Handbook of Naturally Occurring Food Toxicants
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NUTRITIONAL SIGNIFICANCE OF LECTINS

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Lectins or hemagglutinins are proteins which can interact in a very specific way with certain carbohydrates. In its specificity this interaction is comparable to that of an antibody with its antigen or even to the binding of an enzyme to its substrate. The lectins can bind to free sugars or to sugar residues existing in polysaccharides, glycoproteins, or glycolipids, which may be free or may exist in bound form, for example in cell membranes.

The term "hemagglutinin" derives from the visible interaction of lectin-containing material with red blood cells. This agglutination reaction was known since the last century when it was observed that an extract from castor beans would agglutinate a suspension of washed red blood cells of different animal species. This activity was related at this time to the high toxicity of the castor beans. Since these first observations, lectins or lectin-like proteins have been detected in many plant species including fungus and lichens, and also in animals, both invertebrates and vertebrates. The term "lectin" points to the specifity of the reaction (legere = to choose).

In order to produce clumping of erythrocytes and other cells, a lectin must bear at least two receptor sites. The capacity to aggregate red blood cells, which have many surface carbohydrate residues, is a common criterion used to identify lectins. Agglutination is inhibited if the lectin-specific sugar is present in the solution in which the cells are suspended. This is similar to the inhibition a hapten exerts on the reaction between an antibody and its specific antigen and allows study of the specificity of the lectins.

Some lectins will stimulate human and animal lymphocytes to undergo mitosis in vitro, a fact which has been very useful for the study of lymphocyte dynamics and function. Carbohydrate-containing molecules are found in the membranes of many cells and may undergo characteristic changes during embryonic development and malign transformation which may be followed by the use of lectins.

The chemical structure of only a few lectins has been studied in some detail. Many, but not all, are glycoproteins and contain bivalent metal ions (Mn^{++}, Ca^{++}, Zn^{++}). Some can be split in subunits which may be of one or two different types. Several different lectins exist frequently in plant sources and are called "isolectins".

The chemical,[1,2] taxonomic,[3] botanical,[4] immunological,[5] and regulatory[6] aspects of lectins have been reviewed. Compared with this extensive literature, the number of review papers dealing with the antinutritional properties of lectins is rather small.[7,8]

Lectins bound to insoluble support material are useful for affinity chromatography of complex sugar-bearing compounds. At the same time, the lectins can be obtained by affinity chromatography on their specific sugars, immobilized by binding to support material or directly on insoluble polysaccharides like sephardex, sepharose, quitine, etc. Several lectins and immobilized lectins are now commercially available.

FUNCTION OF LECTINS

Very little is known about the function the lectins perform in the organisms in which they occur. There is growing evidence that lectins participate in the recognition processes between cells or between cells and various carbohydrate-containing molecules. Thus they may participate in regulating a variety of normal physiological functions.[6] They also may be involved in defense mechanisms of plants against invasion of harmful microorganisms and insect attack.[9] The possible role played by lectins in the process of recognizing the nitrogen-fixing bacteria of the genus *Rhizobium* by their legume

host has received particular attention. The bacterial cells have sugar-containing substances on their surfaces. There is growing evidence that they may be bound by lectins existing in the roots of legumes, thus establishing the relationship between plants and bacteria.[10]

DETECTION

For screening, the hemagglutinating test is still preferred. Activation of the red blood cells by treatment with trypsin or pronase enhances the sensibility of this test which has been critically evaluated by Burger.[11] Not all blood samples of a given animal species may react in an identical fashion due to the existence of different blood groups.

LECTINS IN FOODS

Lectins have been detected in a great number of edible plants: many legume seeds, potatoes, wheat germ, etc. (Table 1) (see also Reference 74). It is likely that there are still more undiscovered lectins for which the right detection method has not yet been devised. The first lectin to be discovered was the highly toxic ricin from castor beans.[12] It has since been found that a hemagglutinin of low toxicity exists in these seeds together with a toxin. The latter has only one receptor group for sugar residues and therefore will attach itself to the surface of susceptible cells but will not clump them, while the hemagglutinin has two receptor sites.[13] The toxicity of the castor beans stimulated the search for other toxic lectins and led to the discovery of the hemagglutinating activity of the extract of many of the edible legume seeds.[14]

SOYBEAN LECTIN

As early as 1917 it was found that diets prepared with raw soybeans would not support normal growth of experimental animals as do the diets containing heated soybeans, indicating the probable presence of heat-labile, antinutritional compounds in these seeds.[15] Lectins, enzyme inhibitors, and undefined compounds have been implicated.

Liener[16] was the first to isolate a soybean lectin which was toxic when injected into rats. Several isolectins have been detected later in soybeans.[17] The role of the lectin in the oral toxicity of raw soybeans is still a matter of dispute. When the soybean lectin was incorporated into the diet at a level equivalent to the activity found in raw soybean meal, a significant depression of the growth of rats was obtained.[18] On the other hand, Liener et al.[19] could not detect any correlation between the level of hemagglutinating activity in the extracts from different soybean cultivars and the growth-depressing action of the raw beans when added to an experimental rat ration. No such relation was either found between trypsin inhibitor activity and growth-promoting action. The soybean lectin can be removed from a raw seed extract by affinity chromatography. Added to a casein diet, this extract did not cause a significantly different growth depression than did the crude extract.[20] These results seem to indicate that the growth-depressing activity of raw soybeans is due to the interaction of various factors, one of which may well be the lectin. There exist considerable differences between different animal species in their growth response to diets containing raw soybeans, but it is unknown whether this fact is related to the lectin content of the rations.

LECTINS IN BEANS: *(PHASEOLUS VULGARIS)*

Rats fed a diet prepared with raw ground garden beans and supplemented with all essential nutrients will lose weight and die within 1 to 2 weeks. Poor acceptibility and

Table 1
LECTINS FOUND IN EDIBLE PLANTS

Source	Isolation	Molecular weights	Metal requirement	Carbohydrate (%)	Erythrocytes agglutinated	Toxicity
Soy bean *Glycine Max*	17, 18, 19, 31, 32 33	110.000	+	5.0	Rabbit	+ 16
Garden bean *Phaseolus vulgaris*	21, 23, 25, 27, 34, 35, 36	91.000—130.000	+	4.10	All*	+ Type A and C − Type B and D 28, 38, 43
Broad bean[39,40] *Vicia faba*	38, 39	50.000	—	3	All	— 41
Lima bean *Phaseolus limensis*	42	124.000 247.000	+	4.0	Human blood group A	— 41, 43
Lentil *Lens esculenta*	44, 45, 46	52.000	+	0 (?)	Rabbit	—
Garden pea *Pisum sativum*	47, 48, 49	54.000	+	0—0.3	Rabbit	— 50
Field bean *Dolichos lablab*	51, 52	?	—	2	Rabbit	+ 43, 53, 54
Runner bean *Phaseolus cocineus (multifloris)*	55	120.000	+	40	All	+ 41
Horse gram *Dolichos biflorus*	56, 57	109.000 122.000	+	2	Human blood group A	— 43

Table 1 (continued)
LECTINS FOUND IN EDIBLE PLANTS

Source	Isolation	Molecular weights	Metal requirement	Carbohydrate (%)	Erythrocytes agglutinated	Toxicity
Potato *Solanum tuberosum*	58, 59	80.000 100.000	?	5, 2	All	?
Wheat germ *Triticum vulgaris*	60, 61, 62	17.000—35.000	?	 0	Tumor cells	(?) 63
Jack bean *Canavalia ensiformis*	64, 65, 66	112.000	+	0	Rabbit	+ 41, 67

* Only type A beans agglutinate all blood types.[27]

digestibility, enzyme inhibitors, and lectins could be responsible, but there is good evidence that the latter are at least one of the major causes. Experiments by Hanover et al.[21] and by Jaffé[22] clearly established that the lectins are most likely responsible for the toxicity. Since then several authors purified toxic bean lectins.[23-25]

Five heterogeneous proteins can be separated from bean lectin. Each consists of isomeric, noncovalently bound tetramers made of two different subunits.[26] The toxicity of different bean cultivars may be quite different. Four groups of cultivars can be distinguished according to their toxicity and the type of lectins they contain.[27] The latter can be distinguished by their specificity toward red blood cells of various animal species.[28]

A possible explanation for the toxic action of some legumes is that they combine with cells lining the intestinal wall, thus causing localized lesions and a nonspecific interference with the absorption of nutrients.[22] Only lectins resistant to gastric and intestinal digestion can be expected to exhibit such an action.

Etzler and Branstrator demonstrated the binding of several fluorescence-labeled lectins to cells of intestinal vellies of rat intestine.[68] King et al.,[69] and Sotello et al.[70] produced evidence that bean lectins can damage and kill intestinal cells both in vitro and in vivo. Intestinal invertase is strongly inhibited by bean lectin[71] and so is the uptake of vitamin B.[72]

Jayne-Williams and Burgess observed that raw navy beans are toxic for Japanese quail but not for germ-free birds.[24] When the intestines of the latter were infected with several coliform strains, death occurred, which was attributed to impairment of body defense mechanisms by the lectin. Dramatic overgrowth of *Escherichia coli* may occur in the small intestine of rats fed bean lectin and may contribute to the toxic action.[73]

Several cases of human intoxication through the ingestion of raw or partially cooked bean products have been reported.[29,30] Lectins are quite common in foods generally consumed in the U.S. as Nachbar and Oppenheimer[74] have recently pointed out. They observed hemagglutinating activity in about one third of the different food samples tested. Nothing is known about the possible consequences on human health of such widespread exposure.

The data presented in Table 1 summarize some of the published information on lectins in plant food products. The details described by different authors frequently differ from each other in some aspects. One of the reasons is that the lectins from different varieties or cultivars of one plant species may vary considerably in chemical, physical, and biological aspects. Moreover, different isolectins may exist, and subunit aggregation or dissociation depends on the special experimental conditions used. The information on sugar content is also often inconsistent.

The published data on the toxicity of plant lectins are very scarce. Therefore, in the column on toxicity, information on growth-depressing activity of the raw plant material is included, although in most cases it has not been proven that the lectin is the only responsible factor, or even that it is involved as a causative agent of the toxic effect.

Hemagglutination specifity is not well known in many cases. Therefore, only the most frequently used kind of cell is registered.

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