

Review Article

Review on Mineral Malabsorption and Reducing Technologies

Yimer Mihrete

Department of Human Nutrition, Kotebe Metropolitan University, Addis Ababa, Ethiopia

Email address:

luguy00@gmail.com, yimer.mihretie@kmu.edu.et

To cite this article:Yimer Mihrete. Review on Mineral Malabsorption and Reducing Technologies. *International Journal of Neurologic Physical Therapy*. Vol. 5, No. 1, 2019, pp. 25-30. doi: 10.11648/j.ijnpt.20190501.15**Received:** May 15, 2019; **Accepted:** June 28, 2019; **Published:** July 24, 2019

Abstract: This paper is aimed to review the updated scientific information regarding effects on mineral absorption associated with major anti-nutritional factors found in plant foods. Some anti-nutrients may exert beneficial health effects at low concentrations. When they are used at low levels, phytate, lectins, tannins, amylase inhibitors and saponins have also been shown to reduce the blood glucose and insulin responses to starchy foods and/or the plasma cholesterol and triglycerides. In addition, phytates, tannins, saponins, protease inhibitors, goitrogens and oxalates have been related to reduce cancer risks. This implies that anti-nutrients might not always be harmful even though they lack nutritive value. However, most anti-nutrients in plant foods are responsible for deleterious effects related to the absorption of nutrients and micronutrients. For example, phytic acid, lectins, tannins, saponins, amylase inhibitors and protease inhibitors have been shown to reduce the availability of nutrients and cause growth inhibition. Despite this, the balance between beneficial and hazardous effects of plant bioactives and anti-nutrients relies on their concentration, chemical structure, time of exposure and interaction with other dietary components. Due to this, they can be considered as anti-nutritional factors with negative effects or non-nutritive compounds with positive effects on health.

Keywords: Anti-nutritional Factors, Malabsorption, Minerals, Potential Health Benefits

1. Introduction

Anti-nutrients are natural or synthetic compounds that interfere with the absorption of nutrients. Nutrition studies focus on those anti-nutrients commonly found in food sources and beverages. Anti-nutritional factors (ANFs) are compounds which reduce the nutrient utilization and/or food intake of plants or plant products used as human foods or animal feeds and they play a vital role in determining the use of plants for humans and animals [1]. Apart from cyanogenic glycosides, food poisoning arising from anti-nutritional factors, otherwise known as plants' secondary metabolites has not been properly addressed in most parts of the developing world. People have died out of ignorance, poverty and inadequate nutrition information and education, especially within the African societies.

There are reports from time to time of deaths after consumption of some type of beans despite cooking. Also, cases of renal and liver diseases are increasing and these calls

for a need to properly address the issue of thorough and adequate processing of foods/feeds before consumption. Since legumes are often consumed together with cereals, proper processing of cereal-leguminous mixtures could be capable of eliminating these anti-nutrients before consumption [2]. Relatively little is known about the fate of anti-nutrients and toxicants in traditional fermented foods. Toxicants in foods can arise from intrinsic and extrinsic sources. The intrinsic toxicants are those that are components of foods by synthesis or degradation and as such are referred to as naturally occurring food toxicants. An example of some of these toxicants is phytate, cyanogenic glycosides and tannins. Probably all intrinsic toxic substances function as anti-nutrients in foods or their complexes [3].

Chemical substances present in food samples and which have been reported with some level of toxicity in mankind include aflatoxin [4], hemagglutinin [5] and cyanogenic glycosides [6]. Toxicity is the result of interaction between three factors namely the type of organism, concentration of toxin and time of duration [2]. Most plant materials contain

some form of toxic compounds but whether it is toxic or not to animal will depend on the potency of the toxic factor, dosage, the frequency of intake and the natural species in unity to that particular toxic substance [7]. There has been over the past few years a systematic attempt by scientists to elucidate the chemical nature of various naturally occurring toxicants in common and less known foods with a view to developing simpler detoxification procedure for them [8]. For example, in some of the foods which contain intrinsic principles, processing techniques have been developed which make them safe for human consumption. Therefore, this paper is aimed at to review anti-nutritional factors and their effect on mineral absorption.

2. Methods

For this systematic review, many sources of information were assessed and retrieved in Google search engine using terms like *antinutritional factors, phytic acid, lectins, tannins, saponins, amylase inhibitors and protease inhibitors, controlling mechanisms of anti-nutritional factors*, and using time periods such as 2019, 2018 and 2017. The sources are from *published article journals, review, newsletters, magazines, reports, books and dictionaries*.

3. Literature Reviews

3.1. Anti-nutritional Factors in Many Foods

Anti-nutritional factors are substances that when present in animal feed or water reduce the availability of one or more nutrients. It is important to have knowledge of anti-nutritional factors because they can adversely affect the health of human health. Plants contain starch polysaccharides and non starch polysaccharides (NSPs) [9]. A polysaccharide is a chain of sugar molecules (also known as mono saccharides) linked together. Polysaccharides are identified based on the carbon atoms of each sugar involved in the bond and the orientation of the hemiacetal oxygen atom (α/α or β/β). Some polysaccharides are anti-nutritional factors. Starch is made up of glucose molecules connected together in what is referred to as α -glycosides link.

The different orientation of the β -links (compared to α -links) makes them resistant to digestion by endogenous digestive enzymes of animals. NSPs are part of plant cell walls and are closely associated with other polysaccharides or non carbohydrate materials such as protein and lignin. These associations affect the behaviour of the NSPs, especially with regard to solubility. NSPs generally are categorized as water-soluble or insoluble. Plants generally contain a mixture of both water-soluble and insoluble NSPs; the ratio of the two types changes with type and stage of maturity of the plant. Cellulose is insoluble in water and is considered fibre. Arabinoxylans and beta-glucans, two other NSPs, are partially soluble in water. Most NSPs adversely affect digestion in animals consuming them. Soluble NSPs affect the viscosity of the material in the digestive tract. This action, in turn, affects

the ability of the digestive enzymes to reach their target. Absorption of any released nutrients is also reduced. This reduction in nutrient absorption results in reduced feed efficiency. The sticky nature of the digestive material also can result in collection of sticky material around the vent of a chicken) [10].

3.1.1. Phytic Acid

Phytic acid is present in many plant systems, constituting about 1 to 5% by weight of many cereals and legumes. Concerns about its presence in food arises from evidence that it decreases the bioavailability of many essential minerals by interacting with multivalent cations and/or proteins to form complexes that may be insoluble or otherwise unavailable under physiologic conditions [11]. Phytic acid content can be reduced through soaking or other forms of processing [12].

3.1.2. Tannins

Polyphenols (tannins) are usually located in the pericarp and/or testa, especially on pigment cultivars of legumes and millets. Tannin concentration is reported to be higher in coloured seed coats with a range of 38-43mg/g and low in white coated beans (1.3mg/g). However, values ranged from 3.8-5.9mg/g in the cotyledons [13].

3.1.3. Saponins

Saponins are glycosides composed of a lipid-soluble aglycone that consists of either sterol or more commonly, a triterpenoid structure attached to water-soluble sugar residues that differ in their type and amount. The major sources of dietary saponins are legumes, and many types of saponins can be present in the same bean [14]. Saponins are very poorly absorbed. They can kill or inhibit cancer cells without killing normal cells [15]. Most saponins form insoluble complexes with 3- β -hydroxy steroids and are known to interact with and form large, mixed micelles with bile acids and cholesterol [16].

3.1.4. Trypsin Inhibitors

Trypsins inhibitors when ingested by man in large quantity disturb the digestive process and may lead to undesirable physiological reactions [17]. They co-exist with anti α -amylases and are located mostly in the outer layer of the cotyledon of legumes. Trypsins inhibitors from beans interfere with protein digestion and in some species of animals do cause pancreatic enlargement and enhance chemically induced pancreatic tumors [18]. However, heat-treating dry beans generally reduces the trypsin inhibitor content by 80-90% [19]. Other processing methods like soaking in water through leaching, fermentation and germination has been shown to also reduce trypsin inhibitors [20].

3.1.5. Oxalates

Oxalate occurs widely in the plant kingdom; examples of foods containing oxalates are black pepper, parsley, poppy seed, amaranth, spinach, chard, beets, cocoa, chocolate, most nuts, most berries, fish tail palms, New Zealand spinach (*Tetragonia tetragonioides*) and beans. Excess consumption of oxalates may result in kidney disease or even death due to

oxalate poisoning [21]. Oxalic acid can induce toxic as well as anti nutritive effects. To humans, it can be acutely toxic. However, it would require massive doses of 4 to 5 g to induce any toxic effect [15].

The oxalic acid levels usually found in food, however, are no cause for concern. Like phytic acid, oxalic acid reduces the availability of essential bivalent cations. Oxalic acid is a strong acid and, with alkaline earth metal ions and other divalent metal ions, it forms salts that are hardly soluble in water. Calcium oxalate is insoluble in water at neutral or alkaline pH, and dissolves easily in an acid medium. Oxalates produce irritation in the mouth and thereby preventing the absorption of calcium and iron in foods [22].

3.1.6. Occurrence

Anti-nutrients are found at some level in almost all foods for a variety of reasons. However, their levels are reduced in modern crops, probably as an outcome of the process of domestication [17]. The possibility now exists to eliminate anti-nutrients entirely using genetic engineering; but, since these compounds may also have beneficial effects, such genetic modifications could make the foods more nutritious but not improve people's health [23].

3.2. Classification of the Anti-nutritional Factors

The anti-nutritional factors may be divided into two major categories. They are: (1). Proteins (such as lectins and protease inhibitors) which are sensitive to normal processing temperatures. (2). Other substances which are stable or resistant to these temperatures and which include, among many others, polyphenolic compounds (mainly condensed tannins), non-protein amino acids and galactomannan gums [24]. More often than not, a single plant may contain two or more toxic compounds, generally drawn from the two categories, which add to the difficulties of detoxification.

3.3. Methods for Quantification of the Anti-nutritional Factors in Plants

Several methods are used for the quantitative determination of anti-nutritional factors in foods based on reports by different authors. These are: trypsin inhibitor activities are determined according to these studies [6, 15, 17, 25-28].

3.4. Biochemical Effects of the Anti-nutritional Factors

The biochemical and toxicological/adverse effects of plant's secondary metabolites (anti-nutritional factors) have been reviewed by several authors [13]. However, their adverse effects will be briefly highlighted. Anti-nutritional factors diminish animal productivity but may also cause toxicity during periods of scarcity or confinement when the feed rich in these substances is consumed by animals in large quantities [29]. Cyanogenic glucoside on hydrolysis yields toxic hydrocyanic acid (HCN). The cyanide ions inhibit several enzyme systems; depress growth through interference with certain essential amino acids and utilization of associated nutrients. They also cause acute toxicity, neuropathy and death

[30]. Tannins because decreased feed consumption in animals, bind dietary protein and digestive enzymes to form complexes that are not readily digestible [31]. They also cause decreased palatability and reduced growth rate [3].

Saponins cause hypercholesterolemia by binding cholesterol, making it unavailable for absorption. They also cause haemolysis of red blood cells and are toxic to rats [32]. Saponins from *Bulbostemma paniculatum* and *Pentapamax leschenaultii* have also been demonstrated to have anti-spermal effects on human spermatozoa [33]. They significantly inhibited acrosome activity of human sperms and the spermicidal effect was attributed to strong damage of the spermal plasma membrane [34]. Trypsins (protease inhibitor) causes pancreatic enlargement and growth depression [25].

Phytates bind minerals like calcium, iron, magnesium and zinc and make them unavailable [35]. Oxalates, like phytates, bind minerals like calcium and magnesium and interfere with their metabolism. They also cause muscular weakness and paralysis. Oxalates also cause gastrointestinal tract irritation, blockage of the renal tubules by calcium oxalate crystals, development of urinary calculi and hypocalcaemia [31] reported that oxalates cause nephrotic lesions in the kidney. Oxalate, phytate and tannins are anti-nutrients, which could be toxic when consumed in an unprocessed food [16].

The bioavailability of the essential nutrients in plant foods could be reduced by the presence in these plants of some anti-nutritional factors such as oxalates and cyanogenic glycosides [28]. Too much of soluble oxalate in the body prevents the absorption of soluble calcium ions as the oxalate binds the calcium ions to form insoluble calcium oxalate complexes. As a result of this, people with the tendency to form kidney stones are advised to avoid oxalate-rich foods [15]. Gossypols are reported to cause animal and human toxicity and high incidence of irreversible testicular damage. Dietary gossypol can also bring about increased requirement, not only for lysine, but also for iron which it can chelate [36]. At the Plant oestrogens also cause toxicity in animals. For example, it has long been recognized that sheep grazing subterranean clover (*Trifolium subterraneum*) are prone to poor reproductive performance [37]. There are some anti-nutritional factors in some plants, especially leguminous plants, whose mode of action is poorly understood. These are anti-vitamin factors.

Raw kidney beans are believed to contain an antagonist to vitamin E as evidenced by liver necrosis in rats and muscular dystrophy and low concentration of plasma tocopherol in chicks [37]. Anti-vitamin E has also been noted in isolated soya protein, which is suspected to be α -tocopherol oxidase. Unheated soybean flour has been found to be deficient not only in Vitamin B12, but it also contains a heat-labile factor that increases the requirement for vitamin B12 [38]. Alkaloids are also reported to cause alteration of normal foetal developments resulting in foetal malformation in ewes. These are caused by teratogenic alkaloids [39]. Glycoalkaloids are reported to cause haemolysis and toxicity to humans [6].

3.5. Varietals Differences and Effects of Methods of Domestic Processing and Cooking

The losses in B-vitamins and minerals in chickpeas cooked by microwaving were smaller than in those cooked by boiling and auto claving. Germination resulted in greater retention of all minerals and B-vitamins compared to cooking treatments. *In vitro* protein digestibility, protein efficiency ratio and essential amino acid index were improved by all treatments. The chemical score and limiting amino acid of chickpeas subjected to the various treatments varied considerably, depending on the type of treatment. Based on these results, microwave cooking appears to be the best alternative for legume preparation in households and restaurants. Patel [12] reported the effect of blanching on the content of anti-nutritional factors in selected vegetables. Levels of both tannic acid and phytic acid were significantly ($p < 0.05$) reduced by conventional and microwave blanching methods while oxalic acid levels were not significantly ($p > 0.05$) reduced in most of the treatments by either of the blanching methods. In general, they recommended blanching as an effective method for reducing the anti-nutritional factors in green vegetables; however, further investigation on the heating times for both conventional and microwave blanching methods has been suggested. Nkhata [20] reported the effects of extrusion and traditional processing methods on ant nutrients and *in vitro* digestibility of protein and starch in faba and kidney beans. De-hulling significantly increased protein content and greatly reduced condensed tannin and polyphenol levels in both legumes. Extrusion was the best method to abolish trypsin, chymotrypsin, α -amylase inhibitors and haemagglutinating activity without modifying protein content. Furthermore, this thermal treatment was most effective in improving protein and starch digestibility when compared with dehulling, soaking and germination.

Eder [35] reported the methods and devices for reducing the amount of anti-nutritional factors in a mixture of raw material for animal feed. The invention relates to a method for reducing the amount of ant nutritional factors in a raw material mixture for producing an ingredient for animal feed such as cattle fodder or domestic animal feed, which raw material mixture contains at least rape seed in a quantity between 1 and 100%, by subjecting the raw material mixture to a steam treatment for a predetermined time at a predetermined temperature. Due to the steam treatment, the ant nutritional factors are at least partially broken down and determined constituents such as fats also become better accessible, whereby the nutritional value of the final animal feed increases. Plant phytochemicals exhibit diverse pharmacological and biochemical actions when ingested by animals and man [30]. The trypsin inhibitor values were significantly reduced ($P < 0.05$) by the different treatment methods, with cooking being the most effective.

3.6. Effect of Anti-nutritional Factors on Mineral Absorption

3.6.1. Phytic Acid

Phytic acid has a strong binding affinity to minerals such as

calcium, magnesium, iron, copper, and zinc. This could result in precipitation, making the minerals unavailable for absorption in the intestines [22]. Phytic acids are common in the hulls of nuts, seeds and grains. It is primarily present as a salt of the mono- and divalent cat ions K^+ , Mg^{2+} , and Ca^{2+} and accumulates in the seeds during the ripening period. Phytate is regarded as the primary storage form of both phosphate and inositol in plant seeds and grains. In addition, phytate has been suggested to serve as a store of cat ions, of high energy phosphoryl groups, and, by chelating free iron, as a potent natural anti-oxidant [37].

3.6.2. Oxalic Acid and Oxalates

These are present in many plants, particularly in members of the spinach family. Oxalates bind to calcium and prevent its absorption in the human body. Oxalate is an anti-nutrient which under normal conditions is confined to separate compartments. However, when it is processed and/or digested, it comes into contact with the nutrients in the gastrointestinal tract when released, oxalic acid binds with nutrients, rendering them inaccessible to the body [40].

3.6.3. Glucosinolates

Prevent the uptake of iodine, affecting the function of the thyroid and thus are considered goitrogens [25]. They are found in broccoli, Brussels' sprouts, cabbage and cauliflower. A number of plant species produce hydrogen cyanide (HCN) from cyanogenic glycosides when they are consumed. These cyanogens are glycosides of a sugar, often glucose, which is combined with cyanide containing a glycone. Cyanogenic glycosides are classified as phytoanticipins. Their general function in plants is dependent on activation by β -glycosidase to release toxic volatile HCN as well as a ketones or aldehydes to fend off herbivore and pathogen attack [28]. Excessive intake of required nutrients can also result in them having an anti-nutrient action. Excessive intake of fibre can reduce the transit time through the intestines to such a degree that other nutrients cannot be absorbed.

4. Conclusion

In general, anti-nutrients and toxicants are natural or synthetic compounds that interfere with the absorption of nutrients. They are commonly found in food sources and beverages. Because of ignorance, poverty and inadequate nutrition information and education the knowledge of anti-nutritional factors people have died in African countries. Consumption of some type of beans without cooking also reported as a cause of death due to anti-nutritional factors. There are two sources of toxicants, intrinsic and extrinsic or external. The intrinsic toxicants are naturally occurring food toxicants while other toxicants are chemicals such as, aflatoxin, hemagglutinin and cyanogenic glycosides. Also many domestic processing and cooking such as germination, fermentation, dehulling, and blanching and cooking are reported to reduce the toxicants and anti-nutritional factors.

References

- [1] Aartsma Y, Bianchi FJJA, Werf W Van Der, Poelman EH, Dicke M. Herbivore-induced plant volatiles and tritrophic interactions across spatial scales. 2017.
- [2] Estella TF, Jessica PK, Joseph N, Nono NB, Evrard N, Omgba TY, et al. iMedPub Journals Evaluation of the Toxicity of Secondary Metabolites in Aqueous Extracts of *Ficus thonningii* Blume in Wistar rats Abstract. 2018; 1–8.
- [3] Gulati P. EFFECT OF PROCESSING ON IN-VITRO PROTEIN DIGESTIBILITY AND OTHER NUTRITIONAL ASPECTS OF NEBRASKA. 2018.
- [4] Opoku N, Achaglinkame MA, Amagloh FK. Aflatoxin content in cereal-legume blends on the Ghanaian market far exceeds the permissible limit. 2018; (November).
- [5] Hajds G, Gelencser E, Pusztai A, Grant G, Sakhri M, Bardocz S. Biological Effects and Survival of Trypsin Inhibitors and the Agglutinin from Soybean in the Small Intestine of the Rat Biological Effects and Survival of Trypsin Inhibitors and the Agglutinin from Soybean in the Small Intestine of the Rat. 1995; (September 2018).
- [6] Bolarinwa IF, Oke M, Olaniyan SA, Ajala S. A Review of Cyanogenic Glycosides in Edible Plants World ' s largest Science, Technology & Medicine Open Access book publisher. 2016; (October).
- [7] Tsatsakis AM, Vassilopoulou L, Kovatsi L, Tsitsimpikou C, Karamanou M, Leon G, et al. The dose response principle from philosophy to modern toxicology : The impact of ancient philosophy and medicine in modern toxicology science. Toxicol Reports [Internet]. 2018; 5 (October):1107–13. Available from: <https://doi.org/10.1016/j.toxrep.2018.10.001>
- [8] Yue Y, Li M, Wang H, Zhang B, He W. The toxicological mechanisms and detoxification of depleted uranium exposure. 2018; 1–9.
- [9] Composition N, Method C. Nutritional Composition and Bioactive Content of Legumes : Characterization of Pulses Frequently Consumed in France and Effect of the.: 1–12.
- [10] Rööös E, Carlsson G, Ferawati F, Hefni M, Stephan A, Tidåker P, et al. Less meat, more legumes : prospects and challenges in the transition toward sustainable diets in Sweden. 2018; (2010).
- [11] Nissar J, Ahad T, Naik HR, Hussain SZ. A review phytic acid : As antinutrient or nutraceutical. 2017; 6 (6): 1554–60.
- [12] Patel K, Neeharika B, W JS, Kumari BA, Neeraja B, Lakshmi VV, et al. Effect of blanching on anti-nutritional factors of bathua leaves. 2018; 7 (4): 214–6.
- [13] Mattila PH, Pihlava J, Hellström J, Nurmi M, Eurola M, Mäkinen S, et al. Contents of phytochemicals and antinutritional factors in commercial protein-rich plant products. 2018; (October): 213–9.
- [14] Emire SA, Jha YK, Mekam F. Role of Anti-nutritional Factors. 2015; (January 2013).
- [15] Dong X, Guo Z. Exploring the Therapeutic Mechanism of *Desmodium styracifolium* on Oxalate Crystal-Induced Kidney Injuries Using Comprehensive Approaches Based on Proteomics and Network Pharmacology. 2018; 9 (June): 1–15.
- [16] Jesch ED, Carr TP. Review Article Food Ingredients That Inhibit Cholesterol Absorption. 2017; 22 (March): 67–80.
- [17] Katiyar D. Phytochemical and Pharmacological Profile of *Momordica charantia* : A Review Biochemistry and Therapeutic Uses of Medicinal Plants. 2017.
- [18] Rampogu S, Parameswaran S, Lemuel MR, Lee KW. Exploring the Therapeutic Ability of Fenugreek against Type 2 Diabetes and Breast Cancer Employing Molecular Docking and Molecular Dynamics Simulations. 2018; 2018.
- [19] Ngadze RT, Linnemann AR, Nyanga LK, Fogliano V, Verkerk R, Ngadze RT, et al. Local processing and nutritional composition of indigenous fruits : The case of monkey orange (*Strychnos* spp.) from Southern Africa. Food Rev Int [Internet]. 2017; 33 (2):123–42. Available from: <http://dx.doi.org/10.1080/87559129.2016.1149862>
- [20] Nkhata SG, Ayua E, Kamau EH. Fermentation and germination improve nutritional value of cereals and legumes through activation of endogenous enzymes. 2018; (September): 244–58.
- [21] Han H, Segal AM, Seifter JL, Dwyer JT. Nutritional Management of Kidney Stones (Nephrolithiasis). 2015; 137–52.
- [22] Ogundola AF, Bvenura C, Afolayan AJ. Nutrient and Antinutrient Compositions and Heavy Metal Uptake and Accumulation in *S. nigrum* Cultivated on Different Soil Types. 2018; 2018.
- [23] Raman R. Biotechnology in Agriculture and the Food Chain The impact of Genetically Modified (GM) crops in modern agriculture : A review The impact of Genetically Modified (GM) crops in modern agriculture : A review. 2018; 5698.
- [24] N HN, Abbey L, Sk A. An Overview of Nutritional and Antinutritional Factors in Green Leafy Vegetables. 2017; 1 (2): 1–9.
- [25] Nourishment PP. HHS Public Access. 2017; 57 (15): 3313–31.
- [26] Kgosana KG, Africa S, Kgosana K, Access O. The effects of extraction techniques and quantitative determination of oxalates in *Nerium oleander* and feeds. 2009; 1–9.
- [27] Sivakumaran K, Kothalawala S. An overview of the analytical methods for food phytates An overview of the analytical methods for food phytates. 2018; (February).
- [28] Zidenga T, Siritunga D, Sayre RT. Cyanogen Metabolism in Cassava Roots : Impact on Protein Synthesis and Root Development. 2017; 8 (February): 1–12.
- [29] Sultana R, Singh RS. PULSE SECONDARY METABOLITES : A PERSPECTIVE ON HUMAN AND. 2016; (October 2017).
- [30] Altemimi A, Lakhssassi N, Baharlouei A, Watson DG. and Identification of Bioactive Compounds from Plant Extracts. 2017.
- [31] Production O. Hyperoxaluria. 2019; 1–19.
- [32] Larsson R, Gullbo J, Nygren P. Nanoparticulate Quillaja saponin induces apoptosis in human leukemia cell lines with a high therapeutic index. 2010; 51–62.
- [33] Reed KFM. Fertility of Herbivores Consuming Phytoestrogen-containing *Medicago* and *Trifolium* Species. 2016.

- [34] Chikaodiri H. EVALUATION OF NUTRIENTS AND ANTI-NUTRITIONAL FACTORS OF DIFFERENT SPECIES OF AFRICAN YAM BEAN (*SPHENOSTYLIS STENOCARPA*). 2017; 4 (1).
- [35] Eder K, Siebers M, Most E, Scheibe S, Weissmann N, Gessner DK. An excess dietary vitamin E concentration does not influence Nrf2 signaling in the liver of rats fed either soybean oil or salmon oil. 2017; 1–15.
- [36] Cherrak SA, Mokhtari-soulmane N, Berroukeche F, Merzouk H, Elhabiri M, Bensenane B. In Vitro Antioxidant versus Metal Ion Chelating Properties of Flavonoids: A Structure-Activity Investigation. 2016; 1–21.
- [37] Okafor UI, Omemu AM, Obadina AO, Adeyeye BSAO. Nutritional composition and antinutritional properties of maize ogi cofermented with pigeon pea. 2018; (October 2017): 424–39.
- [38] Mozos I, Stoian D, Luca CT. Crosstalk between Vitamins A, B12, D, K, C, and E Status and Arterial Stiffness. 2017; 2017.
- [39] Mazzu-nascimento T, Melo DG, Morbioli GG, Carrilho E, Sales F, Vianna L, et al. Teratogens: a public health issue – a Brazilian overview. 2017; 397: 387–97.
- [40] Susantitaphong P. Secondary Oxalate Nephropathy: Kidney Int Reports [Internet]. 2018; 3 (6):1363–72. Available from: <https://doi.org/10.1016/j.ekir.2018.07.020>