PHYTOALEXINS AND HUMAN HEALTH—A REVIEW

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Abstract. Phytoalexins are compounds which contribute to disease resistance of plants. These compounds may be found either at low levels in healthy plants or may be produced in injured plants. A large number of horticultural crops produce phytoalexins including garden peas, green beans, carrots, sweet potatoes and white potatoes. One group of phytoalexins that have been extensively studied in regard to human health are the glycoalkaloids of white potatoes. These compounds have caused illness when tubers contain excessive amounts of the compounds. The levels of glycoalkaloids in potatoes are a function of variety, climatic conditions, harvesting practices and postharvest procedures. In a recent USDA study, potatoes grown in 1970 at Hastings, FL contained the second lowest glycoalkaloid content when compared with potatoes grown in 39 test plots across the United States. If good cultivating practices and good postharvest procedures are followed, Florida can produce potatoes with acceptable glycoalkaloid content.

In order to maintain high yields from agricultural products, the producers must keep their crops free from disease. This is normally done with the use of chemicals and good agricultural practices. Plants also have defense mechanisms which are chemical barriers, physical barriers and/or response mechanisms that inhibit the growth and limit the penetration of infectious agents (15). A plant's degree of resistance to a specific disease is not a fixed factor but is a function of both genetic and environmental factors i.e., rainfall, temperature, fertility, planting dates and soil reaction (10).

The compounds which plants synthesize in response to infection are known as phytoalexins. The concept of phytoalexins goes back to 1905 when Ward (7) stated "the infection and resistance to infection depend on the power of the fungus protoplasm to overcome the resistance of the cells of the host by means of enzymes or toxins, and reciprocally, in that of the protoplasm of the cells of the host to form antibodies which destroy such enzymes or toxins or to excrete chemotactic substances which repel or attract the fungus protoplasm." The date given to the modern theory of phytoalexins is 1940 when Muller and Borger defined phytoalexin as a specific chemical compound produced by plants when the living cells of the host are invaded by a parasite and the plant tissue undergoes necrosis (13). Such toxins are non-specific, however, different fungi will exhibit different sensitivities to phytoalexins.

Originally the defense mechanism was thought to be confined to the specific area around the infection and not to the entire plant (7). This definition has since been altered slightly to include all chemicals synthesized by plants which impart disease resistance, whether formed in response to mechanical injury, to physiological stimuli, or to the presence of infectious agents (13). A large number of horticultural products will produce phytoalexins including the garden pea (Pisum sativum L.), green bean (Phaseolus vulgaris L.), carrots (Daucus carota L.), sweet potato (Ipomoea batatas L.), and white potato (Solanum tuberosum L.).

Garden Pea

The garden pea (Pisum sativum L.) will accumulate pisatin when the pod is stimulated by fungi, ultraviolet radiation and a number of chemicals such as ethylene, DNA intercalating compounds and various antibiotics (15). However, pisatin synthesis has not been reported when the pod was injured by gross mechanical injury (7). The compound is a weak, but broad spectrum, antibiotic and is degraded both by plant pathogens and enzymes within the pea itself (15). Pisatin also has biological activity on mammalian cells. At concentrations greater than 200 ppm (0.63 mM), pisatin will hemolyze bovine red blood cells and cause a release of cellular potassium within 8 minutes (20, 30). The relationship of this compound to mammalian toxicity is still unknown.

Green Bean

Phaseollin is the major compound produced when green bean pods are inoculated with spores from Monilina fructicola (8). In addition to phaseollin, at least 4 other compounds have been isolated from green beans stressed by micro-organisms. These compounds include phaseollidin, phaseollinoisflavan, kievitone, and coumestrol (15). Phaseollin will be synthesized when the green bean is infected with bacteria, virus and fungi. This differs from pisatin synthesis since the garden pea will synthesize pisatin when infected only with various fungi (15). These compounds also accumulate in beans that are stressed by low concentrations of heavy metals, and metabolic inhibitors of nucleic acid and protein synthesis (15). It is not yet known if these compounds pose a threat to human health; however, in vitro studies show phaseollin will lyse both bovine and sheep red blood cells. The concentration of phaseollin required to lyse 50% of sheep red blood cells is 17.5 ppm (or 0.55 mM) (30, 31).

Carrots

Carrots (Daucus carota L.) contain several compounds that may have potential biological activity in mammals. These compounds include chlorogenic acid which is a stress metabolite and myristicin which may have insecticidal activity. Chlorogenic acid is produced in carrots which are exposed to fungi such as Ceratocystis fimbriata (5, 6). When

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carrots are infected in the laboratory with pathogenic fungi the levels of chlorogenic acid ranged from 410 mg to 644 mg per carrot.

Chlorogenic acid levels may concern some scientists since this compound along with caffeic acid, a structurally similar compound also found in plants, has been shown to inhibit thiamine (vitamin B1) absorption in rat intestine (24, 27). In contrast, some investigators (29) recently reported that caffeic acid caused no impairment in weight gain or in trans-ketolase activity of red blood cells and brain.

Another compound which can be present in carrots is myristicin. This was found to have an insecticidal effect against flies and would act synergistically with the carbamate pesticides such as carbaryl (16). Myristicin is essentially non-toxic to rats with LD50 being 1000 mg/kg body weight (9). However, doses of 400 mg administered to humans will produce excitation in the cerebral region of the brain and larger doses may produce hallucinations (29). The Food and Drug Administration has been interested in the levels of myristicin in carrots. Branen at Washington State University measured the myristicin content of the following varieties; 'Chantenay,' 'Danver,' 'Imperator,' and 'Nantes.' He reported that 20 ppm was the average myristicin content of these carrot varieties (A. L. Branen, personal communication). Therefore, the average 70 kg man would have to eat 5 kg of carrots at one time before showing the first signs of toxicity.

Sweet Potatoes

The toxicity of damaged sweet potatoes (Ipomoea batatas L.) to cattle has been known for about 40 years and the main component, ipomeamarone, was isolated in crude form in 1943 by Hiura (34). In addition to ipomeamarone, 10 other compounds have been isolated from tissue infected with Ceratocytis fimbriata, a pathogen of sweet potatoes. The LD50 of ipomeamarone is 230 mg/kg body weight when administered by injection to rats. In addition, this level of toxin would inhibit growth of Ceratocytis infected with Ceratocytis fimbriata, a pathogen of sweet potatoes. The LD50 of ipomeamarone is 230 mg/kg body weight when administered by injection to rats. In addition, these compounds have been shown to cause liver and lung damage in laboratory animals. Ipomeamarone levels of 9 to 950 mg have been isolated in damaged and blemished sweet potatoes sold in markets in Tennessee and Kentucky. This level of toxin would inhibit growth of Ceratocytis fimbriata (2). In addition, ipomeamarone may be the factor responsible for the bitter flavor of blemished potatoes (32). There is some controversy as to whether sweet potato toxins will be destroyed by cooking. Wilson et al. (35) reported that the baking or boiling of infected sweet potato roots did not destroy the toxins. However, recently Cody and Haard (3) reported that 80% of the ipomeamarone was destroyed in 2 minutes when the root was cooked in a microwave oven and 90% was destroyed after 45 minutes of baking in an oven at 204°C. Since these compounds are found in blemished sweet potatoes sold in markets, further research is needed to determine if processing does indeed destroy the toxins.

White Potatoes

One of the most extensively studied groups of phytoalexins are the glycoalkaloids of potatoes (Solanum tuberum L.). There are 2 primary glycoalkaloids, α-solanine and α-chaconine. The only difference between them is the sugars in the trisaccharide portion of the molecule. α-Solanine has a glucose with 2 rhamnoses, while α-chaconine has a glucose, a galactose, and a rhamnose. This difference appears to have no effect on the toxicity of these compounds (18, 19). Therefore, total glycoalkaloids will be referred to as the combination of α-solanine and α-chaconine. Safety concern for blighted potatoes has been recognized for a number of years since blighted potatoes have been linked to acute poisoning and deaths of humans (1, 11, 12, 28). The oral dose of α-solanine considered to be toxic to man is 3 mg/kg body weight or 210 mg of α-solanine for an average 70 kg man (14). Based on these figures, the morbidity level of total glycoalkaloids in potatoes is assumed to be 20 mg per 100 g of wet tissue, or the average man would have to consume 1 kg of tubers before toxic symptoms appear. Recent concern for glycoalkaloid toxicity of potatoes was raised when Renwick (21) proposed that 95% of the cases of a birth defect known as anencephaly-spina bifida (a serious defect in the development of the central nervous system) could be prevented by eliminating potatoes from the diet. This theory was based on the occurrence of glycoalkaloids in the potato, on the increased synthesis of the glycoalkaloids by blighted potatoes and on epidemiological evidence. Renwick no longer supports the idea that potato avoidance will prevent 95% of anencephaly-spina bifida. However, he still postulates that the glycoalkaloids of potatoes will cause some cases of this birth defect (22). To date, there is no laboratory evidence that α-solanine or α-chaconine will cause this toxicological problem, and most scientists working with α-solanine do not agree with Dr. Renwick's theory.

What do these data mean to the Florida potato industry? As with the previous compounds; α-solanine and α-chaconine are produced when the potato is stressed by exposure to the pathogen, Phytophthora infestans, and to physical agents such as direct sunlight, fluorescent light, and mechanical damage during harvesting and postharvest procedures (26). In addition, the total glycoalkaloid content is a physiological function of variety and of tuber maturity (26). In a recent USDA survey (26), 5 commercial varieties of potatoes were grown at 39 locations across the United States. A summary of the results are presented in Table 1. Differences in total glycoalkaloid content will vary from year to year, even if grown at the same location. Florida

Table 1. The average total glycoalkaloid content per 100 g of fresh weight of commercial potato varieties grown at Hastings, Florida and at various locations across the United States, during the 1970 and 1971 growing seasons.

<table>
<thead>
<tr>
<th>Location</th>
<th>Year</th>
<th>Variety</th>
<th>Average</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>'Kennebec'</td>
<td>'Russet Burbank'</td>
</tr>
<tr>
<td>FL</td>
<td>1970</td>
<td>4.3</td>
<td>4.7</td>
</tr>
<tr>
<td>US*</td>
<td>1970</td>
<td>9.7</td>
<td>7.9</td>
</tr>
<tr>
<td>FL</td>
<td>1971</td>
<td>7.9</td>
<td>11.5</td>
</tr>
<tr>
<td>US*</td>
<td>1971</td>
<td>10.0</td>
<td>8.7</td>
</tr>
</tbody>
</table>

*Data from Sinden and Webb (26).
†Average total glycoalkaloid content reported from 39 experimental stations across the United States.
‡Average total glycoalkaloid content reported from 20 experimental stations across the United States.

potatoes did not have an excessive total glycoalkaloid content and these levels were not significantly different from those from 34 of the reporting stations in 1970 and 17 of the stations in 1971. However, it is important to keep the glycoalkaloid content of potatoes to a minimum, not only from the public health standpoint but also from the consumer acceptance standpoint, since these compounds impart a bitter off-flavor to the commercial product (25, 35). Since potato varieties that contain high glycoalkaloid levels are not used for commercial production, a safe, nutritious and tasty product can be provided if good cultural and postharvest practices are employed.

Summary

There are a large number of naturally occurring chemicals present in food that can injure humans if consumed in very large quantities. However, if good standard practices are used, food will not be hazardous. The difference between toxicity and hazard should be understood. Toxicity is defined as the intrinsic capacity to produce injury when the compound is administered by itself. The level at which a compound is administered may be many times greater than the expected level of exposure. Hazard is the capacity to produce injury under circumstances of exposure (6). All chemicals will produce toxic reaction if ingested in large enough quantities. However, if the exposure to toxic compounds in food is kept to a minimum, the risk taken in eating the food is minimal and all will benefit from being able to eat appetizing and nutritious food.

Even though food purchased in the United States is currently safe, research should continue to determine the effect phytoalexins may have on humans. Also, there always looms the threat that various government agencies may impose impractical restrictions on the level of these compounds in food whether for actual safety reasons, from pressures from consumer activists, or for trade barriers. For example, in 1974 the FDA proposed that reports would have to be made to the agency if new varieties had a 20% loss in specific nutrients or a 10% increase in toxic constituents since these changes would be classified as significant (17). If such potential regulations are to benefit the producers and consumers, a data base must be generated which includes information on the toxicity of the phytoalexins, on the biochemistry of these compounds in crop plants and on the expected dietary levels of the individual compounds. However, this job is very complex and cannot be accomplished within one scientific discipline. It requires a team including plant geneticists, agronomists, horticulturists, phytochemists, phytopathologists and food scientists as well as toxicologists.

Literature Cited