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DOI: <http://ijmer.in.doi./2022/11.01.01>

NATURAL TOXICANTS AS POTENTIAL HEALTH HAZARDS: AN OVERVIEW

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Abstract

The food we consume is not only a rich source of macro and micronutrients but it is also a core of natural toxins which are as harmful as chemical additives. Natural toxicants are secondary metabolites produced by biochemical activities within an organism. These are commonly known as antinutritional factors as they hamper the absorption of primary nutrients by the consumer. They possess a potential risk on human health, as these toxins are not harmful to the organism itself but has deleterious effects on the organisms consuming it, in severe cases it may even be fatal. These toxins are mainly classified as phytotoxins, algal toxins or mycotoxins etc. The present review is to highlight the risks associated with these compounds on human health. The review states different possible factors responsible for the development of such compounds. This also suggests that the different methods of prevention are to be taken into consideration so as to limit the production of natural toxicants or reducing their levels in food.

Keywords: Natural Toxicants, Anti-nutritional factors, Phytotoxin, Mycotoxin.

Introduction

Food being a rich source of nutrients which are required for the growth and development also contains some toxic substances if not prepared and processed as per standards set by authorities. These toxicants can be naturally present in the food or might develop during faulty processing and improper storage. All the foods which are produced by natural methods might not always be safe for consumption. The presence and levels of natural toxicants should also be checked and controlled at various stages of food processing. Natural toxicants are secondary metabolites which are produced by organism as a defence mechanism. These natural toxicants may not be harmful to the organism itself but it is harmful to other species including humans upon consumption. These compounds differ in structures and have difference in biology activity and toxicity.

These metabolites can result in adverse effects on health of the consumers ranging from acute toxicity to chronic poisoning. Acute toxicity includes nausea, dizziness, stomach ache, vomiting, skin allergies but chronic and long-term health effects can lead to permanent damage to vital organ systems likely immune system, kidneys, reproductive system and in severe situations, they can be carcinogenic as well as lethal.

Taking consumer health in consideration WHO in association with FAO of United Nations to form a committee JECFA which is responsible in assessments of health hazards caused by food containing natural toxins. Codex Alimentarius commissions on the basis of JECFA evaluations, sets international standards and codes in order to limit the quantity of natural toxins in food.

How are Natural Toxicants Produced in Food?

Food besides providing essential nutrients, energy and having unique organoleptic attributes, should undergo the standardized procedures so as it to make it safe for consumption according to its intended use. Physical, chemical and microbial contaminations in food including with natural toxicants should be reduced significantly until their minimal exposure limit is achieved. There are about more than 3 lakhs species of plants out of which above 2 thousand of species are poisonous which when consumed can causes minor to severe ailments.

Natural toxicants in food occurs naturally as a defence mechanism or present as derivatives of primary metabolites which are intermediate or end products of metabolic processes. Natural toxicants can be released during the growth of crops or by because of the growth of specific moulds and fungi on these crops during pre-harvesting or in storage results in the formation of their secondary metabolites. Toxicants can also be developed during incorrect processing and preparation of foods. They can be a result of product abuse.

Incorporation of Natural Toxicants in Food

Toxicants are classified on the basis of their origin and producers.



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Based on the origin natural toxicants can be developed during cultivation of crops or rearing of animals, they can also be a ramification of faulty food processing or they might develop because of improper handling, storage and distribution of processed foods. Microbial contamination also leads to the incorporation these secondary metabolites in the food.

Toxins classification based on their producers are stated below with their respective examples.

PLANT TOXINS

Plant Toxins are generally chemicals produced in order to safeguard themselves from predators.

Goitrogens

Goitrogens collectively known as glucosinolates are naturally occurring plant toxins. These substances suppress the uptake of Iodine causing poor cognitive development and increasing the risks of enlarging thyroid gland which results in the formation of goitre. Goitrogens also include thiocyanate and isothiocyanate. They are most commonly found in the brassicaceae which includes vegetables like cabbage, Brussels sprouts, cauliflower, and turnip. They are heat sensitive hence can be destroyed by giving heat treatments.

Tannins

Tannins are class of astringent. They are polyphenolic biomolecules which bind and precipitate proteins and various other organic compounds. In many plant species, tannins are widely distributed and play a major role in protecting them from predation and may also help in regulating plant growth. Traditionally, tannins have been considered anti nutritional, but now it's beneficial and anti-nutritional properties depend upon chemical structure and amount of dosage.

Condensed form of tannins hampers the digestion process by binding with consumed plant protein, thus making them difficult to digest and hindering the actions of digestive enzymes. Tea and coffee are the prime source of tannins. Chocolate liquor contains about 6% tannins. Strawberries contain both hydrolysable and condensed tannins.

Furocoumarins

Furocoumarins are phototoxic and photomutagenic compounds which are mainly found in plants belonging to the Rutaceae (e.g., citrus fruits) and Umbelliferae (e.g., parsnip, parsley, celery, carrots) families. These substances are produced under stressful conditions i.e., when plants face any physical damage. These when consumed causes gastrointestinal disorders in vulnerable groups. These toxins lead to skin infections in response to UVA light or sunlight.

Cyanogenic glycosides

Cyanogenic glycosides when comes in contact with beta-glycosidase or emulsion enzymes results in the formation of prussic acid. Prussic acid that is formed is poisonous in nature and causes tissue necrosis and cellular damage, in severe cases it might be fatal also. Hydrogen Cyanide gas released after the enzymatic activities interferes with oxygen uptake by cells and also hampers their activity mitochondrial cytochrome oxidase. They are mainly found in apple seeds, cherries, peach pit, cassava, almonds sorghum lima beans etc. Traditional methods such as sun drying, boiling, soaking can alleviate the risks of cyanide poisoning as it reduces cyanogenic glycosides levels significantly.

Haemagglutinins

These are present in leguminous variety. They are globulin type of protein that cause agglomeration of RBC's and it leads to anaemia. These are heat labile i.e., they are destroyed or altered by heat. The process of germination does not influence the haemagglutinin property. It interferes with the absorption of essential nutrients and also hinders their uptake. Consumption of improper cooked beans will lead to growth depression due to formation of large amounts of haemagglutinins.

Trypsin Inhibitors

These are naturally found in soya bean, chickpea, Bengal gram, red gram, Lethyrus sativus. It leads to growth retardation and causes hypertrophy of pancreas and release of essential amino acids. They are heat labile and can be destroyed by moist heat treatment. They are present in low amounts in broad beans, peas, mung beans, lupins, and a few varieties of kidney beans.

Canavanines

Canavanine is a non-proteinogenic and potentially toxic arginine antimetabolic, and canaline, found in certain leguminous plants. Its primary metabolite is also a toxic nonprotein amino acid which is found in seeds of Canavalia species. Canavanine has

some intrinsic toxicity. Its toxicity has been linked with auto immunological disease in humans and animals which feed on the plant containing these. It is a non-protein amino acid and is produced in many legumes such as jack beans and Lucerne (alfalfa).

Solanine and Chaconine

Glycoalkaloids which includes solanine, chaconine and tomatine is a class of natural toxicants which are found in higher concentration in Solanaceae family of plants. These chemicals are released in response to stressful conditions by plants. It provides protection to the plant from the attack of phyto-pathogenic fungi, as they are fungicidal in nature. These chemicals are mainly formed as a result of product abuse while preparation or storage. The concentrations of this were found higher in sprouted or unripe green parts of potatoes.



Fig 1: Sprouts development in Potatoes.

Symptoms of acute toxicity includes drowsiness, itching, hyperesthesia, laboured breathing and upset digestive activities. (Shibamoto, T. 1993). They mainly act as acetyl cholinesterase inhibitor resulting in cell membrane disruptions and increased sensitivity. Doses in the range of 1 - 5mg per Kg causes acute toxicity but 3 to 6 mg per Kg intakes can lead to death. (Tise, R. 2010).

Cucurbitacin

Bitter tasting compounds produced by Cucurbitaceae family (including Cucumber, melons, squashes, pumpkins etc.) are known as cucurbitacins. They are chemically called as oxygenated tetracyclic terpenes. They are potent toxins with natural insecticidal and fungicidal properties. These are generally present in low concentration but in response to high temperature, drought, low pH of soil their concentrations in the fruit increases significantly to cause stomach cramps, nausea, abdominal pain as well as diarrhoea. Even higher concentration of cucurbitacin can Toxic squash syndrome. Many evidences of this toxicity have been reported in past years. The LD50 value regarding the intake of this toxin is 5 mg per Kg of body weight. In order to prevent this toxicity, consumers should avoid the consumption of bitter fruits from this family. Minimal environmental stresses should be there when the plant is growing.

Flatulence factors

Flatulence factors are the compounds which when consumed causes gastrointestinal issues and produces carbon dioxide inside the stomach and intestine. Raffinose type oligosaccharides with alpha galactosidic linkage plays major role in flatulence (Prince, K.R. et al 1988). The flatulence produced is determined by the amylase content of the food. These substances are majorly found in pulses and legumes namely bengal gram, soya beans, red gram, green grams etc. and are responsible for digestibility disorders. Overnight soaking of these pulses before cooking has resulted in effective decrease in flatulence factors.



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Phytates

Phytic acid or inositol hexaphosphate are present in plant seeds as a main reservoir of phosphorus as it contains approximately 60 to 80% total phosphorus in cereals, legumes, nuts and oilseeds (Skoglund, E. et al. 2009.). During germination, this acid undergoes degradation and releases phosphorus in order to provide energy to the developing seed. However, phytates can also be degraded using enzymatic or non-enzymatic means.

Phytates in its original forms are more likely to bind and impair the absorption of essential minerals like Iron, zinc, calcium etc. These phytate - mineral complexes are insoluble in intestine so reduces the mineral bioavailability and also it hampers the actions of digestive enzymes, thereby reducing protein and starch uptakes. If taken in moderation phytates were found to be effective against kidney stones and cancer. Germination and soaking of the food grains results in limiting the phytic acid content in food.

Erucic Acid

Erucic acid is a long chain fatty acid with only one carbon-carbon double bond. (Mattson, F.H. 1973). This acid is highly found in rapeseed oil and has severe health impact on animals. This acid tends to get deposit near heart wall and declines the contractile force of heart. High levels of erucic acid can cause myocardial lipidosis. Although no confirmed cases of erucic acid toxicity have been reported in humans till now. Generally natural rapeseeds contain more than 40% of erucic acid but commercially cultivated varieties of rapeseed contain only 0.5% of erucic acid. Acceptable daily intake for this is between the ranges of 0.3 to 4.4 mg per kg body weight.

MYCOTOXINS

Mycotoxins, fungal toxins which are released by moulds and fungi. Class of toxic mushrooms are also included under mycotoxins.

Ergot toxins

Belong to the genus *Claviceps*. This type of fungi grows in rye and related species. Alkaloids produces by them cause ergotism in humans and other mammals. Ergotism is earliest recorded poisoning caused by toxic moulds. In the Middle Ages, human poisoning due to the consumption of rye bread made from ergot-infected grain was common in Europe. Ergot majorly causes abortions in cattle and humans. Early symptoms of this poisoning include vomiting, numbness, itching, rapid or slow heart beats and in severe cases it can cause convulsions, unconsciousness or even death.

Aflatoxin

Aflatoxin is produced by molds namely, *Aspergillus flavus* and *Aspergillus parasiticus* which grow in soil, decaying vegetation and food grains. These toxins mainly affect certain crops like peanuts, corns, cotton seeds etc. They are poisonous, carcinogens and mutagen. Aflatoxin exposure is associated with stunted growth, delayed development, liver damage and liver cancer. Children are mainly affected by the toxin. Aflatoxins are heat stable hence their amount in food cannot be reduced by heat treatments. However, aflatoxin B¹ is the most toxic type, can permeate through the skin.



Fig 2: Aflatoxin contaminated Corn cobs.

Ochratoxin

Ochratoxin A is a naturally occurring foodborne in wide variety of agricultural commodities worldwide i.e., cereal grains, dried fruits, wine and coffee. Its contamination generally occurs when there are poor storage contamination and suboptimal agricultural practices drying of foods.

In 1977, OTA in screen was first detected and become most widely used bio monitoring approaches for human OTA exposure. Half-life for OTA can be increased due to renal absorption, enterohepatic circulation and binding to plasma proteins.

Patulin

Patulin is an organic compound which is classified under polyketide. It is soluble in acidic water and in organic solvents. It is a heat stable lactone, therefore not destroyed by pasteurization or thermal denaturation. It mainly occurs in rotten apple and apple related products. Its toxicity is sulfhydryl groups (SH) due to which inhibition of enzymes occurs. In rodents' models, its oral LD50 have ranged between 20 and 100 mg/kg. Acute toxicity causes gastrointestinal problems, neurotoxicity, pulmonary congestion and edema. In males it causes reproductive toxicities.

Zearalenone (ZEA)

Zearalenone is an estrogenic mycotoxin and produced by *Fusarium* fungi. It affects the reproductive capacity of animals. Because of its toxicity and wide distribution in animal feeds, ZEA is a global public health concern. Zearalenone is particularly found in maize. Its contamination can occur in products made of barely, wheat, oats, rice and sorghum. For the production of zearalenone high humidity and low temperatures are required.

Fumouisin

Fumouisin are produced in cereals by *Fusarium verticilloides*, *Fusarium proliferatum* in crop plants of peanut, maize and grape. More than 15 homologues of fumonisin are known and named as fumonisin A, B, C and P. It was found that by disruption the biosynthesis of sphingolipids, the formation of fumouisin could be controlled.

Poisonous mushrooms

It is another class of toxicants. Mushroom poisoning is termed as Mycetism. Many wild varieties of mushrooms including *Amanita* sps, *Conocybe* sps, *Cortinarius* sps etc are highly poisonous and can cause liver necrosis where as some other mushroom varieties releasing toxins such as muscimol and muscarine causes vomiting, diarrhoea, confusion, hallucinations etc.



Fig 3: Poisonous Varieties of Mushrooms

Usually, the onset of symptoms varies according to the type of mushroom ingested. They are more likely to appear between 6 to 24 hours after the consumption of poisonous species. Late onset of symptoms is more dangerous and lethal than early appearance of



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symptoms. The toxicity of these mushrooms cannot be reduced by processing or even by providing extensive heat treatments. Therefore, it is suggested to avoid the consumption of wild varieties until clearly identified as non-poisonous.

ANIMAL TOXINS

Every animal is not utilized as a source of food by human population but those which are consumed as food are needed to be treated well before consumption to reduce or to totally destroy the harmful microorganisms or toxins present within them. Animal toxins are a complex mixture of polypeptides, enzymes and chemicals which causes cellular injury. These Polypeptides exert their effect through action on ion channels and receptors on the cell membrane. Although no evidence of toxicity because to the consumption of terrestrial animals have been noted till date but there are numerous case studies suggesting the adverse effects on health of seafood poisoning seafood consumption.

Seafood poisoning because of the consumption of marine animals is due to the accumulation of toxins produced by microalgae in shellfish, crustaceans and finfish. The toxins can build up in shellfish as they feed on the algae, especially during algal blooms (or 'red tides'). Clams, oysters, mussels, scallops and crabs are some examples of shellfish that are identified as a prominent source of contamination.

Ciguatera Fish Poisoning

Ciguatera fish poisoning (CFP) is caused by consuming fish which is contaminated with dinoflagellates which produces ciguatoxins. Some fish that can be contaminated with these toxins include barracuda, black grouper, dog snapper, and king mackerel. Symptoms of this poisoning include nausea, vomiting, and neurologic symptoms, such as tingling sensation on fingers and toes. There is as such no treatment for this poisoning.

Paralytic Shellfish Poisoning

Paralytic Shellfish Poisoning (PSP) is one of the most severe toxicities caused after the consumption of a toxin called as Saxitoxin. Onset of symptoms are observed under half an hour after the consumption of poisonous shellfish, crustaceans etc. Initial symptoms include numbness and tingling sensations in whole body, which is followed by loss of coordination, defects in speech. It is fatal as if it affects the respiratory system it can lead to death.

Gempylotoxin

The toxin was named after the family of fish Gemplydiae. Gempylotoxin is composed of waxy esters which are not digestible by humans. Humans after the consumption of escolar fish which belongs to the same family, develops symptoms of this toxicity. Gempylotoxin, as the name suggests is not a toxin but because of the waxy esters which act as laxatives and causes dramatic sensations in some people it is classified as natural toxin.



Fig 4: Escolar Fish

Onset of symptoms generally takes place a few hours following escolar consumption and ceases within 24 to 48 hours. The rectal passage of an oily yellow or orange substance (called keriorrhoea), diarrhoea, nausea, vomiting, abdominal pain, and headache. Keriorrhoea is not associated with a loss of bodily fluids and is not considered life threatening or fatal. Intravenous fluids to restore electrolytes can be given to the patients to stop dehydration.

ALGAL TOXIN

Algal Toxin are the toxins produced by seaweeds and algae. In the past recent years there has been an increase in the frequency and severity of harmful algal bloom Known as HAB' s which further produces bio toxins called Algal Toxins. Certain factors like coastal upwelling or agricultural run-off can increase nutrient levels in water and can cause algal blooms. HAB's are also



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known as red tides and they are responsible for thousands of poisoning incidents due to the consumption of contaminated sea food. Symptoms include vomiting, diarrhoea, and dizziness or, in extreme cases, even death as well as respiratory issues in people who breathe in toxic HAB's outbreaks can have a big impact on local economies which can lead to the closure of fisheries, aquaculture and recreational areas. These Algal toxins can accumulate in the tissues of fishes and hence enter the food chain.

MICROBIAL TOXINS

Microbial Toxins are the toxins which are produced by microorganisms which include bacterial toxin and fungal toxin. Microbial toxins cause infection and disease by directly damaging host tissues and they disable the immune system.

Botulinum Toxin

It is a neurotoxin protein which is produced by the bacterium Clostridium botulinum. It was discovered in sausages. There are 7 types of botulinum species following: A, B, C, D, E, F and G. Out of these species A, B, E and F are the ones that effect humans and among these A is the most lethal one.

Botulinum toxin grows in anaerobic conditions. It prevents the release of acetylcholine from the axon endings at the neuromuscular junctions and, hence causing paralysis. It has been perceived as a lethal threat for many centuries, causing blurred vision, altered speech, muscle weakness further causing paralysis of diaphragm and respiratory failure.

Staphylococcus Enterotoxin

They are water soluble in nature and they can withstand the process of boiling for a time period of 30 mins. Whereas Staphylococcus aureus can easily be destroyed by mild heating. Staph food poisoning is a gastrointestinal disorder caused by eating foods which are contaminated with toxins produced by these Staphylococcus aureus bacteria. These bacteria are present on the skin of animals and humans.

It can come from unhygienic conditions and can cause intoxications. The most common raw material contaminated by Staph is meat products.

General Preventive Measures

The consumption of these toxicants beyond acceptable daily intake can cause severe illnesses in humans or it can be even fatal. So, in order to make food safe as per its intended use, it is required to reduce the production of these metabolites. Mandatory preventive measures suggested by JECFA/WHO should be taken into consideration during preparation, production, processing, storage, distribution and transportation of a food commodity.

When it comes to prevention of the health risks related to natural toxicants, it should be known that they occur in a variety of different crops. One should understand that if the food is "natural", it is not always safe for consumption. Bruised, damaged, discoloured foods should not be consumed. Fruits and vegetables should be washed thoroughly so as to eliminate the risks by water soluble toxins. Foods with off smell and off flavour should be avoided. Simple soaking and fermentation of various food grains results in the reduction of such antinutritional factors significantly. For every particular food product its standardized preparation procedure should be applied. The methods suggested above for the removal of specific toxins should be taken into consideration for the production of particular foods and to assure food safety.

Conclusion & Discussion

A popular notion remains that "natural is good", although it is clear that naturally toxins possess a greater health risk than the synthetic food additives in our food.

Some natural toxins can be formed in food as defence mechanisms of plants, through their infestation with toxin-producing mould, due to improper processing, or storage or through ingestion by animals of toxin-producing microorganisms.

Adverse health effects of such toxins can range from allergic reactions as an acute poisoning to chronic stomach-ache and diarrhoea, convulsions or even death. These toxins don't hamper the biological metabolisms of toxin producing organisms but have adverse effects on the species consuming it directly or indirectly. Anything can be toxic, only dose separates non-toxic from toxic. Even good things in excess can cause toxicity for example antioxidant vitamin A can cause acute toxic effect i.e., hepatotoxicity and more high level can lead to pro-oxidant effect.



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Many case studies regarding the ill effects of natural toxins had come across from various parts of the world. Specific emphasis is placed in the case studies taken under observation on the nature of compounds, distribution of residues in common foods, uptake, toxicology and regulatory issues. For instance, an outbreak caused due to a natural toxicant was seen in Bihar's Muzaffarpur district where many children had died after being infected by a deadly brain disease which was believed to be linked to a toxic substance found in lychee fruit. Lychee toxins are particularly harmful when they are consumed on an empty stomach. Methylene cyclopropyl-glycine (MCPG) is a chemical found in this fruit that affects the brain when body sugar levels are already low due to undernourishment. The toxic substance in lychee causes Acute Encephalitis Syndrome (AES), which is locally known as Chamki Bukhar, which is a form of brain fever that happens due to the inflammation of the brain. The symptoms of the disease include fever, vomiting and unconsciousness or onset of seizures.

Studies of outbreaks in Australia has suggested that Escolar and oil fish are majorly responsible for the disease caused by accumulation of oil in rectum called oily diarrhoea and clinically known as keriorrhea. In order to maintain food safety from farm to folk, it is advisable to follow all the preventive measures suggested by WHO/ JECFA. It is the duty of food suppliers to provide safer foods to the consumer and also consumers are advised to be vigilant.

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