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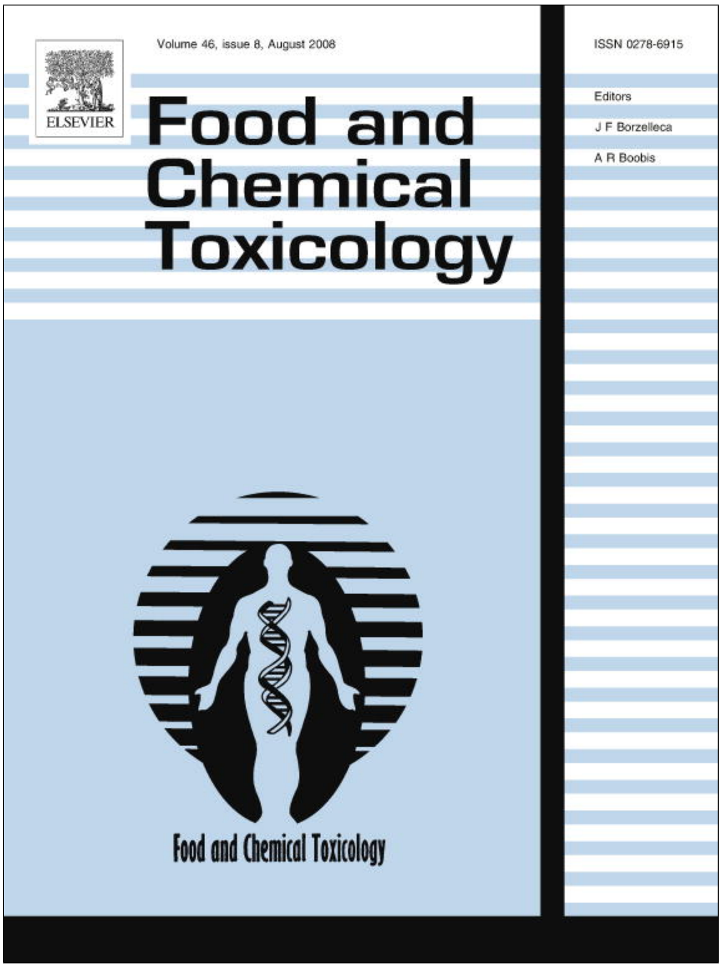

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A human dietary risk assessment associated with glycoalkaloid responses of potato to Colorado potato beetle defoliation

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ABSTRACT

A quantitative human dietary risk assessment was conducted using the glycoalkaloid concentrations measured from tubers of plants defoliated by Colorado potato beetles and undefoliated (control). There was a significantly greater production of glycoalkaloids for defoliated plants compared to control plants for both skin and inner tissue of tubers. The dietary risk posed to different human subgroups associated with the consumption of potatoes was estimated for the 50th, 95th, and 99.9th percentile US national consumption values. Exposures were compared to a toxic threshold of 1.0 mg/kg body weight. Defoliation by Colorado potato beetles increased dietary risk by approximately 48%. Glycoalkaloid concentrations within the inner tissue of tubers, including undefoliated controls, exceeded the toxic threshold for all human subgroups at less than the 99.9th percentile of exposure, but not the 95th percentile.

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1. Introduction

Many secondary metabolites serve as natural pesticides within plants. At certain concentrations, these compounds can be toxic to humans and other animals (Theis and Lerdau, 2003). There are three types of secondary metabolites: terpenes, phenolics, and nitrogen-containing alkaloids. Although terpenes are the largest class of secondary metabolites (Theis and Lerdau, 2003), glycoalkaloids are thought to be the most highly consumed natural toxin in North America (Hall, 1992). However, little is known about the human dietary risks associated with the consumption of these chemicals or how the dietary risks change in response to herbivory of crop plants.

In potato (*Solanum tuberosum* L.), glycoalkaloids serve as natural defense mechanisms against pathogens and insects (Lachman et al., 2001). Because naturally occurring pesticides are synthesized when plants are under stress, it is expected that injury to plant tissue would instigate synthesis of higher concentrations of these compounds in the injured versus uninjured plant tissue. Hlywka et al. (1994) found that tubers from plants subjected to Colorado potato beetle (*Leptinotarsa decemlineata* Say) defoliation contained higher glycoalkaloid concentrations than tubers from undefoliated plants.

Although there are many glycoalkaloids present in potatoes, α-chaconine and α-solanine make up 95% of the total glycoalkaloids present (Friedman and McDonald, 1997); α-solanine is found in greater concentrations than α-chaconine, and α-solanine has only half as much specific toxic activity as α-chaconine (Lachman et al., 2001). Tubers typically have about 75 mg/kg fresh weight (FW) or 500 mg/kg dry weight (DW) total of α-chaconine and α-solanine (Zeiger, 1998). Neither α-solanine nor α-chaconine is regulated in the US. However, the US Department of Agriculture (USDA) has recommended a food-safety level for glycoalkaloids of 200 mg/kg FW or 1000 mg/kg DW (Zeiger, 1998; Bejarano et al., 2000). Levels of α-solanine greater than 140 mg/kg FW or 933 mg/kg DW taste bitter, and levels greater than 200 mg/kg FW or 1000 mg/kg DW cause a burning sensation in the throat and mouth (Lachman et al., 2001).

Although the potential hazard associated with human consumption of potatoes injured by insects has been recognized (Hlywka et al., 1994), there has not been an analytical consideration of the potential human dietary risks associated with increased production of glycoalkaloids as a result of Colorado potato beetle injury. In Pariera Dinkins et al. (2008), we quantified the concentrations of glycoalkaloids in response to Colorado potato beetle and manual defoliation. The objective of this study was to estimate the potential human dietary risk associated with consumption of potatoes with elevated glycoalkaloid levels from plants defoliated by Colorado potato beetles.

Abbreviations: BW, body weight; DW, dry weight; EPA, Environmental Protection Agency; FCID, food commodity ingredient data; FW, fresh weight; LOAEL, lowest-observed-adverse-effect-level; NOAEL, no-observed-adverse-effect-level; USDA, US Department of Agriculture.

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2. Materials and methods

2.1. Quantification of glycoalkaloid concentrations

All experimental methods for injuring potato plants and quantifying glycoalkaloid responses in tubers can be found in Pariera Dinkins et al. (2008).

2.2. Problem formulation

Our human dietary risk assessment focused on the human acute oral exposure to the glycoalkaloids, α-solanine and α-chaconine, in the inner tissue of tubers from plants with no defoliation (control) and Colorado potato beetle defoliation. The initial symptoms of glycoalkaloid toxicity occur within 30 min of consumption and last for approximately 7 h (Friedman and McDonald, 1997). Therefore, in our assessment acute exposure was defined as a single-day total exposure after consumption of skinless tubers. To account for the potential age group and size differences related to exposure, we estimated the risk to different population subgroups in the US (e.g., infants, children 7–12 years, and women 13 years and older who are pregnant).

2.3. Hazard identification and dose-response relationships

Most commercial tubers contain 20–130 mg/kg FW (Zeiger, 1998) or 133–867 mg/kg DW glycoalkaloids. The USDA has recommended a food-safety level for glycoalkaloids of 200 mg/kg FW or 1000 mg/kg DW (Bejarano et al., 2000; Zeiger, 1998). Levels of α-solanine greater than 140 mg/kg FW or 933 mg/kg DW taste bitter, and levels greater than 200 mg/kg FW or 1000 mg/kg DW cause a burning sensation in the throat and mouth (Lachman et al., 2001).

Hellenäs et al. (1992) used seven volunteers who abstained from eating potatoes for two days and were then given potatoes containing glycoalkaloids at a dose of 1 mg/kg body weight (BW) per individual. Six out of the seven subjects experienced burning sensation of the mouth and light to severe nausea and one of the six experienced diarrhea; the initial symptoms were observed 30 min after consumption and lasted for approximately 4 h. Animal studies have shown that in mouse, rat, and hamster tissue, α-chaconine and α-solanine reached their highest concentrations within 6–14 h after ingestion and in less than 35 h, peak concentrations in the blood were reached (Zeiger, 1998).

The symptoms of "solanine" poisoning include nausea, vomiting, diarrhea, stomach and abdominal cramps, headache, fever, rapid and weak pulse, rapid breathing, hallucinations, delirium, and coma (Friedman and McDonald, 1997). Effects on the nervous system include increased heart, pulse, and respiratory rates, sedation, and coma (Zeiger, 1998). Effects from cell membrane disruption include internal hemorrhaging, edema, diarrhea, constriction of the abdominal muscles, and lesions in the stomach and duodenum of the large intestines. Teratogenic effects were observed mainly in the central nervous system and included exencephaly, cranial bleb, encephalocele, and anophthalmia (Zeiger, 1998). Alpha-chaconine exerts teratogenic effects at lower concentrations than α-solanine (Zeiger, 1998).

Tissues that were observed to accumulate α-chaconine and α-solanine were abdominal fat, adrenal glands, blood, brain, heart, kidney, liver, lungs, muscle, pancreas, spleen, testis, thymus, and thyroid. Alpha-chaconine and α-solanine remained unchanged or as solanidine when excreted in urine and feces (Zeiger, 1998).

Peeling reduces the quantity of glycoalkaloids in tubers approximately 30–80% (Zeiger, 1998). Alpha-chaconine and α-solanine are not broken down from cooking or frying because they are heat stable and only begin to break down between 230 and 280 °C (Bejarano et al., 2000).

In humans, the toxic dose for glycoalkaloids is 2–5 mg/kg BW and the fatal dose is approximately 3–6 mg/kg BW (Morris and Lee, 1984). According to Friedman and McDonald (1997), the minimal acute toxic effect level most likely is closer to 1.0 mg/kg BW or less, but there are few human toxicity studies to determine what a toxic or fatal dose would be. An oral LD_{50} for mice is greater than 1000 mg/kg BW (Nishie et al., 1971) and is approximately 590 mg/kg BW in rats (Gull et al., 1970). Although animal studies have shown similar effects when ingesting α-solanine, α-chaconine, and plant material containing these two glycoalkaloids, α-solanine and α-chaconine have been shown to be poorly absorbed (Zeiger, 1998), and to elicit a similar response as observed in humans requires a much greater concentration to be administered.

2.4. Selection of toxic threshold

Many synthetic chemicals have an acute and/or chronic regulatory threshold (acceptable daily intake) that is typically based on a no-observed-adverse-effect-level (NOAEL) from the required toxicity study that generates the lowest dosage necessary to produce the lowest-observed-adverse-effect-level (LOAEL). The data available indicate that humans are more sensitive to α-chaconine and α-solanine than test animals, and because no human oral LD_{50}'s or NOAEL's are available for α-solanine and α-chaconine, the human toxic threshold of 1 mg/kg BW was used based on Friedman and McDonald (1997).

2.5. Exposure assessment

Because peeling potatoes reduces the quantity of glycoalkaloids in potatoes approximately 30–80% (Zeiger, 1998), and because the glycoalkaloid values we obtained from skins were very high compared to typical store-bought potatoes, only the risks for consuming the inner tissue of potatoes were assessed. Alpha-chaconine and α-solanine are found within the tuber, are heat stable, and are not degraded from cooking or frying as they begin to degrade between 230 and 280 °C (Bejarano et al., 2000). Therefore, risks associated with different types of preparation were not assessed. Concentrations of glycoalkaloids from control and Colorado potato beetle defoliation treatments were from Pariera Dinkins et al. (2008).

The human subgroups included the entire US population, all infants, children 1–6 years, children 7–12 years, youth 13–19 years, women 13 years and older who were pregnant, but not nursing, women 20 years and older not pregnant nor nursing, and men 20 years and older. All exposure and risk estimates were determined using the Dietary Exposure Evaluation Model™ (DEEM-FCID™, Ver. 2.03, Durango Software, Exponent, Inc., Washington, DC) based on the USDA's Continuing Surveys of Food Intakes by Individuals (CSFII) food consumption data for 1994–1996, 1998. Food translations within the program to convert foods-as-eaten to commodities were based on EPA, USDA Food Commodity Ingredient Data (FCID) recipe set as of August, 2002.

The acute (one day) food consumption patterns for each of the subgroups listed above were evaluated using the 50th, 95th, and 99.9th percentile US national consumption values for skinless potatoes only. DEEM calculates the acute oral exposure, the risk quotient (see below), and exposure as a percentage of the toxic threshold at different percentiles of US national consumption.

2.6. Risk characterization

The assumptions associated with the dietary risk assessment of glycoalkaloid consumption to all the different human subgroups were: (1) only skinless potatoes were consumed, (2) the only route of exposure was orally through ingestion of skinless tubers, (3) the toxic threshold for a human was 1 mg/kg BW, and (4) the toxic threshold was the same for all ages and sizes within the different human population subgroups.

To determine the risk posed to a subgroup in a population, the estimated glycoalkaloid exposure level was divided by the toxic threshold. The resulting ratio is known as the risk quotient (RQ) and serves as an index of relative risk.

3. Results and discussion

Means and standard errors for glycoalkaloid concentrations in inner tissue of tubers were 174.5 ± 8.59 mg/kg DW for the control and 258.8 ± 23.3 mg/kg DW for Colorado potato beetle defoliation (Pariera Dinkins et al., in 2008). A typical store-bought potato has a mean inner tissue glycoalkaloid concentration of 206 mg/kg DW (Zeiger, 1998). The difference between control and Colorado potato beetle defoliation treatments was statistically significant, and defoliation represented a 48.3% increase in glycoalkaloid concentrations.

The acute oral exposures for the eight population subgroups exposed to glycoalkaloid concentrations in the inner tissue of tubers from control plants at the 50th percentile of exposure ranged from 0.19 to 0.58 mg/kg BW/day, and the risks ranged from 19% to 58.3% of the toxic threshold (Table 1). The acute oral exposures for the eight population subgroups exposed to glycoalkaloid concentrations in the inner tissue of tubers from plants defoliated by Colorado potato beetles at the 50th percentile ranged from 0.28 to 0.86 mg/kg BW/day, and the risk ranged from 28.2% to 86.5% of the toxic threshold (Table 2).

Table 3 compares the RQ's for all eight population subgroups at the 50th, 95th, and 99.9th consumption percentiles for tubers from control plants and Colorado potato beetle defoliated plants. At the 50th percentile, the RQ's were greatest for all infants and least for women 13 and older who were pregnant but not nursing. At the 95th percentile, the RQ's were greatest for children between the ages of 1–6 years and least for women 13 and older who were pregnant but not nursing. At the 99.9th percentile, the RQ's were greatest for all infants and least for women 20 and older who were neither pregnant nor nursing. At the 50th, 95th, and 99.9th percentiles, RQ's were greatest for all human subgroups exposed to tubers from Colorado potato beetle defoliated plants.

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Table 1
Exposure, percentage of toxic dose, and risk quotient for the acute exposure of human subgroups to glycoalkaloids in the inner tissue of tubers from control plants

Control (No defoliation)									
Demographic	50th percentile			95th percentile			99.9th percentile		
	Exposure (mg/kg BW/day)	% Toxic dose	RQ*	Exposure (mg/kg BW/day)	% Toxic dose	RQ	Exposure (mg/kg BW/day)	% Toxic dose	RQ
US population	0.239	23.9	0.24	0.551	55.1	0.55	2.488	248.8	2.49
All infants	0	0	0	0.553	55.3	0.55	4.812	481.2	4.81
Children 1–6	0.515	51.5	0.51	1.131	113.1	1.13	3.753	375.3	3.75
Children 7–12	0.33	33	0.33	0.731	73.1	0.73	2.597	259.7	2.6
Youth 13–19	0.245	24.5	0.25	0.526	52.6	0.53	2.407	240.7	2.41
Women 13+ (pregnant/not nursing)	0.19	19	0.19	0.406	40.6	0.41	1.147	114.7	1.15
Women 20+ (not preg./not nursing)	0.206	20.6	0.21	0.428	42.8	0.43	1.07	106.9	1.07
Males 20+	0.216	21.6	0.22	0.488	48.8	0.49	1.422	142.2	1.42

* RQ = risk quotient.

Table 2
Exposure, percentage of toxic dose, and risk quotient for the acute exposure of human subgroups to glycoalkaloids in the inner tissue of tubers from Colorado potato beetle defoliated plants

Colorado potato beetle defoliation									
Demographic	50th percentile			95th percentile			99.9th percentile		
	Exposure (mg/kg BW/day)	% Toxic dose	RQ*	Exposure (mg/kg BW/day)	% Toxic dose	RQ	Exposure (mg/kg BW/day)	% Toxic dose	RQ
US population	0.354	35.4	0.35	0.817	81.7	0.82	3.69	369	3.69
All infants	0	0	0	0.82	82	0.82	7.135	713.5	7.13
Children 1–6	0.763	76.4	0.76	1.676	167.6	1.68	5.565	556.5	5.57
Children 7–12	0.489	48.9	0.49	1.085	108.5	1.08	3.85	385	3.85
Youth 13–19	0.363	36.3	0.35	0.78	78	0.78	3.569	356.9	3.57
Women 13+ (pregnant/not nursing)	0.282	28.2	0.28	0.603	60.3	0.6	1.7	170	1.7
Women 20+ (not preg./not nursing)	0.305	30.5	0.31	0.635	63.5	0.64	1.586	158.6	1.59
Males 20+	0.32	32.1	0.32	0.723	72.3	0.72	2.108	210.8	2.11

* RQ = risk quotient.

3.1. Estimates of dietary risk

Hlywka et al. (1994) observed a 37.5% increase in glycoalkaloids after defoliation by the same insect (we observed a 48.3% increase). To get a conservative idea of what this means in terms of potato consumption, by taking the average tuber glycoalkaloid concentration (including both inner and skin tissue), 500 mg/kg DW, a person weighing 60 kg would need to consume 120 g DW of potatoes to reach the 1 mg/kg BW toxic threshold. Because an average bagged potato weighs approximately 193 g FW (85% moisture), this translates to 4.1 potatoes. If the glycoalkaloid concentrations within the average tuber were to increase 48.3%, a person weighing 60 kg would need to eat only 81 g DW, which would be 2.8 potatoes.

The US EPA uses the 99.9th population exposure percentile to determine and regulate risk from dietary exposure to pesticides. At this percentile, RQ's for glycoalkaloids in our control tubers (or typical store-bought tubers) would exceed 1.0, and these levels are for the inner tissue only; they do not include the levels measured in the skins of tubers.

Using the exposure levels for adult males 20 years or older, a male weighing 70 kg would need to consume approximately 7 and 20 skinless potatoes to equal the RQ's determined by DEEM at the 95th and 99.9th percentiles, respectively. Approximately 14 skinless tubers of typical store-bought size from uninjured plants would need to be consumed for the exposure of glycoalkaloids to reach an RQ of 1.0. Nine skinless tubers from plants defoliated by Colorado potato beetle would need to be consumed to reach an RQ of 1.0. Again, this reflects the increase in dietary risk from the injury to the plants.

3.2. Uncertainty

The primary uncertainty associated with our human dietary risk assessment is the toxic threshold. Toxic thresholds (e.g., acute LD_{50} and acute, subchronic, and chronic NOAEL's or LOAEL's) for glycoalkaloids either are not available or are not sufficiently robust to set threshold levels. It is unlikely that the 1 mg/kg BW threshold used here is sufficiently conservative because the value has not been established experimentally and is an acute dose known to cause clinical signs of mild toxicity in humans. Indeed, Friedman and McDonald (1997) and Essers et al. (1998) argue that the current

Table 3
Acute risk quotients (RQ) for human subgroups exposed to glycoalkaloids in tubers

Acute risk quotients for human subgroups						
Demographic	50th percentile		95th percentile		99.9th percentile	
	Control	CPB defoliated	Control	CPB defoliated	Control	CPB defoliated
US population	0.24	0.35	0.55	0.82	2.49	3.69
All infants	0	0	0.55	0.82	4.81	7.14
Children 1–6	0.51	0.76	1.13	1.68	3.75	5.57
Children 7–12	0.33	0.49	0.73	1.08	2.6	3.85
Youth 13–19	0.25	0.35	0.53	0.78	2.41	3.57
Women 13+ (pregnant/not nursing)	0.19	0.28	0.41	0.6	1.15	1.7
Women 20+ (not pregnant/not nursing)	0.21	0.31	0.43	0.64	1.07	1.59
Males 20+	0.22	0.32	0.49	0.72	1.42	2.11

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USDA recommended food-safety levels are not sufficiently protective of public health. It is likely, therefore, that an acute NOAEL would be much lower, and a chronic NOAEL (which typically forms the basis for the acceptable daily intake of pesticides) would be even lower than an acute NOAEL. Consequently, it is possible that the toxic threshold could be orders of magnitude less than the value used here, especially given that safety factors of as much as 1000-fold are typically applied to the NOAEL to establish the acceptable daily intake for pesticides.

A complicating factor associated with the uncertainty in toxic thresholds is that animal models (which are used to determine most human toxic thresholds) may not be useful for glycoalkaloids. Both mice and rats are much less sensitive to these toxins than humans.

3.3. Comparative risk

Our results and those of Hlywka et al. (1994) suggest that high levels of Colorado potato beetle defoliation result in an appreciable increase in dietary risk. To manage this risk, growers can use insecticides approved for use on Colorado potato beetles on potato. However, what if the insecticides increase dietary risk greater than that posed by increased glycoalkaloid concentrations? Of the 17 insecticides currently approved in the US for use on potatoes, only four (diazinon, methamidophos, endosulfan, and aldicarb) have been found in quantifiable concentrations in potato tubers in recent USDA Pesticide Data Program surveys (USDA, 2000–2005). The highest levels found for diazinon, methamidophos, and endosulfan would result in acute dietary risks of 0.02–0.07% of the NOAEL at the 99.9th percentile of exposure to the most sensitive population groups. (Aldicarb's dietary risk would be much higher at 49.6% of the NOAEL.) With the possible exception of aldicarb, all other insecticides would seem to pose negligible dietary risks if used to reduce a significant increase in dietary risk from glycoalkaloid production as a result of defoliation.

3.4. Conclusions

It is interesting that the glycoalkaloid concentrations within the inner tissue of tubers exceed the toxic threshold for all population subgroups at less than the 99.9th percentile of exposure. This is both a function of the use of extremely high consumption percentiles as exposure endpoints and the use of 1 mg/kg BW as a toxic threshold. The results also demonstrate the conservative nature of the US EPA's regulation of pesticides. Regardless, the dietary risk assessments presented here support the arguments of Friedman and McDonald (1997) and Essers et al. (1998) that current potato safety levels for glycoalkaloids are not sufficiently protective of public health. If potatoes contained 1000 mg/kg DW of glycoalkaloids – the current USDA potato safety threshold – 65% of the US population would exceed an RQ of 1.0. Clearly, this is cause for concern and more research is needed on the toxicity of glycoalkaloids, especially the determination of acute and chronic NOAEL's.

Our results demonstrate differences in regulatory approaches to toxins in food. The US Food, Drug and Cosmetics Act allows a higher risk for natural food ingredients that may be toxic. The legal standard for such substances is that the food be "ordinarily injurious" which may be contrasted with "may render injurious" for human-made substances. Because tubers typically can be eaten without harm, they are considered safe within the meaning of the law. This increases the importance of information leading to a reduction of risk through proper handling, proper storage, and the use of insecticides to prevent insect damage.

Our work shows that the deleterious consequences of injury by insect pests are not limited solely to considerations of yield and physical appearance. Insect injury to crops also may increase the health risks to humans, livestock, and wildlife through alterations in phytotoxin production. Risk-benefit evaluations of pest management should be expanded to include these poorly understood effects of pest activity.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

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