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REVIEW ARTICLE

Antinutrients in Plant-based Foods: A Review

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Abstract: Modern society has easy access to a vast informational database. The pursuit of sustainable green and healthy lifestyle leads to a series of food choices. Therefore, it is of importance to provide reliable, comprehensive and up-to-date information about food content including both nutritional and antinutritional elements.

Nutrients are associated with positive effects on human health. Antinutrients, on the other hand, are far less popular for the contemporary man. They are highly bioactive, capable of deleterious effects as well as some beneficial health effects in man, and vastly available in plant-based foods. These compounds are of natural or synthetic origin, interfere with the absorption of nutrients, and can be responsible for some mischievous effects related to the nutrient absorption. Some of the common symptoms exhibited by a large amount of antinutrients in the body can be nausea, bloating, headaches, rashes, nutritional deficiencies, *etc*. Phytates, oxalates, and lectins are few of the well-known antinutrients.

Science has acknowledged several ways in order to alter the negative influence antinutrients exhibiting on human health. Mechanical, thermal and biochemical approaches act synergistically to provide food with lower antinutritional levels.

The purpose of this review was to synthesize the availability of antinutrients, clear their effect on the human body, and commemorate possible paths to disable them. This review provides links to the available literature as well as enables a systematic view of the recently published research on the topic of plant-based antinutrients.

Keywords: Antinutritional factors, Plant-based foods, Beneficial effect, Antinutrients, Food content , Biochemical approaches .

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1. INTRODUCTION

Food is an essential part of people's lives. Despite the world produces enough food for everyone, over 800 million people still go to bed hungry [1]. Furthermore, malnutrition and hunger-related diseases cause over 60% of deaths [2]. Eliminating hunger and malnutrition is one of the most fundamental challenges facing humanity [3]. Moreover, food sufficiency is not the last aspect of importance; food nutritional quality is of critical demand as well as the effects of the accepted food portion, in particular. From this point of view, the topic of the present review antinutrients raises essential questions about human health and contributes to the understanding of what people actually eat and what the possible resulting effects can be.

Antinutritional factors are primarily associated with compounds or substances of natural or synthetic origin, which interfere with the absorption of nutrients, and act to reduce nutrient intake, digestion, and utilization and may produce other adverse effects. Antinutrients are frequently related to plant-based, raw or vegan diets and are naturally synthesized in plants [4]. Some of the common symptoms exhibited by a large number of antinutrients in the body can be nausea, bloating, headaches, rashes, nutritional deficiencies, *etc*. [5]. On the other hand, such chemical compounds can be evidently advantageous to humankind when consumed wisely. In fact, plants, for their own defense, primarily use antinutrients.

Although people's sensitivity to antinutrients widely differs adequate food processing is initially recommended to reduce antinutritional factors [6]. A person cannot eliminate antinutrients once they have been introduced to the body. Eliminating and reintroducing specific foods that contain antinutrients can clear the correlation between symptoms and effects on human health. In this regard, the biochemical effects of the anti-nutritional factors are an object of research interest [7 - 10] 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 [11, 12].

Antinutrients are found in their highest concentrations in

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grains, beans, legumes and nuts, but can also be found in leaves, roots and fruits of certain varieties of plants. The major antinutrients found in plant-based foods are phytates, tannins, lectins, oxalates, *etc*. Antinutrients in vegetables, whole grains, legumes and nuts are a concern only when a person's diet is composed exclusively of uncooked plant foods. Oxalate, for instance, prevents calcium from being absorbed in the body by binding with it [13]. Raw spinach, kale, broccoli and soybeans usually contain oxalates [14]. When consuming excessive tannins, which are associated with tea, wine, some fruit, and chocolate, enzymes responsible for protein absorption may be inactivated. Phytates are present in grains, nuts and seeds, while peppers, eggplants, and tomatoes contain lectins. Phytates consumption may lead a lower mineral absorption and lectins are able to cause various reactions to the body [15]. Saponins, on the other hand, have been linked to red blood cells damaging, enzyme inhibition and thyroid function intervention [16].

There are several approaches to oppose antinutritional factors. Modern biotechnology`s techniques could reduce the level of certain allergens and antinutrients in food. Genome editing biotechnology can create mutations and substitutions in plant and other eukaryotic cells based on nuclease-based forms of engineering such as the TALENS (Transcription Activator-Like Effector Nucleases) or the CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)/CRISPR-Associated Systems (CAS) [17, 18]. Providing an enhanced level of prebiotic in the body can positively influence the effects of antinutrients [19]. A classic approach to remove antinutrients is to treat the product thermally, use methods such as extrusion, autoclaving, hydrotechniques, enzymatic and harvest treatments, *etc.* [20].

The nutritional value of foods strongly depends on their nutritional and antinutritional composition. This review was designed to synthesize the availability of antinutrients, clear their effect on the human body, and commemorate possible paths to disable them.

2. ANTINUTRIENTS IN PLANT-BASED FOODS

2.1. Lectins

Lectins, particularly abundant in plants, are proteins or glycoproteins of non-immune origin. They have the ability to bind, without modifying, to either carbohydrates or glycoconjugates (glycoproteins, glycolipids, polysaccharides). They can successfully recognize animal cell carbohydrates, which corresponds to the Latin derivation of the word legere meaning to select [21]. Lectins have a variety of roles. They can bypass human defense system and travel all over the body causing diseases (*i.e.* Crohn's disease, Coeliac-Sprue, colitis, *etc*.) by breaking down the surface of the small intestine [22]. When large quantities of lectins are introduced in the body, the gut wall develops holes, and intestinal permeability, causing the leaky gut syndrome. Lectins can make cells act as if they have been stimulated by insulin or cause the insulin release by the pancreas. Lectins can also cause autoimmune diseases by presenting wrong immune system codes and stimulating the growth of some white blood cells [23, 24]. This may possibly lead to cancer but lectins have not yet been recognized as cancer causing.

Not all variety of lectins are toxic or responsible for intestinal damage. Lectins can be found in plant species such as wheat, beans, quinoa, peas, *etc.* [25]. As grains are a common part of the birds' diet, it has been found that birds themselves are resistant to grains lectins [26]. Acne, inflammation, migraines or joint pains can be caused by the consumption of lectins [27]. Lectins are usually found in the hull so choosing white rice can lower the lectin intake. Heating plant sources in the process of cooking can significantly lower the amount of lectins in them. White potatoes, for instance, have a higher lectin content compared to sweet potatoes [28]. Almonds are also a richer lectin source than peanuts [29].

2.2. Trypsin Inhibitors

Trypsin inhibitors occur in a wide range of foods like chickpeas, soybeans, red kidney beans, adzuki beans, mung beans and other representatives of the Leguminoseae, Solanaceae, and Gramineae families [30]. Ten percent of the world's dietary protein is derived from grain legumes [31]. Trypsin inhibitors redound to the loss of trypsin and chymotrypsin in the gut, thus preventing protein digestion. Excess trypsin synthesis and burden on sulfur-containing amino acids in requirement of the body are due to the release of cholecystokinin triggered by trypsin inhibitors [32].

2.3. Alpha-amylase Inhibitors

Inhibition of α-amylase is considered a strategy for the treatment of disorders in carbohydrate uptake, by reducing insulin levels, as well as, dental caries and periodontal diseases [33]. Amylase inhibitors are substances that bind to alpha amylases making them inactive [34]. Two roles of α-amylase inhibitors have been identified. The primary function of inhibitors is protecting the seed against microorganisms and pests, and the other function is the inhibition of the endogenous α-amylase [35]. However, the instability of this inhibitor under the conditions of the gastrointestinal tract and being a very heat-liable constituent results in its failure to be used as starch blocker [36]. It is used to control human diabetes type two [37] and finds several applications in the food industry [38, 39].

2.4. Protease Inhibitors

Proteases are key cell-process-regulation enzymes that are found in all cells and tissues. Protease inhibitors are commonly present in raw cereals and legumes, especially soybean. Protease inhibitors bind to their target proteins reversibly or irreversibly. Growth inhibition, pancreatic hypertrophy [40], and poor food utilization [41] are associated with protease inhibitors' antinutrient activity. Exopeptidases remove amino acids from the C- or N-terminus, whereas endopeptidases are capable of cleaving peptides within the molecule [42]. Grain eating birds have evolved digestive enzymes that are resistant to grain protease inhibitors [26]. In human volunteers and in animal experiments, high levels of protease inhibitors lead to an increased secretion of digestive enzymes by the pancreas [43].

Table 1. Antinutrients in different foods [29, 68 - 80].

Source	Type	Amount
Legumes (soya, lentils, chick peas, peanuts, beans)	Phytic acid Saponins Cyanide Tannins Trypsin inhibitor Oxalates	386-714 mg/100g 106-170 mg/100g 2-200 mg/100g 1.8-18 mg/g 6.7 mg/100g 8 mg/kg
Grains (wheat, barley, rye, oat, millet, corn, spelt, kamut, sorgho)	Phytic acid Oxalates	50-74 mg/g 35-270 mg/100g
Pseudo-grains: quinoa, amaranth, wheat, buckwheat, teff	Phytic acid Lectins Saponins Goitrogens	0.5-7.3 g/100g 0.04-2.14 ppm
Nuts: almonds, hazelnut, cashew, pignola, pistachio, brazil nuts, walnuts, macadamia, *etc*.	Phytic acid Lectins Oxalates	150-9400 mg/100g 37-144 µg/g 40-490 mg/100g
Seeds: sesame, flaxseed, poppy seed, sunflower, pumpkin	Phytic acid Alpha-amylase inhibitor Cyanide	1-10.7 g/100g 0.251 mg/mL 140-370 ppm
Tubers: carrot, sweet potato, Jerusalem artichoke, manioc (or tapioca), yam	Oxalates Tannins Phytates	0.4-2.3 mg/100g 4.18-6.72 mg/100g 0.06-0.08 mg/100g
Nighshades: potato, tomato, eggplant, pepper	Phytic acid Tannins Saponins Cyanide	0.82-4.48 mg/100g 0.19 mg/100g 0.16-0.25 mg/100g 1.6-10.5 mg/100g

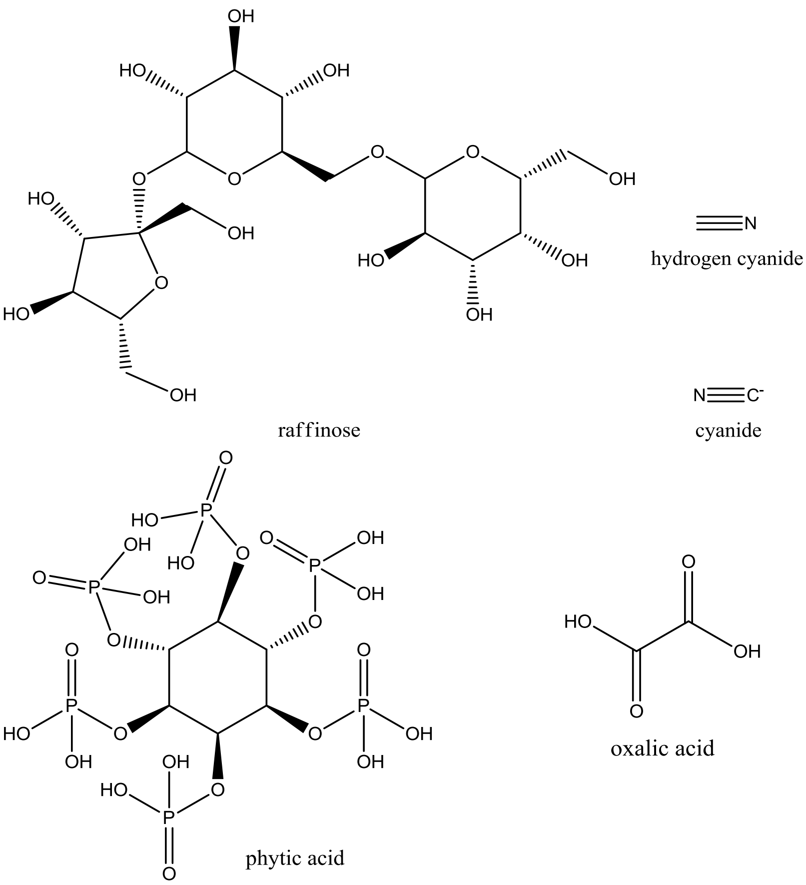

Fig. (1). Structure of some antinutrient substances.

2.5. Tannins

Plant tannins are a major group of antioxidant polyphenols found in food and beverages that attracts research interest with its multifunctional properties to human health. Tannins are oligomers of flavan-3-ols and flavan-3, 4-diols that are concentrated in the bran fraction of legumes [44]. Grapes and green tea are rich in this water-soluble polyphenol [45]. Tannins exhibit antinutritional properties by impairing the digestion of various nutrients and preventing the body from absorbing beneficial bioavailable substances [46]. Tannins can also bind and shrink proteins. Tannin-protein complexes may cause digestive enzymes inactivation and protein digestibility reduction caused by protein substrate and ionisable iron interaction [47].

2.6. Phytates

Phytates occur in several vegetable products. Seeds, grains, nuts and legumes store phosphorus as phytic acid in their husks in the form of phytin or phytate salt. Their presence may affect bioavailability of minerals, solubility, functionality and digestibility of proteins and carbohydrates [41]. Phytic acid is most concentrated in the bran of grains [48]. In legumes, phytic acid is found in the cotyledon layer and can be removed prior to consumption [49]. The digestive enzyme phytase can unlocked the phosphorus stored as phytic acid. In the absence of phytase, phytic acid can impede the absorption of other minerals like iron, zinc, magnesium and calcium by binding to them [50]. This results in highly insoluble salts that are poorly absorbed by the gastrointestinal tract leading to lower bioavailability of minerals. Phytates also inhibit digestive enzymes like pepsin, trypsin and amylase [51].

2.7. Goitrogens

Hypothyroidism is increasing daily worldwide as the thyroid gland is highly sensitive to stress and environmental stimuli [52]. Goitrogens interfere with iodine uptake and thus, affect thyroid function. Vegetables from the genus Brassica *i.e.* broccoli, cabbage, cauliflower, Brussels sprouts and kale are some of the goitrogen rich foods [53]. The consumption of cruciferous vegetables affects triiodothyronine (T3) and thyroxine (T4) levels by causing hypothyroidism [54]. Concomitant factors can be insufficient water consumption and protein malnutrition [55].

2.8. Raffinose Oligosaccharides

Raffinose, stachyose and verbascose, all part of the Raffinose Family Oligosaccharides (RFOs), are synthesized from sucrose. Non-digestible oligosaccharides have a prebiotic effect in the lower intestine by promoting the growth of *Bifidobacterium* and *Lactobacillus* that inhibit pathogenic growth [56]. The absence of appropriate enzyme activity to hydrolyse RFOs (α-galactosidase) leads to the inability of humans and to digest RFOs an allow them to pass through the intestinal wall intact [51, 57]. A correlation between legumes consumption and the likelihood of intestinal discomfort has been drawn leading to symptoms like burping, abdominal pain, and bloating [57]. The presence of RFO in the daily food intake can interfere with the digestion nutrients [58]. RFO can reduce metabolizable energy and protein utilization [59]. Research has shown that RFO removal has improved the digestion of all amino acids increasing the overall nutritional value of the lupin diet [60].

2.9. Saponins

Some saponins (steroid or triterpene glycoside compounds) can be used for food while others are toxic. Saponins with a bitter taste are toxic in high concentrations and can affect nutrient absorption by inhibiting enzymes (metabolic and digestive) as well as by binding with nutrients such as zinc. Saponins are naturally occurring substances with various biological effects. In the presence of cholesterol, saponins exhibit strong hypocholesterolemic effect [61]. They can also lead to hypoglycemia [62] or impair the protein digestion, uptake vitamins and minerals in the gut, as well as lead to the development of a leaky gut [63].

2.10. Oxalates

Some organic acids can have antinutritional factors. Oxalic acid can form soluble (potassium and sodium) or insoluble (calcium, magnesium, iron) salts or esters called oxalates that are commonly found in plants *i.e.* leafy vegetables or synthesized in the body [64]. Insoluble salts cannot be processed out of the urinary tract once processed through the digestive system. Calcium oxalate can have a deleterious effect on human nutrition and health by accumulating kidney stones [65]. Cruciferous vegetables (kale, radishes, cauliflower, broccoli), as well as chard, spinach, parsley, beets, rhubarb, black pepper, chocolate, nuts, berries (blueberries, blackberries) and beans are some of the foods with high amounts of oxalates [66]. Most people can induct normal amounts of oxalate rich foods, while people with certain conditions, such as enteric and primary hyperoxaluria, need to lower their oxalate intake. In sensitive people, even small amounts of oxalates can result in burning in the eyes, ears, mouth, and throat; large amounts may cause abdominal pain, muscle weakness, nausea, and diarrhea [67].

Table **1** is revealing some food sources with the typical antinutrients contained in them as well as the amounts variables.

2.11. Exorphins

The alcohol-soluble proteins (proalimins) of cereal grains and dairy products called gliadins can be further degraded to a collection of opioid-like polypeptides named exorphins in the gastrointestinal tract [81]. Behavioral traits such as spontaneous behavior, memory, and pain perception can be affected by the bioactivity of food-derived exorphins [82]. Exorphins can also influence gastric emptying and intestinal transit by increasing its time [83]. The digestion of milk produces alpha-casein-derived exorphins [84]. Recent research suggests that epigenetic effects of milk-derived opiate peptides may contribute to gastrointestinal dysfunction and inflam-mation in sensitive individuals [85].

Fig. (**1**) pinpoints some of the widely speard antinutrients in plant-based foods.

2.12. Contextual Antinutrients

Some supplements or foods rich in certain nutrients can create reactions of an antinutrient nature. For instance, calcium-rich foods can impede iron absorption. There is also a mutual antagonism between zinc and copper during the absorption process, taking place in/on the intestinal epithelium [86]. Research literature suggests that phytosterols [87] and phospholipids [88] may reduce cholesterol absorption when added to nonfat foods. Some foods can interfere with medication absorption [89]. The most well publicized food-drug interaction is that of grapefruit and a variety of drugs. Bergamottin found in grapefruit juice inactivates drug-metabolizing enzymes. This is the reason why food interaction warnings are listed on some medical labels. Studies have found that resveratrol, found in red wine and peanuts, inhibits platelet aggregation, and high intakes could increase the risk of bleeding when consumed with anticoagulant drugs [90]. Canadian researchers have documented that black tea was a more powerful enzyme inhibitor than single-ingredient herbal teas (St. John's Wort, feverfew, cat's claw, *etc*.) [91]. Another well-known food-drug interaction is that of foods containing tyramine (chocolate, beer, wine, avocados, *etc*.) and mono-amine oxidase inhibitors (type of antidepressant) [92]. The most medically consequential food-drug interaction is that of vitamin K-rich foods (*e.g.* broccoli, spinach) and Coumadin, an anticoagulant prescribed to thin the blood and prevent clots [93].

3. ANTINUTRIENTS AND HUMAN HEALTH

While antinutrients can be problematic, some may also provide health benefits. The consumers should be aware of any possible effect whether beneficial and/or negative. Moreover, concentration-dependent effects must be considered. Data may be manipulated in respect of health related advantages so that chronic diseases management becomes possible [32].

Antinutrients are valuable active ingredients in food and drinks. When used at low levels, phytic acid, lectins and phenolic compounds as well as enzyme inhibitors and saponins have been shown to reduce blood glucose and/or plasma cholesterol and triacylglycerols. Furtermore, saponins are reported to act effectively in maintaining liver function, preventing steoporosis as well as platelet agglutination [94]. Meanwhile, phenolic compounds from plant sources, phytic acid, protease inhibitors, saponins, lignans and phytoestrogens have been demonstrated to reduce cancer risks. Another group of anti-nutrient compounds, like tannins, were found to possess possible antiviral [95], antibacterial [96] and antiparasitic effects [97].

Some compounds such as phytoestrogens and lignans have also been linked to induction of infertility in humans. Therefore, it is prudent to examine all aspects of food antinutrients, including their potential health benefits and methods of analyses [32].

The above mentioned implies that antinutrients could be valuable tools for managing various diseases. They might not always be harmful even though they lack nutritional value. What is most important is focusing on dosage intake in order to find the balance between beneficial and hazardous effects of plant bioactives and antinutrients, in addition to the chemical structure, time of exposure and interaction with other dietary components. Many factors influence their activity. They can both be considered as antinutritional factors with negative effects or non-nutritive compounds with positive health effects. Consumers' awareness is crucial especially when abnormal health conditions are established.

4. DISABLING ANTINUTRIENTS

Removing undesirable food components is essential to their quality improvement. Different techniques *i.e.* soaking, cooking, fermentation, radiation, germination and chemical treatment can come in as handy instruments for antinutritional disabling [98, 99]. The combination of several of the above-mentioned methods may be more effective in removing anti-nutrients than using a sole technique.

Soaking: Soaking can be seen as one of the easiest physical processes to remove soluble antinutritional factors. Soaking in distilled water, 1% $NaHCO_3$ and mixed salt solutions reduced total phenols, ortho-dihydroxyphenols, tannins and phytates by 33, 41, 35 and 21 percentages respectively [100]. Soaking decreased the total protein, soluble sugar and tannins, in soybean flour [101]. Soaking and sprouting grains, nuts, seeds, and beans are an excellent way to deactivate enzyme inhibitors [102]. However, lectin is not affected by this method of deactivation.

Fermentation: Fermenting assorted grain flour with *L. acidophilus* at 37°C for 24 h led to the reduction of phytic acid and polyphenol content [103]. Recent research has shown a general noticeable reduction in the entire antinutrient properties of soybean for a day of fermentation [104]. Ojokoh *et al*. [105] have studied the effect of fermentation on the antinutritional composition of breadfruit and cowpea flours showing a significant reduction of the hydrogen cyanide, oxalate and phytate content. Fermentation is reported to increase the protein content in chickpea by 13% and decrease the content of phytic acid by 45% [106]. Adeyemo *et al.* [107] assessed the effects of fermentation of sorghum at 0, 72 and 120 hours on trypsin inhibitor, protease inhibitor, phytate and tannin. A significant reduction of trypsin inhibitor (69%); protease inhibitor (30%); phytate (60%) and tannin (72%) was observed at 120 h with *L. plantarum* used as starter culture. On the other hand, *L. brevis* as starter appeared to be effective at 120h with 58% reduction of trypsin inhibitor; 40% of protease inhibitor; 70% of phytate and 56% of tannin.

Sprouting (Germination): Germination is one of the most effective processes for the reduction of anti-nutritive compounds *i.e.* phytate levels [108]. The trypsin inhibitor activity, amylase inhibitor activity and phytate content of soy-bean variety MACS-13 decreased with sprouting [109]. Kanensi *et al*. [110] report a lower antinutrient level of germi-nated amaranth seeds. The levels of tannins and phytate were insignificant. To overcome the antinutritional levels, Kajla *et al*. [111] also adopted the germination process in flax seeds. Other authors reaffirm that germination leads to increased nutritional and decreased anti-nutrients content in plant-based foods [112].

Heating: Cooking whole grains, beans and vegetables can reduce certain antinutrients such as phytic acid, tannins, and oxalic acid. Protease inhibitors are easily denatured by heat treatment due to their protein nature [113]. Research has shown that antinutrient levels are reduced with controlled heating at a temperature less than boiling for at least 15 minutes [114]. Autoclaving can also drastically decrease the content of tannins, phytic acid, hydrogen cyanide, trypsin inhibitors and oligosaccharides [6]. Cooking sweet potato leaves with lemon reduced polyphenols with 56% and lowered the oxalate levels [115]. Boiling bambara groundnut seeds for a period of 60 min significantly lowers the raffinose content and improves protein digestibility of the seeds [116].

Gamma radiation: Gamma radiation appeared to be a good procedure to decrease the level of trypsin inhibitor, phytic acid and oligosaccharides of broad bean between 5 and 10% [117]. However, Hassan *et al*. [118] documented that a 2 kGy dose had no significant change in the tannin content of two maize cultivars. Similar observations were reported by El-Niely [119] and Fombang *et al*. [120]. Low doses of gamma irradiation (0.5 and 1.0 kGy) Faba bean seeds significantly reduced antinutritional factors such as tannin and phytic acid [121]. Gamma radiation can be applied as a safe postharvest method to minimize antinutrients of millet grains [122].

Genomic technology: Genomic resources can be used as pathways to RNA interference and removing of antinutrient factors, but this technology has yet to be tried out *in vivo* [123]. Shukla *et al*. [124] designed zinc-finger nucleases construct to mutate the IPK1 gene in maze, one of the phytic acid biosynthesis genes because corn contains high levels of phosphorus stored in the form of phytic acid. Genome editing technology can increase crop quality but there is an ongoing argument about genetically modified organisms' safety [125].

CONCLUSION

Antinutritional factors are widespread food compounds that are especially challenging for those choosing a predominantly plant-based diet *i.e*. vegan, vegetarians, *etc*. Antinutrients can exhibit beneficial health effects if present in small amounts or cause nutrient deficiencies. Uninformed consumers may deal with some misleading information when the latter is not sufficiently available. Antinutrients may induce their undesirable effects when consumed above their upper limit. Harmful effects can also be due to antinutritional breakdown products. Thus, the presence of lectins, tannins, alkaloids, and saponins, goitrogens, inhibitors, *etc*. in foods may induce various reactions when the consumer is presented with little knowledge related to the environmental influence on the detoxification capacity of the human organism. Classic approaches and modern agricultural biotechnological programs can serve as antinutritional removal tools. However, health risk factors can be avoided when a daily sustainable diet lying on a sound scientific basis is introduced.

CONSENT FOR PUBLICATION

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CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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