Phytochemistry 117 (2015) 51–64

Contents lists available at ScienceDirect

Phytochemistry

journal homepage: www.elsevier.com/locate/phytochem

Review

Toxic proteins in plants

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ARTICLE INFO

Article history:
Received 21 March 2015
Received in revised form 25 May 2015
Accepted 27 May 2015

Keywords:
Plant protein
Toxicity
Biological activity
Mode of action
Plant defense
Biotechnological application

ABSTRACT

Plants have evolved to synthesize a variety of noxious compounds to cope with unfavorable circumstances, among which a large group of toxic proteins that play a critical role in plant defense against predators and microbes. Up to now, a wide range of harmful proteins have been discovered in different plants, including lectins, ribosome-inactivating proteins, protease inhibitors, ureases, arcelins, antimicrobial peptides and pore-forming toxins.

To fulfill their role in plant defense, these proteins exhibit various degrees of toxicity towards animals, insects, bacteria or fungi. Numerous studies have been carried out to investigate the toxic effects and mode of action of these plant proteins in order to explore their possible applications. Indeed, because of their biological activities, toxic plant proteins are also considered as potentially useful tools in crop protection and in biomedical applications, such as cancer treatment. Genes encoding toxic plant proteins have been introduced into crop genomes using genetic engineering technology in order to increase the plant's resistance against pathogens and diseases. Despite the availability of ample information on toxic plant proteins, very few publications have attempted to summarize the research progress made during the last decades. This review focuses on the diversity of toxic plant proteins in view of their toxicity as well as their mode of action. Furthermore, an outlook towards the biological role(s) of these proteins and their potential applications is discussed.

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http://dx.doi.org/10.1016/j.phytochem.2015.05.020
0031-9422/

1. Introduction

Being sessile organisms plants are exposed to a multitude of stress factors from their environment. In addition to the unsuitable influences from their surroundings, there is also the constant threat from predators and pathogens. To cope with a diversity of unfavorable conditions plants have undergone evolutionary adaptation such as the elaboration of sophisticated defense strategies and the synthesis of an impressive diversity of natural bioactive compounds, some of which are toxic (Maag et al., 2014). Among the different toxic compounds reported in plants is a large group of low molecular weight compounds, among which alkaloids, terpenoids, tannins and glycosides (Mithöfer and Boland, 2012). Although these small molecules do not have a primary function in plants they play an important role because of their toxicity to animals, arthropods as well as to bacteria and viruses (Cushnie et al., 2014; Mithöfer and Boland, 2012). Furthermore plants also synthesize an arsenal of proteins such as lectins and ribosome-inactivating proteins (RIPs), that help the plant in its continuous battle for survival (Lannoo and Van Damme, 2014; Virgilio et al., 2010).

Plants express a variety of toxic proteins that confer resistance against herbivores and pathogens. Some well-known families of toxic proteins include lectins, ribosome-inactivating protein, protease inhibitors, α-amylase inhibitors, ureases, arcelins, antimicrobial peptides and pore-forming toxins. Most of these proteins tend to accumulate in the vulnerable parts of the plant such as seeds and vegetative storage tissues. In fact, the first proteins classified as RIPs, arcelins, canatoxins and lectins all originated from seeds where these proteins are highly abundant (Carlini and Guimarães, 1981; Olsnes, 2004; Osborn et al., 1988). Research on toxic plant proteins has resulted in numerous data, showing evidence that these noxious proteins are involved in plant defense against phytophagous predators and pathogens, including bacteria, fungi, viruses, nematodes, and insects (Carlini and Grossi-de-Sá, 2002).

It is important to note that toxic proteins have been identified throughout the plant kingdom and have also been discovered in edible crops. For example, lectins have been reported in bean, tomato, potato, banana and garlic (Van Damme et al., 1998a). Similarly, RIPs have been identified in several edible plants, including pumpkin, cucumber, beet, and cereals (Barbieri et al., 2006). Since some of these crops are also eaten raw, knowledge about the toxic proteins in these plants is also important with respect to food safety.

Despite the availability of an enormous amount of information on toxic compounds and proteins in plants, a recent comprehensive overview of toxic proteins in the plants is lacking. This review focuses on the different classes of toxic proteins reported in plants (Table 1), with particular emphasis on their toxicity and mode of action. Furthermore, the potential applications of toxic plant proteins are discussed.

2. Different classes of toxic proteins in plants

2.1. Lectins

Lectins are a class of proteins endowed with carbohydrate-binding activity. They are defined as proteins with at least one non-catalytic domain that binds reversibly with specific mono- or oligosaccharides (Peumans and Van Damme, 1995). Although the majority of lectins have been characterized from plants, these proteins have also been reported in animals, insects, viruses, fungi and bacteria (Van Damme, 2014). Analysis of completed genome sequences and transcriptome data suggests that lectins are ubiquitous in the plant kingdom. Up to now, several hundreds of plant lectins have been identified, purified and at least partially characterized (Van Damme et al., 1998a,b).

Lectins are globular proteins with a carbohydrate-binding site which enables them to specifically recognize and bind particular carbohydrate structures. It should be emphasized that the carbohydrate specificity of lectins is highly diverse. Although some lectins recognize and interact with monosaccharides such as mannose, glucose, galactose, fucose, most plant lectins preferentially bind to more complex oligosaccharides like N- and O-linked glycans (Ghazarian et al., 2011). The carbohydrate-binding site typically consists of five to six amino acids that bind the hydroxyls of the sugar residues mainly by hydrophobic interactions. The specific interaction between the lectin and the carbohydrate involves the formation of a network of hydrogen bonds and is often reinforced by a hydrophobic stacking of the pyranose ring of the sugar to the aromatic ring of aromatic residues (tyrosine, tryptophan or phenylalanine) located in the close vicinity of the carbohydrate binding site (del Carmen Fernández-Alonso et al., 2012).

The affinity of lectins for their substrate is usually rather weak when compared to the antigen–antibody interactions (Kd $\sim 10^{-8}$–10^{-12} M). The binding affinity of a lectin towards monosaccharides is typically in the order of $\sim 10^{-3}$ M (Duverger et al., 2003; Lis and Sharon, 1998). However it should be emphasized that most lectins preferentially recognize oligosaccharides or more complex glycans by multivalent interactions, resulting in a considerable increase of the binding affinity to Kd values of 10^{-6}–10^{-8} M (Duverger et al., 2003; Liang et al., 2007).

Since the family of lectins groups all proteins that specifically interact with carbohydrate structures without altering the substrate, a large number of very diverse proteins complies with this

Table 1
Overview of toxic plant proteins.

Family	Source	Structural features	Biological activity	References
Lectin	Ubiquitous in plants	One or more CRDs	Carbohydrate-binding activity	Van Damme et al. (2008), Van Damme (2014)
Ribosome-inactivating proteins	Widely distributed	N-glycosidase domain	N-glycosidase activity	Peumans et al. (2001), Shang et al. (2014)
Protease inhibitors/α-amylase inhibitors	Widely distributed, rich in storage tissues	N/A	Inhibition of protease/α-amylase	Leung et al. (2000), Murdock and Shade (2002), Svensson et al. (2004)
Urease and canatoxin-like proteins	Mainly in legumes	A 10 kDa region, with a β-hairpin motif	Ureolytic activity Pore-forming activity	Follmer et al. (2001), Barros et al. (2009)
Arcelins	Seeds of *Phaseolus* sp.	Legume lectin fold	N/A	Acosta-Gallegos et al. (1998), Zaugg et al. (2013)
Thionins	A number of monocot and dicot plants	~5 kDa cysteine containing proteins	Increase of cell membrane permeability	Stec (2006)
Cyclotides	Widely distributed	Cyclic cysteine knot	Pore-forming activity	Craik et al. (2012)
Pore-forming toxins	Some plants, e.g. *Enterolobium contortisiliquum*, wheat	Membrane-spanning region (ß-barrel/α-helical)	Pore-forming activity	Bittencourt et al. (2003), Puthoff et al. (2005)