, modulates glutamate uptake [131] and prevents neurodegeneration with cognitive impairment caused by the intracerebroventricular-streptozotocin in diabetic oxidative damage rat model [132].

Ripa et al [133] scrutinized the antinociceptive and central nervous system (CNS) reduction activity of the methanol extracts of seeds and peels of *Nephelium longan* in rats. Both extracts displayed dose dependent suppression of motor activity and exploratory behavior in the tested models in the case of CNS depressant activity.

In Alzheimer's disease (AD) an in vitro approach demonstrated the anti-cholinesterase and antioxidant activities of an aqueous extract of avocado leaves and seeds to be beneficial in Alzheimer's disease treatment [134]. Avocado *P. americana* (var. Colinred) peel extract can protect and prevent transgenic *parkin Drosophila melanogaster* fly against paraquat-induced oxidative stress, movement impairment and lipid peroxidation, in a model of Parkinson's disease [135].

The anti-stress, antidepressant and memory enhancing effects of banana (*M. sapientum* L.*)* fruit peel extract in male mice have been investigated with the confirmation of significant reductions in time immobility during forced swimming test (FST) suggesting antidepressant like effects [136]. Learning and memory assessment showed a reduction in time to reach platform in both short-term and long-term memory test, this suggested increased memory function in banana peel treated animals. Liu et al. identified a compound isochromanone, (±) 7, 8-dihydroxy-3-methyl-isochromanone-4 (1), a nature product contained in banana (*M. sapientum* L.) peel which displayed potent antihypertensive activity in renal hypertensive rat models [137]. Isochromanone, (±) 7,8-dihydroxy-3-methyl-isochromanone-4 has moderate ACE inhibitory activity and beneficial effects in reducing blood pressure, which indicates that ACE is its potential target, or at least one of its potent targets (Table 8).

Others

Skin care Peel extracts are innovatively used as basis for the sustainable production of safe, anti-aging, cosmetic products, with great potential for adding value to agro-industrial development. Peel extracts of litchi and rambutan, and that of tamarind seed are reported to suppress melanin production in B16F10 melanoma cells through tyrosinase and tyrosinase related proteins-2

Table 8 Neuroprotective properties of some peels and seed extracts

Plants	Bioactive compounds	Test organism	Conc/ body weight	Therapeutic activities	Mechanism of action	References
N. longan peel and seed	tannins (ellagitannins) corilagin and acetonyl-geraniin	Rats	250 and 500 mg/ kg	CNS depressant and antinociceptive activities	motor activity suppression and exploratory behavior in the tested models. Reduction of pain sensation in rat via the prostaglandin pathways.	[133]
Citrus unshiu (Chinpi) peel	hesperidin, narirutin, naringenin, and nobiletin	Mice	30, 100, and 300 mg/kg	preventing corticosterone-induced neurotoxicity	increased in tropomyosin receptor kinase B (TrkB), brain derived neurotrophic factor (BDNF) level, and cyclic AMP-response element-binding protein (CREB) in the cerebral cortex and hippocampus regions	[89]
P. americana (Avocado) peel	B-type procyanidins and epicatechin	*Drosophila melanogaster*	1- 5 mg/ mL	Neuroprotective Effects	Exert antioxidant activity	[135]
Citrus peel	Naringenin	Rat	50 mg/ kg/day	ameliorated anxiogenic-like behaviour impairment	Naringenin modulates activity and expression of ectonucleotidases such as adenosine triphosphate diphosphohydrolase and 50-nucleotidase, enzymes which control extracellular ATP and hydrolyze adenosine concentrations in the synaptic cleft.	[129, 138]
G. kola seed	Flavinoids (bioflavonoid), xanthenes and benzophenones	*C. gariepinus*	150 mg/ L – 350 mg/L	antidote for anticholinesterase agents	Stabilize and normalize the concentrations of the acetylcholinesterase and acetylcholine neurotransmitter, for effective and efficient flows of signal.	[127]
M. sapientum L.(banana) *peel*		Rat	400 mg/ kg	anxiolytic effects, antidepressant	Reduction in immobility time, memory strengthening possibly via its antioxidant mechanism. Reduce the anxiety /fear like effects produced increased the short term memory as well as long term memory	[136]

inhibition, a focal point for research into preventing skin hyperpigmentation, a clinical sign of cutaneous aging, with litchi extract being the most potent [139].

Epidermal pretreatment with Pomegranate peel (5–10 mg/0.1 ml/well) prior to UVB-induced skin damage antagonizes the matrix metalloproteinases compounds involved in the degradation of skin connective tissues, collagen components, the markers of oxidative stress and genotoxicity [140]. Hesperidin which is a flavanone glycoside found in citrus fruit peels, ameliorates UV radiation-induced skin damage by blockage of oxidative stress and inflammation in HaCaT cells [141].

Sucrier banana peel extracts contain an effective agent for hyperpigmentation inhibition) [114] treated B16f10 mouse melanoma cells with peel extract of sucrier banana, the extract inhibited melanogenesis process through p38 signaling pathway in B16F10 mouse melanoma cells by reducing the expression of melanogenesis related protein such as microphthalmia-associated transcription factor (MITF) and tyrosinase protein after 24 h incubation with α-melanocyte stimulating hormones (MSH).

Anti- rheumatic Rheumatoid arthritis is a multisystemic chronic autoimmune disorder known to affect about 1–2% of the world population. It is associated with significant morbidity and increased mortality [142]. Oxidative stress, imbalance of pro-oxidants/antioxidants play important roles in the pathogenesis of rheumatoid arthritis [143–146]. Proinflammatory cytokines like interferon-γ (IFN-γ), interleukin-1β (IL-1β), IL-6, IL-17, prostaglandin E2 (PGE-2), and tumor necrosis factor-alpha (TNF-α) are highly expressed in the rheumatoid joint and play key roles in the pathogenesis of rheumatoid arthritis [147, 148]. Several workers reported that the methanol extract of *A. comosus* fruit peel extract exhibited a reduction in paw necrosis, and an anti-rheumatic activity by increasing the levels of SOD, CAT and GPx in liver, kidney and spleen, and by decreasing the levels of CRP and PGE2 prostaglandin in serum of arthritic rats in a complete Freund's adjuvant rat model [149].

Tangeretin a major phytochemical in tangerine peels also have a therapeutic effect on Rheumatoid arthritis by decreasing the oxidative stress damage, inhibiting the clinical signs of joint swelling and modulating inflammatory cytokine expression, including reductions of the accumulation of MDA products, attenuating the levels of IL-1β, TNF-α, IFN-γ, and PGE2 levels, increasing the IL-10 and antioxidant enzymes activity through upregulating/activation of Nrf-2 signaling pathway [150].

Antiobesity In a bid to understand the full benefit of pomegranate extracts as a dietary supplement in the management of metabolic syndromes like inflammation and insulin resistance related to obesity, Harzallah and coworkers studied the pomegranate seed oil and peel extracts combination [67]. Pomegranate seed oil increases energy expenditure, decreases plasma levels of the pro-inflammatory cytokines TNF-α and IL-6, and enhances insulin sensitivity [67]. Both extracts exhibit a potential insulin sensitizer property mediated through their anti-inflammatory properties [67]. The immature *Citrus sunki* peel extract was reported to have anti-obesity effect by increasing β-oxidation and lipolysis in the adipose tissue of high fat diet-induced obesity mice [151].

Antiobesity effects of potato peel in terms of the composition of the bioactive potato peel compounds, phenolic compounds and glycoalkaloids reduced weight gain in mice f a high-fat diet. Gene expression of adipose and liver of mice fed high-fat mouse diets supplemented with 10 and 20% red potato peels showed a decreased expression of fatty acid synthetase (FAS), the glucose transporter (GLUT4, coded by SLC4A2, solute carrier family 4, anion exchanger, member 2), stearoyl CoA desaturase 1 and 2 (SCD1 and SCD2), and lipoprotein lipase (LPL) genes associated with lipid metabolism [152].

Antithyroidal Parmar and Kar revealed that *M. paradisiaca* peel extract possesses antioxidative and antithyroidal activity [63]. Although there is limited evidence supporting an antiperoxidative property of *M. paradisiaca* extract, the observed LPO-inhibiting effect appears to be mediated through dopamine, which is found in banana and is also known to have antioxidative properties. In the same study *C. sinensis* peel was found to have antioxidative, antithyroidal, and insulin stimulatory properties, as it could reduce LPO in hepatic, cardiac, and renal tissues; *C. sinensis* also inhibited serum T_4 concentrations and raised insulin levels (Table 9).

Conclusion

It is well understood that peel and seed are often discarded and generate a lot of waste in the environment hence causing pollution but this review have proved that seeds and peels are of a great value and can be utilized to make affordable, accessible and promising chemopreventive product, dietary agents or nutraceuticals in the clinical management of wide range of diseases and maintenance of a healthy body because of its numerous bioactive compounds. Research studies on cell culture, animal models and clinical trials have established that treatment based on naturally occurring phytochemicals and derivatives of plants have shown promising chemopreventive effects in various kinds of diseases. This review revealed the richness, medicinal values and relevance of peels and seeds of different fruits and vegetables and justified that phytochemicals from peels and

Table 9 other therapeutic properties of some peels and seed extracts

Plants	Bioactive compounds	Test organism	Conc/ body weight	Therapeutic activities	Mechanism of action	References
Tangerine peel	Tangeretin	Rats	(50 mg/kg)	rheumatoid arthritis protection	Decreased the oxidative stress damage through decreasing the IL-1β, TNF-α, IFN-γ, and PGE2 levels, regulates inflammatory cytokine expression, suppression of the accumulation of MDA products, enhancing the IL-10 and the activity of antioxidant enzymes through upregulation of Nrf-2 signaling pathway.	[150]
Apple peel	Ursolic acid	Mice	(50 mg/kg)	rheumatoid arthritis	decreased the levels of stress mediators related to synovial inflammation, such as KC/CXCL-1 levels by 95%, TNF-a levels by 76%, and IL-1b levels by 57%,	[125]
A. comosus fruit peel	Flavonoids, tannins, triterpenoids and phytosterols	Freund's adjuvant rat	500 mg/kg b.w.	Anti-rheumatic activity	Rat paw swelling reduction, increased levels of SOD, CAT and GPx in liver, kidney and spleen, and reducing the levels of C-reactive proteins (CRP) and prostaglandins (PGE2) in serum of arthritic rats.	[149]
Potatoes peel	phenolic compounds and glycoalkaloids caffeic acid chlorogenic acid, tryptophan, α-solanine, α-chaconine, tyrosine	Mice cell based assays	10 and 20%	Antiobesity/ Supplement for weight loss	decreased expression of the gene for fatty acid synthase, less fat storage, as indicated by a reduced expression of the stearoyl-CoA desaturase-1gene, reduced transcription of the insulin-responsive glucose transporter and reduced transcription of the lipoprotein lipase gene	[152]
C. sinensis × *Poncirus trifoliata* (citrange) fruit peel	neoeriocitrin, narirutin, naringin, hesperidin, neohesperidin, poncirin, naringenin, nobiletin and tangeretin.	Female mice	1% *w/w*	Ameliorate obesity	The down-regulation of expression level of peroxisome proliferator-activated receptor γ *PPARγ*) and its target genes, Reduction of the expression levels of liver X receptor (LXR) α and β, which are involved in lipid and glucose metabolism	[153]
immature *Citrus sunki* peel				Ameliorate obesity	increased β-oxidation and lipolysis in the adipose tissue of high fat diet-induced obesity mice	[151]
pomegranate seed oil	linolenic acid,	Mice		decreased weight gain	higher levels of leptin, lower levels of adiponectin	[66]
Mimusops balata peel and seed	Taxifolin	Mice	300 mg/kg	antiulcerogenic activity	gastric volume reduction, pH, total acidity, and pepsin activity in the gastric juice maintained GSH levels, reduction of LPO content, inhibition of neutrophil migration	[154]
Banana (*M. sapientum* L.) peel	7,8-dihydroxy-3-methyl-isochromanone-4	Rats		antihypertensive activity	ACE inhibitor	[137]
purple passion fruit peel	Quercetin, edulilic acid	Humans	150 mg/d	reduces wheeze and cough and improves shortness of breath in adults with asthma	Nitric oxide lowering effect, inhibit histamine release, arachidonic acid metabolism, and cytokine production	[20]
Orange peel	Hesperidin	Human skin keratinocyte line HaCaT cells	220 μg/ml)	Photoprotection, antioxidative and anti-inflammatory capacities in skin injuries	Reduced UVA-induced oxidative stress and inflammatory response, elevate SOD activity and significantly decreased MDA content and increased the total antioxidative capacity levels	[141]
litchi and rambutan peel and	Phenols	B16F10 melanoma cells	0.25 mg/ml 0.0001–	skin aging treatment	Extracts suppress melanin production in B16F10 melanoma cells through inhibition of tyrosinase and TRP-2	[139]

Table 9 other therapeutic properties of some peels and seed extracts *(Continued)*

Plants	Bioactive compounds	Test organism	Conc/ body weight	Therapeutic activities	Mechanism of action	References
tamarind seed			0.01 mg/ml			
Citrus limetta Risso peel	flavonoids, carotenoids, dietary fiber, sugars, polyphenols, essential oils, and ascorbic acid	mice/cell lines	20 μL/ ear/ time	alleviates skin inflammation	reduced lipid peroxidation, the 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced ear thickness, ear weight, pro-inflammatory cytokines production and ameliorate the histological damage in the ear tissue	[119]

seed extract exhibit several ameliorative potentials which are enormous and useful in the treatment of several kinds of diseases. In vivo and in vitro and clinical studies have confirmed that phytochemicals of peel and seed extract have antioxidative, antidiabetic, hepatorenal protective, antithyroidal, anti-inflammatory, antibacterial, cardiovascular protective, neuro-protective effects, anticancer and wound healing activities. Peels and seed extracts have been evaluated and comprehensively established as chemopreventive agent, it would therefore be necessary to use them as conventional therapeutic drugs to augment their therapeutic effect at relatively lower doses, evaluate their therapeutic effect on metal toxicity and focus on the development of inexpensive and cheap therapy from natural products.

The use of these phytowastes as nutraceuticals, also goes a long way to fulfilling the three R's of waste management. Their efficacy of usage compliments the reduction of waste generation, the reuse and recycling of products of veritable importance, in the maintenance of a healthy environment, economic resourcefulness, and positive health care outcomes.

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