Beneficial attributes and adverse effects of major plant-based foods anti-nutrients on health: A review

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Beneficial attributes and adverse effects of major plant-based foods anti-nutrients on health: A review

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ABSTRACT

Anti-nutrients are the biomolecules that if present in food along with nutrients, can reduce either the absorption or the utilization of nutrients. The physiological importance of anti-nutrients is been debated for a long time because the researches point at various effects on different anti-nutrients in foods. Some anti-nutrients show both beneficial and harmful physiological effects that depend on molar ratios between nutrients and anti-nutrients and some other factors. Previous studies suggested that anti-nutrients if are consumed in a adequate amount they may act as a useful natural drug to ameliorate human health. They can have physiological importance in the nutrition of the organism. In this review, we have compiled the beneficial attributes of major plant-based anti-nutrients to improve health conditions, along with their potential adverse effects.

1. Introduction

Due to high amounts of nutrients, plant seeds are considered to be nutritionally rich sources of food with great importance to human nutrition. They contain ample amounts of numerous essential nutrients like-lipids, peptides/proteins, amino acids, starch, dietary fiber, vitamins, and minerals [1]. A majority of food products consumed in homes or restaurants have plant products as their main ingredients. Food crops like legumes and cereals are considered economically very important. Plant-based protein sources are far more economical than animal-based protein sources because they provide much more food production per unit area dedicated to production [2]. The ratio of animal-based food production per unit area dedicated to production is particularly high with less food produced from more effort. Given the economical and nutritional value of plant-based foods, they are still preferred less in the presence of animal-based foods because of anti-nutrients, that are present in plants which can influence every aspect of food.

Anti-nutrients are the compounds commonly produced in natural plant foods/or their derived feedstuffs, through several mechanisms at the metabolism level [3]. Some groups of anti-nutrients are phytic acids, tannins, polyphenols, enzyme inhibitors, saponins, and lectins. Fig. 1 shows the major anti-nutritional factors present in plant foods. Anti-nutrients reduce the bioavailability of minerals, digestibility of protein, and may also lead to toxicity [4]. They are not frequently characterized based on their effects but rather on the type of molecules. This creates a situation in which anti-nutrients can be included in a category that also includes molecules that are not just anti-nutrients but also have other effects [5]. Most of the secondary metabolites, acting as anti-nutrients, elicit very harmful biological responses, while some of them are widely applied in nutrition and as pharmacologically-active agents [6]. Anti-nutrients are still being studied and reduction strategies will only be experiments with unprecedented results if they are not done with complete understanding [7]. Their impact on different organisms is varied to the fact that they can have entirely different effects on different organisms. Their general effects are well known but the molecules these groups include show a variety of effects that cannot be generalized. Therefore, all the possible effects of an anti-nutrient molecule should be studied before making any reduction strategies to avoid any future unprecedented adverse effects.

Cooking is a traditional processing method that are proven and

Abbreviations: ATP, Adenosine triphosphate; EDTA, Ethylenediaminetetraacetic acid; PA, Phytic acid; TA, Tannic acic; CVDs, Cardiovascular diseases; WGA, Wheat Germ Agglutinin; TLC, Thin Layer Chromatography; NPDR, Non-Proliferative Diabetic Retinopathy; SOD, Superoxide dismutase; HEC, Human embryonic carcinoma cell; TLRs, Toll-like receptors; AC, Acute colitis; ROS, Reactive oxygen species; GNA, Galanthus Nivalis Lectin; EGFR, Epidermal growth factor receptor; TNF, Tumor necrosis factor; IL, Interleukin; DPPH, 2,2-diphenyl-1-picrylhydrazyl.

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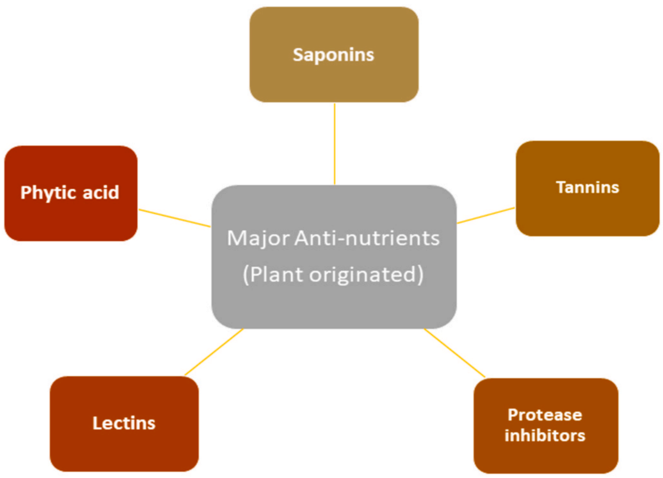

Fig. 1. Major plant originated anti-nutritional factors.

observed to reduce the anti-nutritional components in plant-based foods/food products. Moreover, fermentation, milling, germination, soaking, and puffing techniques also enhance the digestibility of proteins as well as improve the nutritional value of plant-based foods [8]. Many scientific studies report the beneficial as well as adverse effects of plant-based foods anti-nutrient factors are listed in Tables 1 and 2 respectively.

In this paper, we have summarized the recent clinical evidence of key anti-nutritional constituents of plant-based foods, which are known for their potential beneficial and adverse effects on health.

2. Major anti-nutrients of plant foods

2.1. Tannins

Tannins are the bitter-tasting polyphenolic compounds in food [9]. The dryness of the tongue after a strong tea is because of the tannins in the tea. A tannin molecule having 10 galloyl groups attached to glucose is usually regarded as tannic acid although numerous molecules like this are characterized under the same name [10].

Characterization of tannins based on structure: (i) Hydrolyzable tannins from plants that can be hydrolyzed into their constituent phenolic acids and carbohydrates. Have gallic acid as their base unit, i.e. gallotannins and ellagitannins. (ii) Condensed tannins are polymers of the flavan-3-ols present in plants. They are depolymerized into anthocyanidins under oxidative conditions, i.e. Proanthocyanidins (iii) Pseudo tannins are phenolic compounds of lower molecular weight. The base units of tannins were found separately in plants, i.e. Gallic acid and Falvan-3-ols. (iv) Phlorotannins are oligomers of phloroglucinol found in brown algae.

Tannins are present in food items such as pomegranate, strawberries, cranberries, blueberries, raw nuts like hazelnuts, walnuts, and pecans, almonds, cloves, tarragon, cumin, thyme, vanilla, and cinnamon, most legumes, peanut, chocolate, apple, grape and berry juices, packaged fruit juices [11,12].

2.2. Phytic acid

Phosphorous is a key component of ATP, of a seed that has stored energy for the future contains a lot of phosphorous. Most of the phosphorous stored in seed is in the form of phytic acid [13]. In the protein storage vacuoles present in the aleurone layer of seed embryo, which creates a problem as phytic acid is involved in so many crucial

Table 1
Adverse effects shown by major anti-nutrients of plant-based foods.

Anti-nutrients	Sources	Responses & findings	References
Tannins	Tea (*Camelia sinensis*)	(Lower serum Hemoglobin) 53.85% of the sample (student) who have consumed tea had low Hb level.	[105]
	Mango (*Mangnifera indica*)	(Binds with iron to form complexes affects growth of gut microbes) Due to iron complexing properties it can prevent growth of food spoilage bacteria and *Escherichia coli*	[107]
	Sorghum (*Sorghum bicolor*)	Decline milk production and impact lactation when fed in different concentrations to cows	[109]
	Cocoa (*Theobroma cacao*), Pomegranates (*Punica granatum*), Cranberries (*Vaccinium subg. oxycoccus*), and Grapes (*Vitis vinifera*).	Isolated tannin extract inhibit the α- amylase and glucoamylase *in vitro*	[118]
Saponins	*Vernonia amygdalina*	(Lyse the erythrocyte) Saponin had high haemolytic effect on blood group-O and genotype-SS.	[127]
	Neem (*Azadirachta indica*)	Observed inhibition of amylase enzyme in *T. castaneum* insects after 4 days feeding	[130]
Phytic acid	Wheat (*Triticum aestivum*)	(Reduce the absorption of magnesium) Addition of phytic acid lowered the magnesium absorption in healthy humans, in a dose-dependent manner	[133]
	Bean (*Phaseolus vulgaris*)	Reduce the efficiency of iron absorption in the women subjects.	[135]
	Bean (*Phasiolus vulgaris*)	(Reduce the efficiency of iron absorption) Phytic acid reduced the iron bioavailability of iron-biofortified beans	[138]
	Rye (*Secale cereale*)	(Not improve iron status) High phytate rye bread comsumptions not showing any improvement in the iron status of Swedish females	[141]
Lectins and hemagglutinins	Bean (*Phasiolus vulgaris*)	Decrease in body weight and food intake in the experimental animals (Sprague Dawley rats) when using a dose of 50 mg/kg on alternate days for six weeks.	[93]
	Moringa oleifera	Chitin binding activity and enzyme binding activity (reduce the growth of larvae, impaired the larval weight gain by 50% and impacted the pest's major digestive enzymes activity)	[145]
	Moringa oleifera	Inhibiting nutrition and affecting the growth of larva of *A. aegypti*	[146]
	Bean (*Phasiolus vulgaris*)	Phytohemagglutinins induces diarrhea in human by inhibiting electrogenic Na (+) absorption	[151]
Protease inhibitors	Soybean (*Glycine max*)	(Inhibits trypsin activity) due to Bowman–Birk inhibitor (BBI) with stevioside (STE)	[154]
	Soybean (*Glycine max*)	Soyabean trypsin inhibitor Inhibits the trypsin/protease enzymes in the larval midgut of *P. xylostella*	[156]

Table 2
Beneficial properties shown by major anti-nutrients of plant-based foods.

Anti-nutrients	Sources	Responses & findings	References
Tannins	Grapes (*Vitis vinifera*)	Grape seed proanthocyanidin extract (GSPE) improved the blood pressure conditions in the middle-aged Japanese adults with prehypertension conditions	[42]
	Grape (*Vitis vinifera*)	Reducing the severity of Hard Exudates HE (Non-Proliferative Diabetic Retinopathy) After 9 months of GSPE group showed a considerable improvement in HE severity	[43]
	Pistacia weinmannifolia	(Prevent lipid peroxidation in neuronal cells) Pistafolia A (gallotannin) could scavenge both superoxide anion and hydroxyl radicals and dose-dependently	[55]
	Fruits of *Capparis moonii*	Acts like insulin and increase glucose intake by cells	[57]
	Caesalpinia spinosa	Extract of *Caesalpinia spinosa* which is a rich source of gallotannin was reported to reduce the occurrence of the primary tumor in breast cancer	[60]
Saponins	Notoginseng (*Panax notoginseng*)	Panax notoginseng saponins reduce the apoptosis of cardiomyocytes suffering from oxidative stress, in mouse model	[64]
	Balanites aegyptiaca	(Improves the glycaemic markers and the lipid profile) Controlling the blood glucose level and lipid profile in people suffering from type 2 diabetes	[65]
	Allium minutiflorum	(Anti-fungal effect) Novel saponins showed a significant antifungal activity depending on their concentration (minutoside B > minutoside C ≫ minutoside A)	[71]
Phytic acid	Rice (*Oryza sativa*)	Phytic acid extracted (Rice bran) can reduce the risk of developing colon cancer in rats	[79]
	Canola (*Brassica napus* L.)	DPPH free radicle scavenging activity indicating their behavior as antioxidants	[80]
	Rice (*Oryza sativa*)	(Prevent breast, ovarian, and liver cancer) Phytic acid extract induced growth inhibition in liver, breast, and ovary cancer cells with 50% (IC50) values of 1.66, 3.78, and 3.45 mM, respectively	[86]
	Rice (*Oryza sativa*)	Phytic acid can reduce hyperlipidemia and oxidative stress by increasing lipid excretion and activating antioxidants and lipogenic enzymes	[88]
Lectins and hemagglutinins	Wheat (*Triticum aestivum*)	(Potential Therapeutic Agent for Leukemia) Wheat Germ Agglutinin (WGA) can target leukemia cells (acute myeloid leukemia (AML)) and agglutinate them	[92]
	Phaseolus acutifolius (Tepary bean)	Apoptotic effects on colon cancer	[93]
Protease inhibitors	Soybean (*Glycine max*)	(Anti-inflammation and anti-HIV effect) BBI action inhibits HIV effect, showed that BBI down-regulated the expression of CD4 receptor and induced the production of the CC chemokines in macrophages.	[96]
	Potato (*Solanum tuberosum*)	(Immunomodulation, antileishmanial drugs) Potato tuber extract 3 (PTF3) showing protective immune response with increased antimicrobial substances and up-regulation of pro-inflammatory cytokines.	[98]
	Peanut (*Arachis hypogaea*)	(Good hungriness-reducing effect) Supplementation with trypsin inhibitor in peanut paçoca significantly decreased fasting glucose, body weight gain, and food intake.	[100]
	Tamarind (*Tamarindus indica*)	(Reduce food intake and inflammation) Tamarind seed trypsin inhibitors (TTI) reduced food intake in animals with metabolic syndrome, tumor necrosis factor-alpha was lower in animals receiving TTI.	[101]

physiological processes in the plant, so it will not be a good strategy to completely remove it from a plant's body [14]. Its concentration in food and body plays a major role in its negative effect. As it is a negatively charged and highly reactive biomolecule, it can interact with all the positively charged nutrient molecules [15]. Considering its importance in the plant body, there is no surprise that it is present in all the plant foods, in high concentration until the seed starts to germinate. It is found in all the major food crops of the world including maize, wheat, rice, and barley. Phytic acid is retained during the dormant phase, However, during germination, it is broken down and used by the seed. The phytase enzyme and other phosphatases get activated during germination and break phytates into their constituent molecules [16,17].

Its ability to reduce the utilization of micronutrients in the body makes it an anti-nutritional factor in diet. enhancement of micronutrient quality of food is a big challenge since a lot of factors come in the way of efficient micronutrient delivery [18,19]. Improving the starch content, on the other hand, has been the motive of many food crop improvements. There is evidence of phytic acid affecting the uptake and bioavailability of iron. Iron, in our diet comes in two forms, heme iron, and non-heme iron. Heme iron is provided by non-vegetarian food sources while non-heme iron is provided by plant food sources. Both types can be utilized by our body [20]. The absorption of iron happens in the proximal part of the duodenum. While weak chelators are helpful because they make iron more soluble, strong chelators act as inhibitors. EDTA is an example of a weak chelator while phytic acid is an example of a strong chelator [21]. Polyphenol groups that have a catechol group in their structure can inhibit iron absorption. Tannic acid, which falls in this group, is an even greater inhibitor of iron absorption than phytic acid. The effects of phytic acid can be reversed to some extent by meat and ascorbic acid in the diet but they can't do the same to the effects of tannic acid [22,23]. When metals like iron and zinc are present in the gut along with phytic acid in a ratio of more than 10:1 (PA: metal), absorption of iron and zinc is inhibited [7].

2.3. Saponins

Saponins are bitter-tasting plant secondary metabolites of steroid or triterpenoid aglycone molecules attached to one or more sugar chains [24]. Based on the structure of aglycone, saponins are classified into two groups-steroid and triterpenoid saponins. Since saponins can inhibit microbial growth and fungal growth, they are thought to be a defense mechanism evolved by plants. Saponins are present in a great variety of plants whether wild or cultivated. Triterpenoid saponins are more abundant in cultivated plants [25,26]. Triterpenoid saponins are confirmed in many important legumes such as soybeans, beans, peas, etc. They are also reported in tea, spinach, sugar beet, quinoa, and ginseng. While steroid saponins are reported in oats, capsicum peppers, tomato seed, asparagus, etc., [27].

2.4. Lectins and hemagglutinins

Lectins can target carbohydrates and reduce their absorption, can be very detrimental to one's health and nutrition. The lectins that we are concerned with here, are those that can target carbohydrate metabolism [6]. The first lectin ever to be discovered was a toxin named ricin, by Herrmann Stillmark (1888). But Lectins were first scientifically described by Boyd and Shapleigh in 1954. They are the proteins that can target monosaccharides and oligosaccharides and bind to them in a reversible manner which compromises their absorption. Other types of molecules that have sugar components in them like glycoproteins and glycolipids are also targeted for binding. There are hundreds of them in nature [28]. They are also called hemagglutinins because they can agglutinate erythrocytes. While lectins are present in plants, animals, fungi, and bacteria, plant lectins are studied for their anti-nutrient behavior [29]. Interestingly, in fungi and bacteria, lectins perform numerous physiological functions like-protection from pathogens, storage of sugar, and transport of biomolecules. While some of them are harmful, even considered toxins, few specific examples of lectins are reported to be beneficial. There are several examples of lectins being able to reduce several types of cancers. Cooking can help in reducing them, but once they get inside the body, they are very hard to degrade and the body is not able to eliminate them effectively. In high concentrations like in raw kidney beans, lectins are reported to cause severe abdominal pain, vomiting, and diarrhea [30,31].

The lectins present in plants are generally grouped based on their structures and sugar-binding specificity. According to this classification, they are grouped into four categories that are called hololectins, chimerolectins, superlectins, and merolectins [32]. Some examples include legume lectins, Galanthus nivalis lectin (GNA), and cyanovirins. Raw red kidney beans contain a higher amount of lectin which can cause nausea, vomiting, and diarrhea when these beans are consumed raw. These kidney beans have lectins levels of about 20000–70000 hemagglutinin units making even five raw beans dangerous [33,34]. But cooking them solves the anti-nutrients problem. Raw soybeans contain high amounts of hemagglutinin units but they are eliminated while pressure cooking. Raw wheat contains higher amounts of lectins called wheat germ agglutinin that is unknowingly reduced during cooking and other processing methods. While wheat germ contains about 300 μg/g some products of wheat like pasta does not contain any significant amount of lectins at all [35]. Peanuts contain lectins that can act as anti-nutrients if they are eaten raw or roasted [36]. However, they are nutritious enough to be healthy even if they have some amount of anti-nutrients.

2.5. *Enzyme inhibitors*

Enzyme inhibitors can reduce the functionality of a digestive enzyme if they are present in the body. Three major types of digestive enzymes can be affected by these enzymes. The enzymes that can be affected by these inhibitors are proteases, amylases, and lipases [37]. These enzyme inhibitors are specific to their target enzymes and can be characterized based on the type of enzyme they target. Hence, they are grouped into three groups named protease inhibitors, amylase inhibitors, and lipase inhibitors [38]. While the protease inhibitors can be easily regarded as harmful as they can greatly affect the growth of a child, the amylase inhibitors and lipase inhibitors in a balanced quantity can be beneficial because they can prevent lifestyle-induced diseases. So, the most problematic types of enzyme inhibitors are protease inhibitors. In the human body, seven types of proteases perform physiological functions. Six of these proteases can be inhibited by naturally occurring protease inhibitors. Trypsin and chymotrypsin inhibitors are widely distributed among a great variety of plant foods [5,39,40]. Soybean trypsin inhibitors are greatly studied because soybean is a very important food crop. The Bowman-Birk family of protease inhibitors is found in a great variety of leguminous food crops. Barley is known to have trypsin inhibitors. Potato is known to have a protease inhibitor [5,41].

3. Health beneficial attributes of anti-nutrients

3.1. *Tannins*

Some findings indicate that proanthocyanidins might be good for health in particular quantities. For example, proanthocyanidins present in grapes were shown to have a potential for helping people suffering from hypertension. It was a randomized, placebo-controlled clinical trial, in which proanthocyanidins were linked to the improvement of blood pressure conditions in people suffering from hypertension [42]. Doses were of two types in this study, the low dose was 200 mg/day while the high dose was 400 mg/day. The study spanned 12 weeks. Grape seed proanthocyanidin extract has shown great promise in recent years for disease treatments. In another randomized control trial, it was found that proanthocyanidin can help people suffering from Non-Proliferative Diabetic Retinopathy (NPDR) [43]. Highlighted in this study was the proanthocyanidin's ability to reduce the severity of hard exudates (HE) which are complications associated with NPDR. In this trial, people suffering from retinal thickening with HE caused by NPDR were given grape seed proanthocyanidin extracts orally for 12 months. The improvement in the conditions was detected by analyzing the severity of HEs using fundus photography. Diabetic macular edema is the cause of visual impairment that occurs in people suffering from diabetes and reducing the severity of HE is an important way to treat it. This research highlights the potential of proanthocyanidins to treat a complication related to diabetes in humans. In another study, on proanthocyanidins, oligomeric proanthocyanidins were reported to affect the health of periodontal tissue. The randomized control trial reported that supplementary ingestion of capsules containing oligomeric proanthocyanidins can prevent bleeding of the gums that happens in gingivitis [44]. Gingivitis is the inflammation of dental tissue which can lead to other complications if untreated. This research gives a treatment opportunity to people suffering from gingivitis by the use of oligomeric proanthocyanidins supplementation. Highlighting the importance of tannins in oral hygiene.

There is much evidence of the beneficial effects of the tannic acid molecule on health which will be discussed in this section. Tannic acid has the potential to prevent complications that are caused by cardiovascular disease progression. In a study in mice, tannic acid was found to be able to prevent myocardial fibrosis [45]. Myocardial fibrosis is caused by the exaggerated activation of the β-adrenergic receptors and the inflammation mediated by certain toll-like receptors (TLRs) which causes myocardial interstitial collagen fibers to accumulate. Tannic acid was able to prevent these collagen fibers to accumulate and prevent myocardial fibrosis. In one study, tannic acid is considered to be a good natural antioxidant that can be used in ground chicken packaging [46]. Tannic acid can exert a vasodilation effect on the cells of the endothelium.

Tannic acid was also studied for its possible application in cancer prophylaxis and adjuvant cancer therapy [47]. Many anti-carcinogenic properties of tannic acid were highlighted, reporting that-it can exert anti-carcinogenic effects via its anti-oxidant and anti-inflammatory effects, it can exert an anti-mutagenic and anti-tumorigenic effect, it can reduce several cancerous properties of cancer cell lines. The pathways through which this molecule can exert its anti-carcinogenic effects were given to bio-signaling pathways such as EGFR/Jak2/STATs and enzymatic pathways such as inhibition of PKM2 glycolytic enzyme. Further, tannic acid was also reported to be able to make the cancer cells responsive to chemotherapy by overcoming the multidrug resistance in them. In a study on mice endothelium cells, it was reported that tannic acid (in the absence of channel blocking molecules) can stimulate an influx of calcium ions in the cells by activating the calcium ion channels [48]. In another study related to cancer prevention, tannic acid was found to have an anticancer property on the growth of prostate cancer cells (PCa) [49]. Prostate cancer cells abuse lipid signaling and metabolism for their survival and proliferation. Since lipid metabolism is so important in the proliferation of prostate cancer, strategies to prevent prostate cancer can be made by targeting the lipid metabolism of PCa cells. This is exactly what this study reported the tannic acid doing to the PCa cells. It was able to disrupt the lipid metabolism of prostate cancer cells by targeting the lipids and was also able to induce oxidative stress in the endoplasmic reticulum of the PCa cells. Not only this, but it was also able to improve the membrane permeability of PCa cells to the drug treatment. In a study on adult male rats, tannic acid was confirmed to have neuroprotective properties because it was able to prevent neuronal death and inflammation [50]. The neurological condition known as sporadic dementia of Alzheimer's type (SDAT) was induced by intracerebroventricular (ICV) injection of streptozotocin (STZ) in mice. STZ promoted an increase in neuronal death and the levels of proinflammatory cytokines, and tannic acid was able to restore these changes. This study highlighted that tannic acid can prevent the memory deficit and it can re-establish the normal working of the brain in rats with induced SDAT. It may be possible that tannic acid can help in preventing the damage caused by Alzheimer's disease. There is yet another study that suggests that tannic acid (TA) possesses the ability to cause apoptosis in human embryonic carcinoma cells [51]. Gallotannin is a type of tannin with various health effects. It can affect the epithelial cells of the kidney and prevent the formation of kidney stones [52]. Kidney stones can form because Calcium oxalate monohydrate (COM) crystals can bind to the surface of renal endothelial cells. Gallotannin can prevent kidney stone formation because of the following reason-it can enhance antioxidant enzyme superoxide dismutase (SOD) activity in response to oxalate. In addition to this, it can also reduce the expression of monocyte chemoattractant protein-1 (MCP-1) and osteopontin (OPN). Overall, the study showed that gallotannin prevents the retention of COM crystals and also the harmful responses that these crystals can elicit. It can prevent countless people from developing a disease that can ultimately lead to kidney failure.

The harmful effects of acute colitis (AC), like colon shortening and colon tissue damage along with the secretion of tumor necrosis factors and interleukins, can be reduced by gallotannin called Corilagin [53]. Ulcerative colitis is one of the complications of inflammatory bowel disease. Corilagin can help in the treatment of acute colitis by reducing the production of pro-inflammatory mediators such as TNF-α, IL-1β, and IL-6. The study indicated that corilagin can reduce the symptoms of DSS-induced colitis in mice. It might be due to the reduction in the inflammatory responses of the colon and intestinal epithelial cell apoptosis via inhibition of NF-κB activation.

In, another finding, a four weeks dosage of gallotannin was able to reduce the concentration of creatinine in plasma which is a studied and confirmed indicator of diabetic nephropathy [54]. Diabetic nephropathy is one of the complications of diabetes and can lead to end-stage renal disease. Gallotannin administered to STZ-induced diabetic rats can prevent the cleavage of Poly (ADP-ribose) polymerase (PARP), which in turn can delay diabetic nephropathy.

A Gallotannin named Pistafolia A was investigated and confirmed to be able to scavenge hydroxyl radicles and superoxide anion and prevent lipid peroxidation [55]. This means Pistafolia A can be used to prevent or cure neurodegenerative diseases. In the study, gallotannin was able to reduce the peroxynitrite-induced oxidative neuronal damage and apoptosis. The antioxidant capacity of Pistafolia A was reported to be superior to an analog of vitamin E, Trolox.

Gallotannin can reduce the poly-ADP ribosylation and impart a cytoprotective effect [56]. In a study on the HaCat cell line, gallotannin was able to protect cells that are under oxidative stress. Gallotannin was able to inhibit poly (ADP-ribose) glycohydrolase (PARG) when in 50 microM concentration. Two new types of gallotannins extracted from the fruits of *Capparis moonii* in 2010 were reported to mimic the action of insulin and increase glucose intake by cells through some molecular mechanisms [57]. To treat Alzheimer's disease many natural compounds have been tested for their ability to inhibit amyloid beta-peptide aggregation. In an *in vitro* study, two specific types of gallotannins having different galloyl residues were reported to have a desirable effect of preventing the aggregation of amyloid-beta lipid aggregation [58]. Amyloid b-peptide aggregation into toxic fibrils is one of the major processes occurring during the progression of Alzheimer's disease.

Human embryonic carcinoma cells (HEC) are self-renewable and pluripotent. Cancer stem cell pathways are very active in these cells which can be detected by their markers. One of these pathways is Wnt/β-catenin. Inhibiting these pathways can ensure effective targeting by the drug. Tannic acid can do exactly this, it can inhibit the Wnt/β-catenin cancer stem cell pathway. In this study, the inhibition of Wnt/β-catenin signaling, and the reduction in cancer cell markers were detected by Western blotting and PCR. TA can induce sub-G1 cell cycle arrest and apoptosis. It was detected by fluorescence-activated cell sorting analysis in this study. By regulating the reactive oxygen species in mitochondria, tannic acid can induce extrinsic apoptosis in the cells of HEC cells. The study confirmed the importance of tannic acid as a dietary phytochemical that can act as cancer chemoprevention. gallotannin is known to have an anticancer effect in particular types of cells because it can induce cell cycle arrest and apoptosis. A study on human colonic cancer cells reported the cancer prevention effect of ghallotannin by the means of S-phase cell cycle arrest [59]. It also reported that gallotannin was not toxic to normal human colonic cells. It emphasized the non-toxic and anti-cancer effects of gallotannin. In another study related to gallotannin mediated cancer prevention, an extract of *Caesalpinia spinosa* which is a rich source of gallotannin was reported to reduce the occurrence of the primary tumor in breast cancer [60]. The study highlighted the importance of gallotannin as a therapeutic alternative capable of generating an immune response against residual tumor cells and eliminating the cancer stem cells. Investigations into the anti-cancer effects of specific gallotannins have confirmed its anticancer effect and pointed out the possible mechanisms it may use to achieve the anticancer result [61].

A specific gallotannin extracted from *Euphorbia* species can inhibit the lipopolysaccharide stimulation and production of nitric oxide to prevent inflammation caused by the same [62]. Some gallotannins inhibit bacterial growth so efficiently that they are suggested to be used to prevent tomato crops from bacterial wilt. In a study, 10 types of gallotannins were suggested to be used as a measure to prevent bacterial wilt in tomato crops [63].

3.2. Saponins

The saponin extracted specifically from a traditional herb of China can help in cardiovascular diseases. In a randomized control trial performed on the mouse, Panax notoginseng saponins were reported to be able to reduce the apoptosis of cardiomyocytes suffering from oxidative stress [64]. It was achieved by reducing oxidative stress damage and balancing cell signaling pathways related to mitochondrial function. It means saponin can be used in the prevention of cardiovascular diseases (CVD). It is important as the prevention of CVDs can be achieved by a healthy diet and investigations into the components of food. *Balanites aegyptiaca* fruits contain five steroidal saponins and seven phenolic compounds which could be can helpful in the management of type 2 diabetes. In a randomized controlled clinical trial, the saponin and phenolic extract of this fruit was reported to be beneficial in controlling the blood glucose level and lipid profile in people suffering from type 2 diabetes [65]. The dosage of the extract was 400 mg per day and the study spanned 8 weeks.

The tumor-suppressing properties of many different types of saponins are well documented. The application of saponins with tumor suppression therapies is also advised. Saponins can cause apoptosis and cell cycle arrest in tumor cells [66]. Saponins are the components of food that can impart health benefits in optimal conditions.

In an application away from humans, tannins and saponins together can be used to reduce the energy loss caused by methane production in ruminant animal livestock. Several studies have bolstered the idea of regulating tannin and saponin contents in the feed given to ruminant livestock to reduce their methane production and conserve energy at the same time [67].

Many types of saponins possess beneficial attributes like preventing cardiovascular diseases, cancer, liver damage, and hyperglycemia.

Findings also suggest many more beneficial effects including immunomodulation, neuronal protection, and anti-inflammatory effect [68]. Saponins can act as effective adjuvants in vaccination procedures even in low quantities. There is a lot of evidence supporting their efficiency in acting as an adjuvant in vaccination processes [27]. Many chemical studies have studied the mechanism by which pentacyclic triterpenoid and saponins show an anti-cancer effect [69]. Some types of saponins can reduce blood cholesterol levels by causing a decline in intestinal cholesterol absorption. Some specific saponins named steroid saponins may be the reason behind the cholesterol-lowering effect of garlic [70]. Investigations into the food components that can reduce cholesterol levels are important because they can help in detecting beneficial foods for this purpose. Some specific types of saponins found in *Allium minutiflorum* were found to have an efficient anti-fungal effect [71]. A specific type of saponin present in the Ginseng herb called Ginsenoside was found to have an anti-cancer effect on human prostate cancer cells [72]. It underlined the importance of saponin as an anticancer component of food. This can be an important nutritional approach for cancer prevention. The specific saponins that are present in *Sorghum Bicolor* have been studied to have an antimicrobial effect on pathogenic gram-positive bacteria specifically [73]. Certain saponins can help in reducing cholesterol in the blood. A saponin that named Diosgenin, which is a steroidal saponin extracted from Yam, can reduce the cholesterol in serum and liver, increase plasma HDL, and improve antioxidant efficiency [74]. Food components that can reduce the occurrence of cardiovascular diseases and improve antioxidant efficiency are very important in the prevention of diseases by the means of healthy nutrition. Some specific examples of saponins showed an anti-tumor effect but are devoid of any hemolysis effect. Two examples of saponins like these were given by Gauthier et al. [75], explaining their possible application in tumor therapy and prevention because they don't have the hemolysis effect like the other saponins.

3.3. Phytic acid

The topical application of inositol hexaphosphate can help in the recovery after breast surgery. In a randomized control trial, it was found that inositol hexaphosphate can help women receiving chemotherapy after breast surgery avoid the side effects of their treatment [76]. In another randomized, double-blind, placebo-controlled, crossover study, it was found that inositol hexaphosphate (Phytic acid) can help in reducing the amount of uric acid in the serum of people with hyperuricemic conditions while fasting. Thiry one human subjects were given 600 mg of inositol phosphate (IP6) twice daily and at this concentration, phytic acid was able to help people suffering from hyperuricemia [77]. It indicates that hyperuricemia can be managed by adding healthy amounts of phytic acid to the diet. Diabetes-related complications can be reduced by dietary intake of IP6. It can prevent metal-catalyzed protein glycation that is seen to trigger diabetes-related diseases. In a randomized crossover trial, 1 and 2 μM concentrations of IP6 were linked to lower occurrence of metal-catalyzed protein glycation end products [78]. Since protein glycation end products are considered the pathophysiological mechanisms of diabetes progression, dietary phytic acid can be important in the prevention of this disease. Phytic acid from rice bran can reduce the risk of developing colon cancer in rats [79]. The tannins and phytic acid present in 27 varieties of Canola (*Brassica napus* L.) have been found to show DPPH free radicle scavenging activity indicating their behavior as antioxidants [80]. Phytic acid is proven to be able to reduce the pathology of amyloid-beta protein in the cell and mice models, showing that it can use in the prevention of Alzheimer's disease [81]. In the food industry, phytic acid can be used to prevent the oxidation of stored apple juice because it can inhibit the polyphenol oxidase enzyme responsible for oxidation [82]. In the case of environmental impact, phytic acid can prevent the corrosion of iron in acidic conditions, indicating a possible environmental application [83]. Although there is not much understanding about the beneficial effects of phytic acid, evidence of its antioxidant effects is constantly increasing [84]. Phytic acid is stated as a better chelating agent than EDTA and even less toxic when used in dentistry procedures [85]. With its antioxidant effect becoming popular, it was found that phytic acid may also be able to prevent breast, ovarian, and liver cancer if its effects on cell lines are replicated in the body [86]. These results were derived from biochemical assays and antioxidant assays. For a 50% reduction in cancer growth, different concentrations of phytic acid, ranging from 3.45 to 1.66 mM, were found to be sufficient. Along with this anti-cancer effect, phytic acid also showed an antioxidant effect. The study concluded that dietary antioxidants and anti-cancer agents in preventing cancer progression and maintain health in an organism. According to one study, phytic acid may be able to help alcoholics because phytic acid and other polyphenols were able to prevent cells from alcohol-induced oxidative stress by blocking ROS [87]. A study in mice confirmed that phytic acid can reduce hyperlipidemia and oxidative stress by increasing lipid excretion and activating antioxidants and lipogenic enzymes [88]. The weight gain caused by a high fat diet was also suppressed by feeding rice bran and phytic acid. They also exerted a normalizing effect on the hepatic lipogenic enzymes. Reduction in the activities of the intrinsic antioxidant enzymes was also reverted by rice bran and phytic acid. It confirmed that dietary components like phytic acid is playing a significant role in maintaining the healthy functioning of lipid metabolism and antioxidant activity. Another *in vitro* study on human colonic epithelial cells highlighted the efficiency of phytic acid in inhibiting lipid peroxidation [89]. Phytic acid at the concentrations of 100 μM and 500 μM effectively inhibited the decay of linoleic acid showing an inhibitory effect on lipid peroxidation. Lipid peroxidation can lead to carcinogenesis and cell death and phytic acid's ability to prevent this is of importance in the field of cancer prevention and health management. It reflects the efficiency of phytic acid in the management of reactive oxygen species in the cell. Phytic acid may also help in dealing with type 2 diabetes because it can improve insulin sensitivity in the adipocytes [90]. Phytic acid in concentrations in the diet can impart numerous health benefits like cancer prevention, antioxidant activity, glucose metabolism regulation, etc.

3.4. Lectins and hemagglutinins

Lectins are known to affect cancer cells in a way that can be utilized in cancer therapy and diagnosis. Lectins are recently being explored for their application in targeted nano-vaccines that can be used in cancer immunotherapy [91]. In a very elaborate study, it was reported that A dietary lectin called Wheat Germ Agglutinin (WGA) can target leukemia cells and agglutinate them when ingested in small amounts with no effect on normal cells [92]. It is also more efficient than other lectins in its anticancer effects. The dose- and time-dependent manner of WGA was also explored in the study along with its binding and killing potential. Although the anticancer effect of WGA is highly explored, its impact on hematological malignancies has not explored to that extent. Lectins exclusively from the *Phaseolus acutifolius* (Tepary bean) are being explored for their potential in treating colon cancer [93]. The dosage of 50 mg/kg for six weeks was efficient in reducing the tumorigenesis but without any detectable apoptotic activity. The antiproliferative activity was attributed to a decrease of the signal transduction pathway protein *Akt* and an increase of caspase 3 activity. Multiple mechanisms of cancer prevention are already reported from numerous kinds of lectins.

The lectins present in our body normally play certain roles in maintaining immunity by detecting and identifying pathogens by recognizing the glycans on them, i.e. collectins and galectins are types of lectins in our bodies. Lectins from these families are secreted by alveolar epithelium cells and play a role in neutralizing pathogens. They play many roles in the immune function of the respiratory system Casals et al. [94]. A dietary lectin from bananas called banana lectin is showing a promise in beneficial effects as they are reported to be able to inhibit reverse transcriptase activity of HIV-1 [95]. The clinical effects of lectins are to be considered very important in molecular interactions relevant to human nutrition.

3.5. Protease inhibitors

Bowman-Birk inhibitor from soybean may be used in the prevention and treatment of HIV because it is reported to be able to prevent the entry of the virus into the macrophages [96]. The ability of this protease inhibitor to inhibit the entry of HIV is very important because it can indicate the possibility of dietary protease inhibitors acting as defense mechanisms against viral infections and also showing an immunomodulatory effect. In an animal model of Guillain-Barré syndrome, Bowman-Birk inhibitor was suggested to be a potential therapeutic agent [97]. There is a serine protease inhibitor that is present in potato tubers that are reported to be an immunomodulator that can be used in treating visceral leishmaniasis [98]. Ulinastatin is an example of a protease inhibitor present in the human body. In a recent clinical, randomized, control trial, Ulinastatin was suggested to be a good agent to prevent sepsis in critically ill patients if used along with Rhubarb extract [99]. The trypsin inhibitors present in the peanut are thought to be the reason behind the hungriness-reducing effect of peanuts. This effect can be used for several good effects like managing weight and preventing weight gain by eating peanuts as a snack. Hence, investigating particular types of peanuts that have optimal amounts of these trypsin inhibitors is important. A Brazilian peanut type is considered good because it has been reported to have a good hungriness-reducing effect [100]. A trypsin inhibitor specifically present in tamarind is linked to a hungriness-reducing effect that can be used to control weight and prevent weight gain. Research on Wistar rats having obesity-induced metabolic syndrome, the trypsin inhibitor from tamarind was reported to reduce the food intake and inflammation [101]. A specific trypsin inhibitor extracted and identified in *Cassia leiandra* seeds was reported to be good against *Aedes aegypti* mosquitoes [102]. This means it is a naturally occurring compound that can be used to control the mosquito population and prevent dengue virus infection. Most of the time, anti-nutrients are present in food crops of agricultural importance. The food crops grown and consumed worldwide are not at all anti-nutrient-free. For example, Chickpeas are popularly regarded as nutritious and delicious but people also need to be careful because of their rich anti-nutritional constituents. The food preparations of chickpea are planned in a manner that reduces anti-nutritional components. Raw chickpea is known to have protease inhibitors and amylase inhibitors along with many other anti-nutrients [103].

4. Adverse effects of anti-nutrients

4.1. Tannins

Tannin has been linked to a decline in serum transferrin receptor activity and hemoglobin by a study in stunted overweight adolescents [104]. The tannins present in tea have been connected with lower serum hemoglobin levels [105]. The study concluded that tannins in a diet can profoundly influence the hematological iron conditions of a person and tannins can be introduced in a diet from various food products and drinks. Exploring the numerous molecular interactions of different molecules with nutrients is very important in the field of nutrition. Because these interactions can completely derail the iron enrichment strategy made for the reduction of the prevalence of anemia in a population. Through hydrogen bonding and hydrophobic association, tannins can bind to proteins and phospholipids with greater affinity than sugars [106]. Thus, interfering with the structure and function of these molecules. As proteins and phospholipids are crucial for life, therefore, the molecules that can affect their functioning should be kept in check. Tannins behave as anti-nutrients because of their binding property to nutrients. Tannins that are present in mango (*Mangnifera indica*) can bind with iron to form complexes that in turn affect the growth of gut microbes [107]. Molecules that can adversely affect the iron status and microbiome's health can greatly reduce the health of a person because the normal functioning of both of these physiological functions is essential for health. In a study on rat intestinal α-glucosidases, it was found that ellagitannin and galloyl glucose can harm the maltase and sucrase activity [108]. In a study performed on lactating cows, it was reported that dietary intake of a condensed type of tannins can bring a decline in milk production and impact lactation in a dosage dependent manner [109]. Tannins are known to inhibit pancreatic lipase which can reduce lipid absorption [110]. In higher quantities, they can be harmful to lipid nutrition, and in optimal lower quantities, they can be used to treat or prevent dyslipidemias. Some specific tannins can affect the structure of some specific proteins. They are confirmed to negatively affect the structure of bovine serum albumin protein structure. Tannins like pentagalloyl glucose, gallic acid, and ellagic acid can make the bovine serum albumin to unfold when administered in the high concentrations of 100–500 μM, according to research [111]. Plants that are rich in tannins, when their unused parts are thrown as litter into the soil, can create an unbalance in nature. Too many tannins from too much plant litter can negatively affect the necessary enzymes in the soil and create an unbalance in nature [112]. A type of condensed tannin called procyanidin can make complexes with α-amylase and irreversibly inactivate the enzyme's functionality [113]. Tannin is another anti-nutrient that is also considered a great concern for damage in humans, it also forms complexes which are not easily digestible interfere with proteins, and may block the functions of the digestive enzymes [114]. In a previous study by Butler [115], it was reported that tannins can cause adverse effects on the nutritional status by damaging the intestinal layer, reducing iron absorption, and imparting some carcinogenic effects. Tannins can inhibit enzymes like α -amylase, trypsin, and lipase in dosage dependent manner. Tannins specifically from sorghum are reported to inhibit enzymes like α-amylase, trypsin, and lipase in rabbits and also reduce the absorption of calcium when they are in high concentration in their diet [116]. This enzyme inhibition ultimately caused a decline in the weight gain of rabbits. The efficiency of tannins to inhibit the trypsin enzyme depends on their degree of polymerization. The procyanidin tannins and other polyphenols present in wine can inhibit trypsin enzyme activity [117]. Tannins can interact with proteins because they have many hydroxyl groups that can have a hydrophobic association with proteins. Plant food like pomegranate, cranberry, and cocoa contain some specific types of tannins called proanthocyanidins and ellagitannins that can interact with digestive enzymes like α-amylase and inhibit their action [118]. Digestive enzymes are very important in maintaining the proper functioning of physiological processes. Tannins inhibit these enzymes can greatly cause an impact on the health and development of a developing child. While the excess concentration of tannins is harmful, the optimal concentrations seem to contribute towards the maintenance of a balanced blood glucose level.

4.2. Saponins

In legumes, saponins are the anti-nutrients that are mainly for preventing infections due to microbes and herbivory. Saponins, in legumes at lower doses moderately show toxicity but at high concentrations in diet cause problems [119]. It can change the integrity of the intestinal epithelial cells and alter the permeability of the intestinal epithelial layer, which can let toxic substances present in the gut easily enter the circulatory systems and cause toxicity [120]. A previous study by Jenkins and Atwal [121] reported that dietary saponins can reduce the growth, feed proficiency in chicks, and also affect the absorption of vitamin A and E as well as lipids. Certain types of saponins can cause erythrocytes to undergo programmed cell death and can also cause cell rupture. Saponins were reported to be able to lyse erythrocytes by damaging the membrane structure [122]. Even a saponin concentration of 15 μg/ml can start causing erythrocytes cell deaths because some saponins can induce a high cytosolic influx of calcium ions that can damage the cell membrane. Moreover, saponins are recently being explored for their effects in treating numerous diseases, it should be taken into account that their harmful effects will target people that have iron or erythrocyte-related diseases [123]. Their property of causing erythrocyte cell death was also stated by Makkar et al. [124], and this property was attributed to their ability to interact with the membrane molecules of erythrocytes. Their efficient ability to kill erythrocytes is also suggested by Sharma et al. [125] to be useful in determining saponins by the TLC method using erythrocytes for detection. Studies on finding a way to eliminate the erythrocyte-killing property of steroidal saponins so that they can be used for theirbeneficial properties are pointed out by many researchers like Liu et al. [126]. Saponins present in the leaves of *Veronia amygdalina* show an ability to lyse the erythrocyte [127]. Along with its use in traditional medicine in Nigeria, this shrub (*Veronia amygdalina*) is also used as a soup ingredient and is being explored for its phytochemical content. Saponins present in the shrub can have both beneficial and adverse effects but the strong hemolytic effect is concerning. Although saponins usually remain in the gastrointestinal tract, they can get into the blood in some cases like the eroded intestinal mucosa. This means these saponins can cause some serious pathological conditions in people that have eroded the intestinal mucosal layer because of a disease. There are several recent studies aimed at finding out the types of saponins present in plants and their physiological effects in humans that are either beneficial or adverse. Saponins were evolved by the plant to discourage insects from feeding on them. Several mechanisms were used by the plants to achieve this. One of them is shown by some saponins that can bind and inhibit the enzymes in the body of insects and interfere with the physiological processes of insects. Several saponins and phenolic compounds were studied and their inhibitory effects on five types of α-carbonic anhydrase enzymes were reported in a study by Koz et al. [128]. By binding and inhibiting the α-carbonic anhydrase enzymes, these plant-produced saponins can interfere with the abilities of insect physiology like respiration, acid-base balance, etc. A concentration of 500 μg/ml can inhibit pancreatic lipase activity, which can reduce lipid absorption. Saponins from the *Panax ginseng* herb are reported to inhibit pancreatic lipase activity and reduce lipid absorption preventing weight gain in mice fed on a high-fat diet [129]. Specific saponins that are present in Neem (*Azadirachta indica*) can inhibit amylase enzymes in some insects and even kill them by this inhibition [130]. Although the effects of saponins are not extremely harmful in humans but can impact a whole population of insects, by increasing death rates in their population. Saponins are used in the defense mechanisms of a plant but in humans, they may create nutritional complications. Several studies suggest the ability of saponins to bind with pancreatic lipase and reduce the absorption of lipid [131].

4.3. Phytic acid

In fishes, phytic acid is reported to be particularly dangerous in high concentrations. In a study on grass carp (*Ctenopharyngodon idella*), phytic acid was fed during 60 days of growth. Different concentrations were fed to different groups. Skin hemorrhage and lesions along with a reduction in immune function were found [132]. The concentration of phytic acid below 1.70% of the total diet was found to be critical. Although the interactions of phytic acid with other minerals and micronutrients are much explored, the dosage-dependent manner of phytic acid on magnesium absorption is not that explored. But in a study, it was presented that, phytic acid, in the amount that it is normally present in the white wheat bread, can reduce the absorption of magnesium [133]. Magnesium is very crucial in numerous metabolic processes and the detections and exploration of dietary molecules that can affect the absorption of it are important in the view of nutrition science. Phytic acid can affect the amount of magnesium our body can absorb from white bread. In earlier research by Prasad et al. [134], it was reported that Egyptian boys from the study who consistently consumed bread and beans were found to be deficient in zinc. It is now very well accepted that phytate present in food crops is one of the main causes of zinc deficiency. Phytate-like anti-nutrients affect the zinc in a dose-dependent manner. The polyphenolic compounds and phytic acid together can greatly reduce the efficiency of iron absorption and utilization in young women [135]. In humans, phytic acid can inhibit the absorption of essential minerals and cause mineral deficiencies. Taking care of phytic acid concentrations in a diet is a good idea to avoid these mineral deficiencies. In animals, on the other hand, several types of livestock suffer from growth retardation and other defects when subjected to a diet with high levels of phytic acid [136]. Phytic acid can impair the absorption of magnesium, calcium, and iron but according to research done on mice, its deleterious effect can be reduced by the introduction of fructo-oligosaccharides in the diet [137]. This gives us a chance to reduce the harmful effects of a diet rich in phytic acid by adding healthy foods that can counteract these harmful effects. The efforts in the reduction of iron deficiency resulted in an iron bio-fortified bean but the benefits were prevented by the presence of phytic acid, which indicates that bio-fortification alone can't be the solution [138]. In an *in vitro* study on the Caco-2 epithelial cell model, it was given that phytic acid in the presence of CaCl2 reduced iron absorption [139]. Iron is an important micronutrient that performs many physiological functions either in the form of a co-factor or a protein component. Unlike non-heme iron, inorganic iron can have its absorption disrupted by many molecules including phytic acid. Even though phytic acid is present in cereals, the bio-fortification of cereal-based food products with iron is the main strategy to tackle the problem of anemia by the Governments. A study on piglets found out that phytic acid can reduce growth performance and the ability of sodium absorption in the intestine [140]. Consumption of bread with low phytate bread may not help in improving iron absorption in the body according to a dietary intervention study. A twelve-week, randomized dietary intervention study done on Swedish women found out that while the high phytate containing wholegrain rye bread did not affect the iron status, the low phytate containing wholegrain rye bread was able to reduce the iron in the blood [141]. The normal bread contained phytate in the concentration of 77 mg/100g while the bread with reduced phytate had less than 1 mg of phytate per 100g of bread. High phytate diets can reduce iron status. Mediterranean diets are high in phytate. Although they are high in phytate, that is not found to have any effect on iron and selenium status. In a one-year randomized clinical trial, no improvement in iron and selenium status was achieved by introducing the Mediterranean diet in elderly Europeans [142].

4.4. Lectins and hemagglutinins

The lectins specifically in black kidney beans are known to be able to bind to hemoglobin and immunoglobulin E. However, this activity is affected by low pH and high temperature. Prolonged high-temperature treatment can reduce the negative effects of lectins from black kidney beans [143]. They are also reported to increase the growth of cancer cells [144]. In experimental animals, the lectins present in Tepary bean have been reported to have anti-nutritional effects like a decrease in body weight and food intake when given in a dose of 50 mg/kg [93]. Indicating that the excess consumption of lectins-rich food can be detrimental to one's health. In insects, some lectins are reported to be harmful. A water-soluble *Moringa oleifera* lectin found in *Moringa oleifera* seeds has a chitin-binding activity and enzyme binding activity that can prevent larvae from *Anagasta kuehniella* from growing [145]. It shows many harmful effects on larval nutrition. These effects that it causes on nutrition are negative but their application can be positive. For example, they can be used in pest control. Similar effects of this water-soluble lectin from *Moringa oleifera* seeds are also reported to do the same with *Aedes aegypti* larvae, inhibiting nutrition, and affecting the growth of larva [146]. This effect is negative but its application in mosquito population control is positive. In a study on mice, it was reported that a specific type of lectin called concanavalin A can induce liver injury in high dietary concentrations (10 mg/kg) and this effect can be prevented by a compound called Nobiletin [147]. Concanavalin A is so efficient in inducing liver injury that its ability is extensively studied for its mechanism. Concanavalin A is used to induce liver injury in studies that are aimed to find compounds that can prevent and treat liver injury. Concanavalin A is being extensively researched for its application in pest control because of its negative effect on insect survival. Promising examples of its application exist. For example, it can be used for pest control of *Bactericera cockerelli* because it can cause apoptosis of the pest's midgut cells [148]. According to Jönsson et al. [149], the human leptin hormone system may not be well adapted to a cereal-based diet and the occurrence of diseases like obesity and diabetes might be because of this. It suggests that the constituents in the cereal-based diet that can be the cause of these diseases might be lectins. It was stated based on the experiment on pigs that cereal-based diets that have lectins in them cause leptin resistance whereas cereal-free diets prevent leptin resistance [150]. Specific lectins present in red kidney beans and jack beans can cause Diarrhoea [151]. Lectins can affect the intestinal mucosa and cause a myriad of harmful effects like-nutrient loss, infections, reduced absorption, and agglutinate RBCs.

4.5. Protease inhibitors

Another class of anti-nutrient is a protease inhibitor, mainly trypsin and chymotrypsin are the protease inhibitors which are found in plant-based foods and cause various concerns. It was reported that the presence of these inhibitors in the raw legumes is responsible for the retardation of growth. Trypsin inhibitors decrease protein digestibility and pancreatic hypertrophy [152]. Because of this, these inhibitors can have a huge impact on a child's growth. A protease inhibitor is present in soybeans and it belongs to the Bowman-Birk family of protease inhibitors. It can very efficiently reduce protein digestion. As soy milk is consumed globally nowadays, the prevalence of protease inhibitors can happen due to food-production defects. So, the strategies for treating these inhibitions are being explored. Epigallocatechin gallate can make complexes with soybean protease inhibitors and prevent its adverse effect possibly [153]. Milk produced from soybean called soy milk can have residual soybean protease inhibitors that can be deactivated by Stevioside [154]. Hence, it is needed to prevent protease inhibitors from acting on it. The knowledge of molecular interactions that can prevent the antinutrients from acting is very important if we want to eliminate the effects of these molecules. The addition of these anti-nutrient reductions or inactivation processes in industrialized production methods can make these food products healthy. This can improve the palatability, production, and acceptance of these food products. The Kunitz trypsin inhibitor that is present in soybean is studied extensively for years now and several reduction strategies are confirmed in documentation [155].

Protease inhibitors can adversely affect the digestive enzymes of insects and therefore, they can be used in pest control. Soybean trypsin inhibitor is reported to be able to inhibit the trypsin enzyme of the diamondback moth and inhibit its growth [156]. Although, these defensive strategies used against insect pests are functional in the crop system they could create nutrition-related problems in humans.

5. Conclusions

Anti-nutrients show both beneficial and adverse effects. The adverse effects are caused by unbalanced concentrations. While the beneficial effects are imparted due to the optimal concentrations of anti-nutrients. It might be unbalanced in certain conditions and it is not just the mere presence of these anti-nutrients that is the cause of problems.

Interestingly, sometimes both effects are shown by the same molecule. However, many anti-nutrient molecules show only adverse effects. Anti-nutrients include a large number of molecules that are frequently present together in different concentrations and combinations in foods. This creates a situation in which a standard large-scale strategy cannot be applied to all foods. The complete elimination of the anti-nutrients may not be the solution either. Coordination among the clinical findings is needed to get a better understanding of all the possible effects of an anti-nutrient molecule. The outcome of a collective understanding of an anti-nutrient molecule may encourage a better strategy for reduction. Even it may clarify whether we need to remove them or not. While exploring the numerous molecular interactions of different molecules with nutrients is very important in the field of human nutrition. Therefore, all the possible effects of anti-nutrients must be examined thoroughly in human subjects before proceeding with a full-scale reduction strategy.

Credit author statement

All authors equally contributed to Writing- Original MS draft preparation, Reviewing and Editing of manuscript. All authors approved the final manuscript for submission.

Conflict of interest

The authors declare no conflict of interest.

Ethical statement

This study does not involve any human nor animal testing.

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Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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