ANTINUTRITIONAL PROPERTIES OF DIETARY LECTINS

Abstract

Lectins are a class of specific proteins widely distributed in nature, which selectively detect and bind reversibly to carbohydrates and glycoconjugates. Lectins have been isolated from various sources, including plants, algae, fungi, and body fluids of invertebrates and lower vertebrates. The majority of regularly consumed edible plant foods contain lectins. When it comes to food, lectin comes under antinutritional factors since harmful local and systemic reactions might trigger during ingestion. However, the characteristic property of lectins being resistant to animal and insect proteases and their ability to recognize and affect other molecules in a distinct way makes them play a vital role in plant defense.

Keywords: Lectin, antinutritional factors, toxic substance, carbohydrate binding protein

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I. INTRODUCTION

Lectins are a class of natural bioactive proteins and glycoproteins of non-immune origin widely distributed in nature that reversibly bind to carbohydrates and glycoconjugates (Kennedy *et al.,*1995; LIS and SHARON 1981). Lectins have been isolated from numerous sources such as plants, algae, fungi, and body fluids of invertebrates and lower vertebrates. (Mishra *et al.,* 2019; Peumans and Van Damme 1995). Plant lectins are referred to as phytohemagglutinins. When it comes to food, lectin comes under antinutritional factors (Thompson 1993; Vasconcelos and Oliveira 2004a). Lectins bind to the membrane glycosyl groups of the cells, lining the digestive tract because of their ability to withstand digestion by the gastrointestinal tract. This interaction could cause several adverse local and systemic reactions, placing this class of biomolecule as a toxic or antinutritive substance. *(Kumar et al.,* 2012; Pusztai, Bardocz, and Ewen 2008a; Vasconcelos and Oliveira 2004a). The first outbreak of lectin poisoning was reported by the Public Health Laboratory Service in 1976 when a party of schoolboys and adults ate raw kidney beans, *Phaseolus vulgaris*, which had been soaked in water for a day (Bender and Reaidi 1982). Later, Rodhouse surveyed the same poisoning incidents between 1976 and 1989, leading to the conclusion that lectin is responsible for all the events (Rodhouse *et al.,* 1990). The carbohydrates and proteins that are undigested and unabsorbed in the small intestines reach the colon where the bacteria flora ferments them to short-chain fatty acids and gases. These may contribute to some of the gastrointestinal symptoms prevalent with the consumption of lectin-associated foods (Thakur *et al*., 2019). Lectin comes under one of the five major classes of plant defense proteins, which include protein inhibitors, α-amylase inhibitors, lectins, chitinases, and polyphenol oxidases (Fürstenberg-Hägg, Zagrobelny, and Bak 2013). Keeping these views, we intend to compile the role of lectin as plants defense molecules and its implications as antinutritional properties on human dietary lectins.

II. CLASSIFICATION OF LECTINS

Because of their vast diversity, the classification of lectins is still evolving. Based on structure, lectins are classified as (1) Merolectins, with only one carbohydrate-binding domain, are small monovalent proteins with a single polypeptide and are incapable of precipitating glycoconjugates or agglutinating cells (Macedo, Oliveira, and Oliveira 2015; Peumans and Van Damme 1995; Santos *et al.,* 2016). (2) Hololectins, which are lectins exclusively with carbohydrate-binding domains, in which two or more are identical or very similar. They comprise all lectins with multiple binding sites and can undergo cell agglutination or glycoconjugate precipitation (Santos *et al.,* 2016). (3) Chimerolectins, which do not contain any carbohydrate domains but are 'chimeric' proteins holding a carbohydrate-binding domain tagged with other domains having enzymatic activity. The carbohydrate-binding domain doesn't affect the functions of the enzymatic domain. Chimerolectins can function as hololectins or merolectins depending on the quantity of sugar binding sites (Mishra *et al.,* 2019). (4) Superlectins, which consist of molecules with two or more distinct carbohydrate-binding domains. They have two distinct carbohydrate-binding domains that can detect sugars with different structural characteristics (Santos *et al.,* 2016).

Based on binding affinity to carbohydrate moiety, lectins are classified as (1) Glucose/mannose binding lectins; (2) Galactose and *N*-acetyl-D-galactosamine binding lectins; (3) L-fucose binding lectins; (4) *N*-acetyl-D-galactosamine binding lectins and (5) Sialic acids binding lectins (Bah, Fang, and Ng 2013; Mishra *et al.,* 2019).

Lectins are also grouped into 12 families based on the similarity of amino acid sequences of these proteins and the structure of their carbohydrate-recognition domains (CRD). These families include *Agaricus bisporus* homologs, Amaranthin domain, class V chitinase homologs, *Euonymus europaeus* family, *Galanthus nivalis* agglutinin family, proteins with hevein domains, Jacalins, Cyanovirin domain proteins with legume lectin domains, Lys M domain proteins, the Nicotiana tabacum agglutinin family and the ricin-B domain (Hendrickson and Zherdev 2018; Macedo, Oliveira, and Oliveira 2015).

Another classification of plant lectin is base on sequence data. They are categorized into four groups based on evolutionarily-related proteins *viz*: (1) Legume lectins; (2) Chitin-binding lectins; (3) Type 2 RIP (ribosome-inactivating proteins); and (4) Monocot mannose-binding lectins (Damme *et al.,* 1998).

III. LECTINS IN FOODS

Lectins are present in commonly edible foods such as tomato, potato, beans, peas, carrots, soybeans, cherries, blackberries, wheat germ, rice, corn, garlic, peanuts, mushrooms, avocado, beetroot, leek, cabbage, tea, parsley, oregano, spices, and nuts, and also in several non-cultivated plant species (Vasconcelos and Oliveira 2004b). Plant tissues are reported to have more lectin content compared to animal tissues (Hamid *et al.,* 2013). When it comes to food, lectin comes under antinutritional factors. The lectins bind to the membrane glycosyl groups of the cells lining of the digestive tract because of their ability to withstand digestion in the gastrointestinal (GI) tract. This interaction could cause several adverse local and systemic reactions in the GI tract, placing this class of biomolecule as an antinutritive substance (Kumar *et al.,* 2012; Pusztai, Bardocz, and Ewen 2008a). Several lectins from many vegetables and fruits have been discovered as potent food allergens. Few of them have been listed as potential food allergens by the WHO/IUIS Allergen Nomenclature Sub-Committee. Examples include, restricted number of proteins such as Tri a 18 (Wheat Germ Agglutinin) and a few chitinases with a hevein domain including Mus a 2 (banana), Bra r 2 (turnip), Cas s 5 (chestnut), Zea m 8 (corn), and Per a 1 (avocado), and contact allergens from Hev b 6 (hevein) and Hev b 11 (class I chitinase having a hevein domain) from the rubber tree *Hevea brasiliensis*, have also been included in the list. A few other plant lectins have also been identified as potential food allergen according to their ability to bind IgE, degranulate mast cells and basophils, and initiate interleukin responses in susceptible individuals (Barre *et al.*, 2020).

The exposure of heterotrophic organisms, including humans, to functionally active lectins is a common event. The lack of public knowledge concerning the deleterious effects of dietary lectins on the gut and other part of GI tract has led to several food poisoining outbreaks. The first outbreak of lectin poisoning was reported by the Public Health Laboratory Service in 1976 when some people ate raw kidney beans, *Phaseolus vulgaris* (Bender and Reaidi 1982). Later, the same poisoning incidents were surveyed between 1976 and 1989 concluding that lectin is responsible for all the events (Rodhouse *et al.,* 1990). The carbohydrates and proteins that are undigested and unabsorbed in the small intestines reach the colon where the bacterial flora ferments them and produce gases. These may, contribute to some of the gastrointestinal symptoms associated with the intake of lectins from food (Thakur *et al.,* 2019).

When consumed, lectins in human may causes vomiting, nausea, bloating and diarrhoea. It was also reported that, animal fed with lectins, show symptoms of appetite loss, decrease in body weight and even death of the animal (Liener et al.,, 1986; Lajolo et al.,, 2002).

Lectins are comparatively resistant to digestion in GI tract, and many of them may undergo further modification leading to remain as active throughout the digestive processes. And those bound to the mucosa become important as antinutritional lectins (Pusztai and Bardocz, 1996; Sunil *et al* 2012). After binding to the mucosal cells, lectins may cause changes in cellular morphology and intermediary metabolisms leading to frequent disruption of brush borders and other main absorptive cells. It may cause reduction in the absorptive surface area and absorption of essential nutrients and become hyperplasia (Otte et al., 2001; Sasaki *et al*., 2002). Another secondary toxic effect of accumulated lectins in the small intestine is the overgrowth of intestinal bacteria which ultimately lead to overproduction of bacterial toxins. This also may aggravate in the worsening of animal health (Grant, 1999; Ilka *et al.,* 2004; Sunil *et al.,* 2012).

IV. LECTINS AS PLANT DEFENSE MOLECULE

Plant lectin plays a vital role against fungi, bacteria, and insects (Souza Cândido et al., 2011). Lectin comes under the five major classes of defense proteins which include protein inhibitors, α-amylase inhibitors, lectins, chitinases, and polyphenol oxidases. The first defense lectin discovered was the glucose/mannose-specific concanavalin A (ConA) from Canavalia ensiforms (Jacobean) (Fürstenberg-Hägg, Zagrobelny, and Bak 2013). Plants accumulate part of their nitrogen reserve in the form of carbohydrate-binding proteins, which can be used as passive-defense proteins (Peumans & Van Damme,1995). Lectins play a major role in plant defense against herbivorous insects by penetrating, destroying, or modifying the peritrophic membrane (Konno and Mitsuhashi 2019). Chrispeels & Raikhelb also closely analyzed the protective role of lectin and several chitin-binding proteins (Chrispeels & Raikhelb,1991). One of the most crucial characteristics of lectins is their ability to survive in the digestive system of insects, thereby claiming their significant insecticidal potential. They act as antinutritive and/or toxic substances by binding to membrane glycosyl groups lining the digestive tract, leading to an array of harmful systemic reactions in insects (Belete 2018). Plant lectins also have the advantage of remaining stable under a wide pH and temperature range, and being resistant to animal and insect proteases (Souza Cândido *et al.,* 2011). Many reports show how these bioactive defense proteins often interfere with their digestion. Esch and Schaffrath, discussed the possibility that Jacalin-Like Lectin (JRL) domains as a decoy in fusion proteins that help to alert plants of the presence of attacking pathogens (Esch and Schaffrath 2017). A small-sized lectin from Rhizomes of stinging nettle inhibits the growth of several phytopathogenic and saprophytic chitin-containing fungi (Broekaert *et al.,* 1989).*Oliveira* and his team reported *Cratylia argentea* lectin and its insecticidal activity upon *Callosobruchus maculatus* larvae which attack cowpea (*Vigna unguiculata*) seeds, reinforcing the hypothesis that lectins take part in the mechanisms against herbivory (Oliveira *et al.,* 2004).

Plant genomes encode a plethora of RLKs (receptor-like kinases), RLPs (receptor-like proteins), and lectins to protect themselves against the vast array of pathogenic bacteria, viruses, fungi, oomycetes, and pest insects. A large diversity of membrane-bound and soluble PRRs (pattern recognition receptors) responsible for recognizing carbohydrate structures of pathogens and initiating stress response have been described to carry lectin domains (De Schutter and Van Damme 2015).

V. EFFECT OF LECTINS ON HUMANS.

Most plants seem to contain lectins, although the majority of them do not bind to cells of higher animals (Damme *et al.,* 1998; Van Damme, Lannoo, and Peumans 2008). Their resistance to heat denaturation varies, as does their resistance to proteolytic enzyme degradation during passage through the digestive tract. The latter also appears to depend on the animal species ingesting (Pustzai 1990,). Since many cellular receptors and other components of the intestinal tract's epithelium are equipped with carbohydrate-rich side chains, lectins may bind to the cells depending on their carbohydrate specificity. They may elicit responses that are related to the function of the receptors/components (Krogdahl and Bakke 2015). Some can interrupt the mucosal barrier whereas others may secure beneficial microflora, have anti-inflammatory properties, or even prevent cancer (Pusztai, Bardocz, and Ewen 2008b).

The lack of public knowledge concerning the deleterious effects of dietary lectins on the gut and health has led to several food poisoning outbreaks. When consumed in excess by sensitive individuals, they can cause primary physiological reactions, including severe intestinal damage disrupting digestion and causing nutrient deficiencies, provoking IgG and IgM antibodies causing food allergies and other immune responses, and binding to erythrocytes, simultaneously with immune factors, causing hemagglutination and anemia (Fekadu Gemede 2014)

Many lectins from many vegetables and fruits have been discovered as potential food allergens. Few have been listed as potential food allergens by the WHO/IUIS Allergen Nomenclature Sub-Committee, consisting of a restricted number of proteins such as Tri a 18 (wheat germ agglutinin, WGA) and a few chitinases with a hevein domain, which includes Mus a 2 (banana), Bra r 2 (turnip), Cas s 5 (chestnut), Zea m 8 (corn), and Per a 1 (avocado), contact allergens Hev b 6 (hevein) and Hev b 11 (class I chitinase with hevein domain) from the rubber tree *Hevea brasiliensis*, have also been included in the list. A few other plant lectins have also been identified as potential food allergens according to their ability to bind IgE, degranulate mast cells and basophils, and initiate interleukin responses in a various allergic individual (Barre *et al.,* 2020).

The social behavior of cells depends on membrane glycosylation, including cell communication, adhesion, and migration. Once they are consumed, different biological properties are observed at biochemical and molecular levels. Binding between lectins and surface cell molecules or internalization into cells involve a wide variety of signals that are important for cell regulation, including Cell agglutination or aggregation, induction of apoptosis or cell cycle arrest, down-regulation of telomerase activity, inhibition of angiogenesis, increased drug sensitivity of tumor cells, direct effects on the immune system by altering the production of various interleukins (Krogdahl and Bakke 2015), or by activating specific protein kinases. Consuming lectins also sequesters the body's supply of polyamines, thereby inhibiting cancer cell growth. Some lectins can bind with ribosomes to prevent protein synthesis Ferriz-Martínezet *et al.,* (2010).

The overall impact of dietary lectins on human health is still an area of ongoing research and debate. While some lectins can have negative effects, others might have potential health benefits, such as their potential to modulate the immune system or act as prebiotics to support beneficial gut bacteria (Pusztai, Bardocz, and Ewen 2008b).

VI. CONCLUSION

Lectins are antinutritional or toxic substances detrimental to various plant-eating organisms. This property is associated with their high resistance to proteolysis in the gastrointestinal tract of various organisms and to their capacity of binding and modulate epithelial cells lining of the small intestine. In plants, lectins are effective defense molecules and insect resistant transgenic plants produced by the expression of lectin genes are already a reality. This approach could increase crop productivity and reduce the usage of pesticides. However, their effect on human consumption should also be investigated thoroughly since many of the food lectins are proven to be antinutritional and toxic to humans.

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