Integrated Laboratory Systems

α-Chaconine
[20562-03-2]

and

α-Solanine
[20562-02-1]

Review of Toxicological Literature

Prepared for

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EXECUTIVE SUMMARY

α-Chaconine and α-solanine were nominated for testing based on their frequent occurrence in high concentrations in commonly ingested foods and the lack of carcinogenicity data for either compound.

Both α-chaconine and α-solanine are glycoalkaloids which exhibit antifeedant, fungicide, and pesticide activities. α-Chaconine has been used as a nematicide, and both glycoalkaloids have been used in the treatment of asthma and epilepsy. α-Chaconine and α-solanine occur naturally in potatoes (*Solanum tuberosum*) and other members of the Solanaceae family. Solanine is also present in apples, bell peppers, cherries, sugar beets, and tomatoes.

The two glycoalkaloids are produced commercially by extracting the major alkaloids with water, and then preparing a crude glycoalkaloid extract from the weakly acidic plant extract. Both chemicals contain the same solanidine moiety, but differ in their attached trioses. Production and import volumes were not found.

Human exposure predominantly occurs via the consumption of foods containing α-chaconine and α-solanine. In 1993, the average annual per capita consumption of potatoes in the U.S. was estimated to be 61 kg, which correlates to an average daily consumption of 167 g of potatoes. The glycoalkaloid content in potatoes varies significantly depending on environmental conditions during growing, mechanical injury, length of storage, and potato variety. The average glycoalkaloid content is 0.075 mg/g potato. This, in turn, would result in the ingestion of 12.75 mg glycoalkaloids/ person/ day (0.18 mg/kg) based on the average per capita consumption and an average body weight of 70 kg. Deep frying at temperatures of ≥170°C is effective in lowering the glycoalkaloid levels. Boiling is not effective and microwaving is only slightly effective. Similarly, freeze drying and dehydration reduce the glycoalkaloid content of potatoes only slightly or not at all. Peeling reduces the quantity of glycoalkaloids in potatoes since 30 to 80% of the glycoalkaloids are found in the outer peel. Baked and fried potato peels are a major source of large quantities of α-chaconine and α-solanine in the diet.

Poisoning resulting from ingesting potatoes containing high levels of glycoalkaloids has been demonstrated in a number of case studies. Symptoms, which generally occur 8 to 12 hours after ingestion, include gastrointestinal disturbances and neurological disorders. One study analyzing case reports of poisoning determined that glycoalkaloid doses of 2 to 5 mg/kg (0.0023-0.0058 mmol/kg) induce toxic symptoms in humans, and doses of 3 to 6 mg/kg (0.0035-0.007 mmol/kg) are fatal.

In one epidemiologic study, a regional correlation between the severity of potato late-blight (which causes increased glycoalkaloid levels) and the incidence of congenital spina bifida was reported, but other studies found no correlation between the consumption of potatoes and the incidence of birth defects.

The relationship between the consumption of potatoes and cancer risk has been investigated but remains undetermined. Case-control studies reporting increased risks of digestive tract tumors (e.g., colon, esophagus, rectal, and stomach cancer) associated with high levels of potato consumption are matched by an equal number of studies reporting a decreased risk for

these same cancers. Other studies have suggested that there is an increased risk for cancers of the brain, breast, endometrium, lung, and thyroid associated with the consumption of large quantities of potatoes, but a causal relationship between diet and cancer in these studies was not definitely proven.

Pharmacokinetic studies have shown that in humans, consumption of potatoes resulted in increased serum levels of α-chaconine, α-solanine, and the metabolite solanidine. Animal studies generally showed that α-chaconine and α-solanine are poorly absorbed. In mice, rats, and hamsters, α-chaconine and α-solanine reached peak tissue concentrations within 6 to 14 hours. Peak concentrations of α-solanine in plasma were reached in less than 35 hours. Tissues which accumulated α-chaconine and α-solanine included abdominal fat, adrenals, blood, brain, heart, kidney, liver, lungs, muscle, pancreas, spleen, testis, thymus, and thyroid. Both α-chaconine and α-solanine were excreted in the urine and feces (in varying amounts) either unchanged or as the metabolite solanidine. *In vitro*, rumen microorganisms were found to hydrolyze the glycoalkaloids to solanidine, much of which was then reduced to 5β-solanidan-3β-ol. No solanidine was identified in the milk of cows fed tater meal (an animal feed known to contain high levels of glycoalkaloids).

Acute toxicity values for several species have been reported. For α-chaconine, the intraperitoneal (i.p.) LD_{50} is 19.2 to 27.5 mg/kg (0.023-0.032 mmol/kg) for mice and 84 mg/kg (0.099 mmol/kg) for rats. For α-solanine, the oral LD_{50} dose is 590 mg/kg (0.68 mmol/kg) for rats; the i.p. LD_{50} dose is 30 to 42 mg/kg (0.035-0.048 mmol/kg) for mice, 67 to 75 mg/kg (0.077-0.086 mmol/kg) for rats, and less than 40 mg/kg (0.046 mg/kg) for monkeys. For rabbits, the i.p. LD_{Lo} dose is 50 mg/kg (0.059 mmol/kg) for α-chaconine and 40 mg/kg (0.046 mmol/kg) for α-solanine. The i.p. LD_{50} dose for solanine hydrochloride is 42 mg/kg (0.046 mmol/kg) for mice.

Acute, short-term, and subchronic animal toxicity studies identified similar effects from administration of α-chaconine, α-solanine, or plants or extracts containing the glycoalkaloids. Effects on the nervous system included increased heart, pulse, and respiratory rates, sedation, and coma. Effects resulting from cell membrane disruption included internal hemorrhaging, edema, diarrhea, constriction of the abdominal muscles, and lesions of the stomach and duodenum. α-Chaconine was a potent cholinesterase inhibitor, and α-solanine exhibited weak to moderate cholinesterase inhibition. In some studies, hepatotoxic effects were induced. Concordant with human case reports and animal toxicity studies, *in vitro* studies also found that α-chaconine andα-solanine disrupted cell membranes and inhibited cholinesterase activity. No chronic exposure data were found.

α-Chaconine, α-solanine, or plants or extracts containing these glycoalkaloids were embryotoxic and teratogenic to experimental animals. Teratogenic effects in mammals were primarily central nervous system abnormalities (e.g., exencephaly, cranial bleb, encephalocele, and anophthalmia). Some studies found no neural tube defects, but reported a high incidence of other abnormalities, including mild hydronephrosis, hydroureter, and irregular or fused ribs. α-Chaconine appeared to exert teratogenic effects at lower doses than α-solanine.

No carcinogenicity data were found for either compound.

Limited genotoxicity data were found for α-chaconine and α-solanine. α-Chaconine was not mutagenic at concentrations up to 2300 µmol/plate in *Salmonella typhimurium* strains TA98 and TA100 with or without metabolic activation. However, analysis of pooled data from two experiments with α-chaconine in strain TA98 without metabolic activation suggested weak mutagenic activity. Based on data from multiple experiments, α-solanine at concentrations up to 2300 µmol/plate was not mutagenic in strains TA98 and TA100 with or without metabolic activation. In a DNA-Cell-Binding assay, solanine, at 25 or 250 µM, did not increase the binding of radiolabeled DNA to *Escherichia coli* Q13 cells. When administered orally at 10 mg/kg to mice, α-[^{3}H]chaconine did not covalently bind to DNA or RNA isolated from the livers. The only other genotoxicity data identified for these compounds was from a mouse micronucleus test. In this study, no increase was observed in the frequency of micronucleated erythrocytes in blood from weanling mice or fetuses from dams dosed i.p. with up to 45 mmol/kg α-chaconine and 90 mmol/kg α-solanine.

One immunologic study indicated that consumption of potato plants containing glycoalkaloids induced dermatitis in Indian buffaloes, while another study reported anti-allergic effects of intravenous (i.v.) administration of solanine hydrochloride to guinea pigs.

Studies conducted to evaluate other biological effects potentially relevant to this evaluation were reviewed. *In vitro* tests using isolated guinea pig ileum indicated a cholinergic action of α-chaconine and α-solanine. Solanine did not impede synaptic transmissions in isolated frog thoracic superficial muscle. *In vitro* studies using isolated frog ventricle or beating rat heart cell cultures found that solanine exerted a positive chronotropic effect and α-chaconine and α-solanine exerted a positive inotropic effect. Both glycoalkaloids were cytotoxic to Chinese hamster ovary cells. Solanine exhibited a hyperglycemic effect in intact rats and a hypoglycemic effect in adrenalectomized rats. α-Chaconine and α-solanine both increased ornithine decarboxylase activity in rats. Low concentrations of α-solanine stimulated the growth of cultured human fibroblasts by shortening the G_1 cell cycle phase. Higher concentrations inhibited fibroblast cell growth, and an abnormal accumulation of cells in the G_2 phase was observed. α-Chaconine inactivated Herpes simplex virus Type I *in vitro*.

In terms of structure-activity relationships, the biological activity of glycoalkaloids is influenced by the nature and the number of sugars composing the carbohydrate moiety attached to the 3-OH position of the aglycone, and the stereochemical orientation of the chaconine diglycosides. Embryotoxicity generally decreased with stepwise removal of sugar units from the chacotriose and solatriose side chains. Based on this relationship, the α forms of the two glycoalkaloids, similar to each other in potency, are more potent than the β forms, which in turn are more potent than the γ forms; solanidine, which contains no sugar units, is the least potent embryotoxin.

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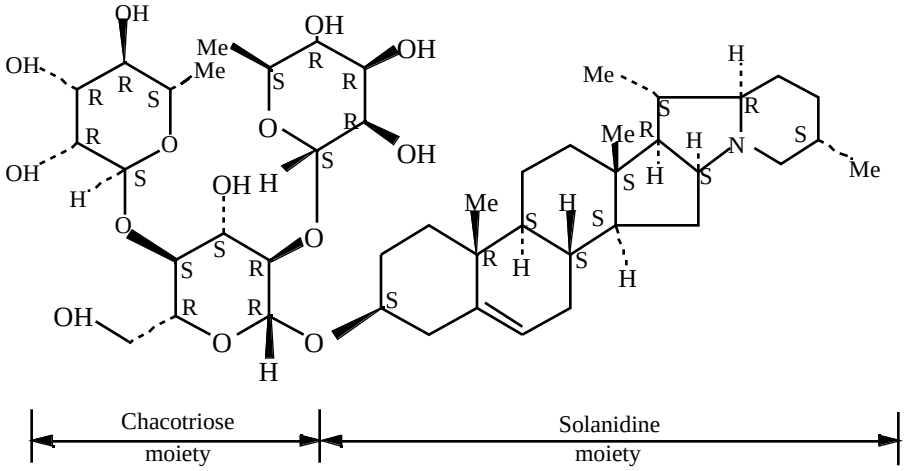
1.0 BASIS FOR NOMINATION

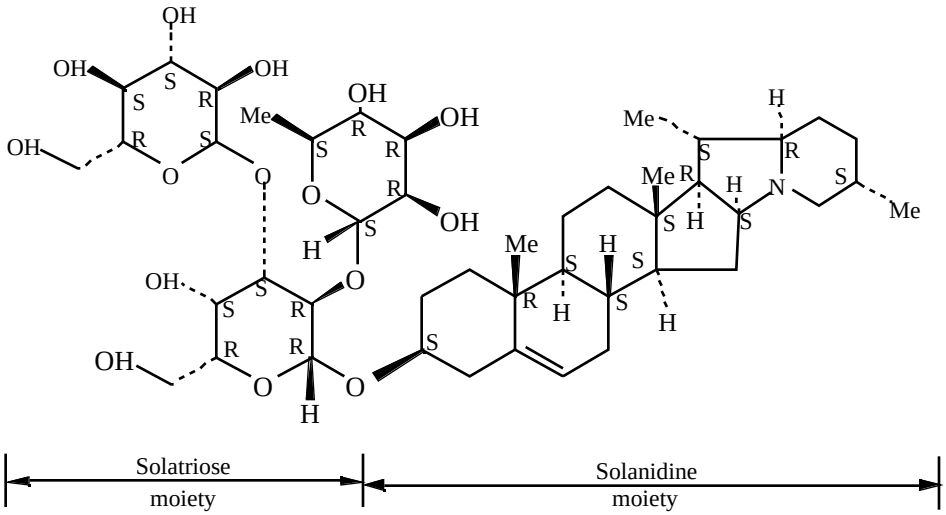
The nomination of α-chaconine and α-solanine by Dr. L. S. Gold, Dr. B. N. Ames, and Dr. T. H. Slone, University of California, Berkeley, for testing is based on their frequent occurrence in high concentrations in foods and the lack of carcinogenicity data.

2.0 INTRODUCTION

α-chaconine
[20562-03-2]



α-solanine
[20562-02-1]


Solatriose
moiety
Solanidine
moiety

2.1 Chemical Identification

α-Chaconine ($C_{45}H_{73}NO_{14}$, mol. wt. = 852.07) is also called:

β-*D*-Glucopyranoside, (3β)-solanid-5-en-3-yl-*O*-6-deoxy-α-*L*-mannopyranosyl-(1→2)-*O*-[6-deoxy-α-*L*-mannopyranosyl-(1→4)]- (9CI)
1*H*-Naphth[2',1':4,5]indeno[1,2-*b*]indolizine, β-*D*-glucopyranoside deriv.
Solanidane, β-*D*-glucopyranoside deriv.

α-Solanine ($C_{45}H_{73}NO_{15}$, mol. wt. = 868.07) is also called:

β-*D*-Galactopyranoside, (3β)-solanid-5-en-3-yl-*O*-6-deoxy-α-*L*-mannopyranosyl-(1→2)-*O*-[β-*D*-glucopyranosyl-(1→3)]- (9CI)
1*H*-Naphth[2',1':4,5]indeno[1,2-*b*]indolizine, β-*D*-galactopyranoside deriv.
Solanidane, β-*D*-galactopyranoside deriv.
α-Solanin
Solatunine

Solanidine ($C_{27}H_{43}NO$, mol. wt. 397.64, CAS No. 80-78-4) is also called:

Solanid-5-en-3-ol, (3β)- (9CI)
1*H*-Napth[2',1':4,5]indeno[1,2-*b*]indolizine, solanid-5-en-3-ol deriv.
Solanid-5-en-3β-ol
Solanidin
Solatubin
Solatubine

The α-chaconine:α-solanine mix (60:40) typically found in potatoes (Slanina, 1990) has a molecular weight of 858.47. However, the proportion of α-chaconine and α-solanine varies widely in different potato varieties (Osman et al., 1976; Fitzpatrick et al., 1977; Wu and Salunkhe 1977c; Ahmed and Müller, 1978; Cadle et al., 1978; all cited by Jadhav et al., 1981).

A 1:1 α-chaconine:α-solanine mix (used in some studies) has a molecular weight of 860.07.

Solanine hydrochloride ($C_{45}H_{73}NO_{15}\cdot HCl$) has a molecular weight of 904.53.

Chemical names mentioned in this document are given as the original authors presented them.

2.2 Physical-Chemical Properties

2.2.1 α-Chaconine

Property	Information	Reference
Physical State	solid	NIEHS (1997a)
Melting Point (^{o}C)	243	NIEHS (1997a)
Solubility	not found	

2.2.2 α-Solanine

Property	Information	Reference
Physical State	slender needles from 85% alcohol	Budavari (1996)
Melting Point (°C)	190-285	NIEHS (1997b)
Dissociation Constant (pK) at 15°C	6.66	Budavari (1996)
Solubility:		
Water	practically insoluble	Budavari (1996)
Organic Solvents	readily soluble in hot alcohol; practically insoluble in ether and chloroform	Budavari (1996)

α-Chaconine and α-solanine are both glycosylate derivatives of the aglycone solanidine (Friedman and Dao, 1992). β_1-, β_2-, and γ-Chaconine and -solanine are formed by stepwise cleavage of the individual sugars of the glycoside, respectively (Friedman and McDonald, 1997).

2.3 Commercial Availability

In the U. S., α-chaconine and α-solanine are available from Fluka Chemical Corp. and Sigma Chemical Co. (CHEMCATS, 1995). α-Solanine is also available in the U. S. from Atomergic Chemetals Corp. and Research Plus, Inc. Both glycoalkaloids are sold in 2 to 50 mg quantities.

3.0 PRODUCTION PROCESSES AND ANALYSES

The major alkaloids of potatoes occur in the form of salts that may be extracted with water, forming a mixture of weakly acidic plant extracts (Jadhav et al., 1981). Using the plant extracts, a crude glycoalkaloid preparation is normally obtained by precipitation with ammonia at a pH above 10 at 70°C (Achterberg et al, 1979; Bushway et al., 1980b; both cited by Jadhav et al., 1981). Individual glycoalkaloids may then be isolated from the crude preparation using a number of chromatographic procedures, including preparative thin layer chromatography (TLC) (Boll, 1962; Fitzpatrick et al., 1978; both cited by Jadhav et al., 1981; Sharma et al., 1979), high-performance liquid chromatography (HPLC) (Bushway et al., 1980b; cited by Jadhav et al., 1981), or column chromatography (Paseshnichenko and Guseva, 1956a; Talley, 1975; McCollum and Sinden, 1979; all cited by Jadhav et al., 1981; Nishie et al., 1975; Chaube and Swinyard,

1976). A clear separation of α-chaconine and α-solanine is achieved by chromatography on paper saturated with monosodium phosphate solution and ethyl acetate-acetic acid-water (11:2:2, v/v/v) as the developing solvent (Paseshnichenko and Guseva, 1956a; cited by Jadhav et al., 1981). α-Chaconine and α-solanine are also separated from potatoes by paper chromatography with a wedge strip procedure (Schilling and Zobel, 1966; cited by Jadhav et al., 1981) or by using rotation locular countercurrent chromatography (RLCC) on the aqueous potato fraction extracted with methanol (Kubo and Fukuhara, 1996). RLCC was followed by removal of methanol, suspension of the residue in water, and partitioning with organic solvents.

4.0 PRODUCTION AND IMPORT VOLUMES

Production and import volumes of α-chaconine and α-solanine were not found, but the data reviewed on production processes provided no indication that α-chaconine or α-solanine are produced on a large scale.

The U.S. production volume for potatoes in 1994 was 23 million tons (21 million Mg) (Famighetti, 1995). As reported in 1981, the annual world-wide production of potatoes was 300 million tons (272 million Mg), making potatoes the third ranking economic commodity (Jadhav et al., 1981).

5.0 USES

Both α-chaconine and α-solanine have pesticidal properties, including antifeedant and fungicidal properties (Beckstrom-Sternberg and Duke, 1997). α-Chaconine also has nematicidal properties. α-Chaconine and α-solanine were effective as larval feeding deterrents for spruce budworm (*Choristoneura fumiferana*) (Bentley et al., 1984). Additionally, solanine hydrochloride has been used as an insecticide (Budavari, 1996). Solanine was formerly used in the treatment of bronchitis, epilepsy, and asthma (Dorland's Illustrated Medical Dictionary, 1994). The genus *Solanum* has sedative and anticonvulsant properties (Budavari, 1996). Jimson weed, which contains solanine, is an ingredient in over-the counter drug preparations used for

treating bronchial asthma attacks and as an anticholinergic for relieving cough and cold symptoms (21 CFR 250.12). However, its effectiveness for either use is questionable.

The presence of glycoalkaloids in potato foliage is desirable in cultivating potatoes because the glycoalkaloids provide resistance to disease and insect infestation (Allen and Kúc, 1968; Sinden et al., 1980; both cited by Matthew et al., 1983).

6.0 ENVIRONMENTAL OCCURRENCE AND PERSISTENCE

α-Chaconine and α-solanine occur naturally in potatoes (*Solanum tuberosum*), constituting 95% of the total glycoalkaloid content in commercially available potatoes (Paseshnichenko and Guseva, 1956b; cited by Matthew et al., 1983). α-Chaconine also occurs in another potato species (*Solanum chacoense*) (Nishie et al., 1975). Specific potato plant tissues which contain α-chaconine and α-solanine are leaves, shoots, stems, blossoms, tubers, eyes, peels, and sprouts, with the greatest glycoalkaloid content in sprouts (Jadhav and Salunkhe, 1975; cited by Maga, 1980). The ratio of α-chaconine to α-solanine is generally 60:40 (Slanina, 1990), but varies considerably among portions of the plant and species (Osman et al., 1976; Fitzpatrick et al., 1977; Wu and Salunkhe 1977; Ahmed and Müller, 1978; Cadle et al., 1978; all cited by Jadhav et al., 1981).

α-Chaconine and α-solanine are synthesized at cut surfaces of potatoes (Locci and Kúc, 1967; Allen and Kúc, 1968; both cited by Beier, 1990), with synthesis being stimulated by mechanical injury and aging (McKee, 1955; Locci and Kúc, 1967; Sinden, 1972; all cited by Beier, 1990). Exposure of potatoes to light in the field or marketplace also causes increased synthesis of the glycoalkaloids (Griebel, 1924; cited by Beier, 1990). Potatoes that have turned green due to light exposure are unsafe for human consumption due to high levels of α-chaconine and α-solanine (Morris and Lee, 1984).

α-Solanine is present in other edible plants, including apples (Lagolo et al., 1991; cited by Hoskins, 1994), bell peppers (*Capsicum annuum*) (about 500 ppm in the leaves) (Beckstrom-Sternberg and Duke, 1997), eggplant (*Solanum melongena*) (Lagolo et al., 1991; cited by Hoskins, 1994), sugar beets (*Beta vulgaris*) (Lagolo et al., 1991; cited by Hoskins, 1994), and tomatoes

(*Lycopersicon esculentum*) (Budavari, 1996). The concentration of α-solanine in tomatoes was less than 50 ppm (0.05 mg/g tomato), with higher concentrations in the viscous materials with high sugar content than in the other parts (Kyzlink et al., 1981).

α-Chaconine and α-solanine are present also in Jerusalem cherries (*S. pseudo-capsium*) (Teat and Ellis, 1981) and solanine is present in bittersweet (*Solanum dulcamara*) (De Vincenzi et al., 1996), black nightshade (*S. nigrum*) (0-40 ppm in the fruit) (Beckstrom-Sternberg and Duke, 1997), ground cherries (*Physalis peruviana*) (Smith, 1994), and Jimson weed (*Datura stramonium*) (Hansen, 1928).

Solanine may be found in effluents from potato starch factories (Brebion et al., 1967) and in the potato waste products generated during potato processing (Bushway et al., 1984). However, solanine is largely biodegradable (Brebion et al., 1967). Some waste products from the starch and potato industries are made into potato and tater meal (animal feeds) (Bushway et al., 1980). Potato meal is a dried potato pulp, which is a waste product from starch manufacturing, and tater meal is prepared from leftover potato food products (Bushway et al., 1980a; 1985).

7.0 HUMAN EXPOSURE

Human exposure predominantly occurs via the consumption of foods containing α-chaconine and α-solanine. In 1993, the average per capita consumption of potatoes in the U.S. was estimated to be 61 kg/year, which corresponds to an average daily per capita consumption of 167 g of potatoes (Willard, 1993; cited by Friedman and McDonald, 1997). Based on a 1983 report by the USDA Economic Research Service (cited by Stofberg and Grundschober, 1984), the U. S. per capita consumption was 8.1 kg/year (22 g/day) for apples and 30.8 kg/year (84 g/day) for tomatoes.

Glycoalkaloid levels vary significantly depending on the potato variety (Maga, 1980), but no variety is completely void of α-chaconine and α-solanine (Hopkins, 1995). Potato breeders attempt to keep the α-solanine content of potatoes below 0.2 mg/g (200 ppm) fresh weight (Smith, 1977; cited by Beier, 1990), but the concentrations of α-chaconine and α-solanine in potato tubers vary between 0.5-635 ppm (0.0005-0.64 mg/g potato) and 5-125,100 ppm (0.005-

125.1 mg/g potato), respectively (Beckstrom-Sternberg and Duke, 1997). In a study by Wolf and Duggar (1946; cited by Beier, 1990), the α-solanine content of 32 Wisconsin potato varieties varied from 0.02 to 0.13 mg/g of tuber. The average glycoalkaloid content is usually 0.075 mg/g potato (Jadhav et al., 1981), which is equal to 12.5 mg/person/day (0.18 mg/kg/day), based on average personal consumption and a body weight of 70 kg (154 lbs.). Although storage for extended periods increases the glycoalkaloid content, Wilson et al. (1983) showed that storing potatoes for 3 months under home storage conditions at 12.2°C did not increase the glycoalkaloid content to levels which are toxic to humans.

Boiling is not effective in decreasing the concentrations of α-chaconine and α-solanine in potatoes (Takagi et al., 1990). Microwaving reduced the alkaloid content by 15%, and deep frying showed mixed results depending on cooking temperature. The authors noted that the critical temperature for the decomposition of both alkaloids in cooked potatoes was 170°C. Freeze drying and dehydration of potatoes reduced the glycoalkaloid content either slightly or not at all (Brain and Turner, 1971; Zaletskaya et al., 1977; both cited by Morris and Lee, 1984).

Thirty to eighty percent of the glycoalkaloids in the potato tuber are found in the outer layers (Meyer, 1895; Bomer and Mattis, 1924; Griebel, 1924; Wolf and Duggar, 1946; all cited by Maga, 1980). Thus, peeling generally reduces glycoalkaloid intake (Lagolo et al., 1991; cited by Hoskins, 1994). However, a study by Mondy and Gosselin (1988; cited by Beier, 1990) concluded that peeling potatoes prior to cooking did not decrease the glycoalkaloid content.

Fried potato peels are a source of large quantities of α-chaconine and α-solanine; one study indicated that fried potato peels had α-chaconine plus α-solanine levels of 1.4 to 1.5 mg/g potato peel (Bushway and Ponnampalam, 1981), which is seven times the recommended upper safety limit (0.2 mg/g potato) (Beier, 1990). Another study found that combined α-chaconine and α-solanine levels in baked or fried peels of commercial potato varieties ranged from 0.02 to 1.1 mg/g potato peel and 0.03 to 1.6 mg/g potato peel, respectively (Bushway et al., 1983). Additionally, the concentration of glycoalkaloids in commercial potato chips varies between 0.1 and 0.7 mg/g of chips (Sizer et al., 1980).

The presence of high levels of glycoalkaloids in potato can be determined by chewing a small piece of the raw potato peel; bitterness indicates high glycoalkaloid content (Wood and Young, 1974; cited by Beier, 1990). Levels of glycoalkaloids above 0.1 mg/g tuber cause a slow developing, hot burning persistent irritation of the sides of the tongue and back of the mouth. An immediate burning sensation is induced by glycoalkaloid levels greater than 0.2 mg/g tuber.

8.0 REGULATORY STATUS

Neither α-chaconine nor α-solanine are registered under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) for use as pesticides.

The potato breeding program of the U.S. Department of Agriculture has an accepted, but non-mandated, guideline of 0.2 mg/g tuber for total glycoalkaloid content of parents and offspring of potential potato varieties (Sinden and Webb, 1972; cited by Beier, 1990).

The solanine-containing plant bittersweet is classified by the U.S. Food and Drug Administration as an unsafe poisonous herb (De Vincenzi et al., 1996). Under 21 CFR 250.12, products containing Jimson weed are misbranded when the packaging contains directions for use in self-medication. Any new OTC cough-cold product containing Jimson weed that is labeled, represented or promoted for use as an anticholinergic requires an approved new drug application under Section 201(p) of the Federal Food, Drug, and Cosmetic Act; in the absence of an approved new drug application, the product is misbranded under Section 502 of the Act.

9.0 TOXICOLOGICAL DATA

Summary: Poisoning resulting from ingesting potatoes containing high levels of glycoalkaloids has been demonstrated in a number of case studies. Symptoms, which generally occur 8 to 12 hours after ingestion, include gastrointestinal disturbances and neurological disorders. One study analyzing case reports of poisoning determined that glycoalkaloid doses of 2 to 5 mg/kg (0.0023-0.0058 mmol/kg) induce toxic symptoms in humans, and doses of 3 to 6 mg/kg (0.0035-0.007 mmol/kg) are fatal.

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The relationship between the consumption of potatoes and cancer risk has been investigated but remains undetermined. Case-control studies reporting increased risks of digestive tract tumors (e.g., colon, esophagus, rectal, and stomach cancer) associated with high levels of potato consumption are matched by an equal number of studies reporting a decreased risk for these same cancers. Other studies have suggested that there is an increased risk for cancers of the brain, breast, endometrium, lung, and thyroid associated with the consumption of large quantities of potatoes, but a causal relationship between diet and cancer in these studies was not definitely proven.

Pharmacokinetic studies have shown that in humans, consumption of potatoes resulted in increased serum levels of α-chaconine, α-solanine, and the metabolite solanidine. Animal studies generally showed that α-chaconine and α-solanine are poorly absorbed. In mice, rats, and hamsters, α-chaconine and α-solanine reached peak tissue concentrations within 6 to 14 hours. Peak concentrations of α-solanine in plasma were reached in less than 35 hours. Tissues which accumulated α-chaconine and α-solanine included abdominal fat, adrenals, blood, brain, heart, kidney, liver, lungs, muscle, pancreas, spleen, testis, thymus, and thyroid. Both α-chaconine and α-solanine were excreted in the urine and feces (in varying amounts) either unchanged or as the metabolite solanidine. *In vitro*, rumen microorganisms were found to hydrolyze the glycoalkaloids to solanidine, much of which was then reduced to 5β-solanidan-3β-ol. No solanidine was identified in the milk of cows fed tater meal (an animal feed known to contain high levels of glycoalkaloids).

Acute toxicity values for several species have been reported. For α-chaconine, the intraperitoneal (i.p.) LD_{50} is 19.2 to 27.5 mg/kg (0.023-0.032 mmol/kg) for mice and 84 mg/kg (0.099 mmol/kg) for rats. For α-solanine, the oral LD_{50} dose is 590 mg/kg (0.68 mmol/kg) for rats; the i.p. LD_{50} dose is 30 to 42 mg/kg (0.035-0.048 mmol/kg) for mice, 67 to 75 mg/kg (0.077-0.086 mmol/kg) for rats, and less than 40 mg/kg (0.046 mg/kg) for monkeys. For rabbits, the i.p. LD_{Lo} dose is 50 mg/kg (0.059 mmol/kg) for α-chaconine and 40 mg/kg (0.046 mmol/kg) for α-solanine. The i.p. LD_{50} dose for solanine hydrochloride is 42 mg/kg (0.046 mmol/kg) for mice.

Acute, short-term, and subchronic animal toxicity studies identified similar effects from administration of α-chaconine, α-solanine, or plants or extracts containing the glycoalkaloids. Effects on the nervous system included increased heart, pulse, and respiratory rates, sedation, and coma. Effects resulting from cell membrane disruption included internal hemorrhaging, edema, diarrhea, constriction of the abdominal muscles, and lesions of the stomach and duodenum. α-Chaconine was a potent cholinesterase inhibitor, and α-solanine exhibited weak to moderate cholinesterase inhibition. In some studies, hepatotoxic effects were induced. Concordant with human case reports and animal toxicity studies, *in vitro* studies also found that α-chaconine andα-solanine disrupted cell membranes and inhibited cholinesterase activity. No chronic exposure data were found.

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other abnormalities, including mild hydronephrosis, hydroureter, and irregular or fused ribs. α-Chaconine appeared to exert teratogenic effects at lower doses than α-solanine.

No carcinogenicity data were found for either compound.

Limited genotoxicity data were found for α-chaconine and α-solanine. α-Chaconine was not mutagenic at concentrations up to 2300 µmol/plate in *Salmonella typhimurium* strains TA98 and TA100 with or without metabolic activation. However, analysis of pooled data from two experiments with α-chaconine in strain TA98 without metabolic activation suggested weak mutagenic activity. Based on data from multiple experiments, α-solanine at concentrations up to 2300 µmol/plate was not mutagenic in strains TA98 and TA100 with or without metabolic activation. In a DNA-Cell-Binding assay, solanine, at 25 or 250 µM, did not increase the binding of radiolabeled DNA to *Escherichia coli* Q13 cells. When administered orally at 10 mg/kg to mice, α-[^{3}H]chaconine did not covalently bind to DNA or RNA isolated from the livers. The only other genotoxicity data identified for these compounds was from a mouse micronucleus test. In this study, no increase was observed in the frequency of micronucleated erythrocytes in blood from weanling mice or fetuses from dams dosed i.p. with up to 45 mmol/kg α-chaconine and 90 mmol/kg α-solanine.

One immunologic study indicated that consumption of potato plants containing glycoalkaloids induced dermatitis in Indian buffaloes, while another study reported anti-allergic effects of intravenous (i.v.) administration of solanine hydrochloride to guinea pigs.

Studies conducted to evaluate other biological effects potentially relevant to this evaluation were reviewed. *In vitro* tests using isolated guinea pig ileum indicated a cholinergic action of α-chaconine and α-solanine. Solanine did not impede synaptic transmissions in isolated frog thoracic superficial muscle. *In vitro* studies using isolated frog ventricle or beating rat heart cell cultures found that solanine exerted a positive chronotropic effect and α-chaconine and α-solanine exerted a positive inotropic effect. Both glycoalkaloids were cytotoxic to Chinese hamster ovary cells. Solanine exhibited a hyperglycemic effect in intact rats and a hypoglycemic effect in adrenalectomized rats. α-Chaconine and α-solanine both increased ornithine decarboxylase activity in rats. Low concentrations of α-solanine stimulated the growth of cultured human fibroblasts by shortening the G_1 cell cycle phase. Higher concentrations inhibited fibroblast cell growth, and an abnormal accumulation of cells in the G_2 phase was observed. α-Chaconine inactivated Herpes simplex virus Type I *in vitro*.

In terms of structure-activity relationships, the biological activity of glycoalkaloids is influenced by the nature and the number of sugars composing the carbohydrate moiety attached to the 3-OH position of the aglycone, and the stereochemical orientation of the chaconine diglycosides. Embryotoxicity generally decreased with stepwise removal of sugar units from the chacotriose and solatriose side chains. Based on this relationship, the α forms of the two glycoalkaloids, similar to each other in potency, are more potent than the β forms, which in turn are more potent than the γ forms; solanidine, which contains no sugar units, is the least potent embryotoxin.

9.1 General Toxicology

9.1.1 Human Data

9.1.1.1 Solanine Poisoning

Solanine poisoning occurs when humans ingest potatoes containing high levels of glycoalkaloids (Rothe, 1918; Wilson, 1959; both cited by Maga, 1980; Harris and Cockburn, 1918); potatoes containing greater than 0.02% (200 ppm) solanine are toxic (Oslage, 1956; cited by Maga, 1980). Several signs of poisoning have been traced to eating potatoes with α-solanine concentrations between 0.1 to 0.4 mg/g (100-400 ppm) (Alfa and Heyl, 1923; cited by Beier, 1990). Symptoms include gastrointestinal disturbances and neurological disorders (Willimott, 1933; Terbruggen, 1936; Ruhl, 1951; Oettingen, 1952; Gonzalez et al., 1954; all cited by Maga, 1980), such as nausea, diarrhea, vomiting, stomach cramps, headaches, and dizziness (Wood and Young, 1974; cited by Beier, 1990). Solanine has caused hemolytic and hemorrhagic damage to the gastrointestinal tract (Konig and Stafze, 1953; cited by Maga, 1980) and to the retina (Ruhl, 1951; cited by Maga, 1980). Symptoms generally occur about 8 to 12 hours after ingestion (McMillan and Thompson, 1979; Morris and Lee, 1984).

According to a calculation by Morris and Lee (1984), 2 to 5 mg/kg body weight (0.0023-0.0058 mmol/kg) is a toxic human dose of glycoalkaloids. Ingestion of 3 to 6 mg/kg (0.0035-0.007 mmol/kg) is fatal. However, Friedman and McDonald (1997) found that indications of toxic effects were observed at 1.0 mg/kg (0.0012 mmol/kg).

After eating 1 to 1.5 kg cooked, peeled potatoes containing 0.24 mg glycoalkaloids/g tubers, 56 German soldiers experienced typical “solanine” poisoning (Pfuhl, 1899; cited by JECFA, 1993). Jaundice and partial paralysis were observed in a few cases. The intake of glycoalkaloids was calculated to be about 3.4 to 5.1 mg/kg (0.004-0.0059 mmol/kg) using an assumed body weight of 70 kg.

In 18 households in Scotland, 61 people suffered solanine poisoning within several hours after eating potatoes containing 0.41 mg solanine/g tubers (Harris and Cockburn, 1918); one five-year old-died. Members of the households who did not eat potatoes experienced no ill effects. The glycoalkaloid intake was estimated as 3.4 mg/kg (0.0040 mmol/kg), based on consumption of

500 g potatoes and a body weight of 60 kg.

In Germany, an outbreak was reported to affect 41 people who had eaten potatoes with a glycoalkaloid content of 0.43 mg/g tuber (Rothe, 1918; cited by Jadhav et al., 1981).

In another case report, 7 family members who ate greened potatoes exhibited poisoning symptoms after 2 days (Hansen, 1925; cited by Jadhav et al., 1981). The mother (age 45) and daughter (age 16) died; the other 5 family members recovered.

Wilson (1959; cited by Hopkins, 1995) reported the experience of a British family, in which 4 of the family members experienced symptoms of vomiting, abdominal pain, diarrhea, and general malaise on three consecutive Sundays after eating a meal including jacket potatoes. A fifth family member who ate only the potato flesh experienced no symptoms. Severity of symptoms was related to the number of potatoes consumed. Solanine levels in the potatoes were determined to be 0.5 mg/g potato, but no analysis of the skin and potato flesh was undertaken. From this incident, it was estimated that severely toxic effects are caused by doses of 4.2 mg/kg (0.0049 mmol/kg) and that mild symptoms are caused by doses of 1.4 mg/kg (0.0016 mmol/kg).

In a pharmacological experiment, test subjects developed potato poisoning symptoms following an oral purified potato glycoalkaloids dose of 2 mg/kg (0.0023 mmol/kg) (Ruhl, 1951; cited by Sinden and Deahl, 1994). Lower doses had little or no effect; higher doses were not tested.

McMillan and Thompson (1979) reported a poisoning incident involving 78 adolescent boys attending a U.K. school, who became ill after eating a batch of potatoes that had been left in stores over the summer term. Seventeen (22%) of the boys who ate the potatoes were hospitalized with symptoms of vomiting, severe diarrhea, abdominal pain, fever, hallucinations, and other nervous system effects. The three most critically ill were comatose or stuporose and had peripheral circulatory collapse at the time of hospital admission. The glycoalkaloid content of the potatoes was measured as 0.25 to 0.3 mg/g peeled, boiled potato. The potatoes left over from the meal had excessive anticholinesterase activity *in vitro*.

In Canada, 61 out of 109 schoolchildren and their teachers became ill after eating baked potatoes containing about 0.5 mg solanine/g potato (Anonymous, 1984; cited by Hopkins, 1995).

Symptoms included nausea, abdominal cramps, headache, vomiting, fever, and diarrhea. The ingested solanine dose was estimated as 2.5 mg/kg (0.0029 mmol/kg).

In a Swedish volunteer study, 7 male volunteers (doctors or medical students) abstained from eating potatoes for 48 hours and were then given a potato dose which provided a total glycoalkaloid dose of 1 mg/kg (0.6 mg/kg [0.0007 mmol/kg] α-chaconine and 0.4 mg/kg [0.0005 mmol/kg] α-solanine) (Hellenäs et al., 1992b). Six of the volunteers experienced a bitter taste, burning of the throat, and mild to severe nausea; one of the six also had diarrhea. Most experienced symptoms within 30 minutes after ingestion of the potato meal, and symptoms persisted for 3-4 hours. No correlation was found between toxicity symptoms and concentrations of the glycoalkaloids in the serum.

A 70-year-old woman experienced vomiting, diarrhea, and bloody stools after drinking the juice of a potato with a concentration of solanine 15-fold greater than that of a normal potato (Gonmori et al., 1993).

9.1.1.2 Birth Defects

A correlation was identified between the severity of potato late-blight (which causes increased glycoalkaloid levels) and the incidences of congenital spina bifida in humans (Renwick, 1972; Renwick et al., 1974). Ireland, with highly suitable weather for blight fungus, has the world's highest incidence of congenital spina bifida (Renwick, 1972). The same correlation was found in other geographical regions. In areas where new potato varieties with higher glycoalkaloid contents were being ingested, the frequency of anencephaly was twice as high as the frequency reported for previous times. Elwood (1976), on the other hand, reported that mortality rates from anencephalus, spina bifida, and other congenital abnormalities in Canada were similar to the incidence of potato blight, but annual or seasonal associations were not identified. The author concluded that the geographical correlation was probably related to other factors, such as socio-economic conditions.

Nevin and Merrett (1975; cited by Hopkins, 1995) conducted a small clinical trial in Belfast. Mothers with a previous child with anencephaly or spina bifida were advised to avoid

eating potatoes if they tried for another child. The incidence of birth defects in offspring of 27 mothers who became pregnant again and maintained the potato-free diet was 8.7%; the incidence of birth defects in the offspring of 56 mothers who continued to eat potatoes was 3.6%. Additionally, another study identified that serum levels of glycoalkaloids were lower in 210 mothers carrying a fetus with a neural tube defect than in 170 mothers carrying an unaffected fetus (Harvey et al., 1986).

9.1.1.3 Cancer Studies

Case-control studies reporting increases in risk for cancers of the colon, rectum (Taijima and Tominaga, 1985; Tuyns et al., 1988; Benito et al., 1990; 1993; Bidoli et al., 1992; Iscovich et al., 1992; Peters et al., 1992; Steinmetz and Potter, 1993; Centonze et al., 1994; all cited by Hopkins, 1995), stomach (Graham et al., 1972; Taijima and Tominaga, 1985; Trichopoulos et al., 1985; La Vecchia et al., 1987; Hu et al., 1988; Demirer et al, 1990; Hansson et al., 1993; Ramon et al., 1993; all cited by Hopkins, 1995), and esophagus (Zeigler et al., 1981; Brown et al., 1988; both cited by Hopkins, 1995) in humans consuming large amounts of potatoes have been matched by a similar number of studies reporting a decrease in cancer risk for the same types of cancers with increased potato consumption (Hopkins, 1995).

The relative risk of cancer of the brain (Boeing et al., 1993; cited by Hopkins, 1995), breast (Iscovich et al., 1989; Levi et al., 1993a; both cited by Hopkins, 1995), endometrium (Levi et al., 1993b; cited by Hopkins, 1995) lung (Sankaranarayanan et al., 1994; cited by Hopkins, 1995), and thyroid (Ron et al., 1987; Franceschi et al., 1989; both cited by Hopkins, 1995) associated with consuming large quantities of potatoes has also been reported. Some studies found a nominal indication of increased risk, but Hopkins (1995) stated that it is premature to assume that the effects were causally related.

9.1.2 Chemical Disposition, Metabolism, and Toxicokinetics

9.1.2.1 α-Chaconine

Peak levels of α-chaconine in the liver were observed within 6 to 14 hours after oral administration of α-[^{3}H]chaconine (10 mg/kg; 0.012 mmol/kg) to female Swiss-Webster mice (Sharma et al., 1983). The α-chaconine distribution in the nuclear, mitochondrial, and microsomal fractions of the hepatocytes was directly proportional to organelle weights, indicating no preferential localization.

α-[^{3}H]Chaconine was poorly absorbed when administered orally at a dose of 5 mg/kg (0.0059 mmol/kg) to male Sprague-Dawley rats (Norred et al., 1976). Sixty and 80% of the dose was excreted in the feces within 12 and 24 hours, respectively. Ten percent of the dose was excreted in the urine within 12 to 24 hours after administration. Peak concentrations of α-chaconine were found in the liver, kidney, spleen, lung, blood, brain, abdominal fat, adrenal, testis, pancreas, muscle, thymus, thyroid, and heart (in decreasing order) within 6 to 12 hours. The major constituent in urine and feces was presumably solanidine, while 25% of the dose was excreted unchanged.

When α-[^{3}H]chaconine was administered intraperitoneally (i.p.) to male Sprague-Dawley rats at doses of 5 to 25 mg/kg (0.0059 and 0.029 mmol/kg), most of the dose was eliminated in the urine (Norred et al., 1976). At doses higher than 10 mg/kg (0.012 mmol/kg), only a negligible amount of the dose was excreted in the feces. α-Chaconine accumulated in the liver, spleen, kidney, pancreas, fat, lung, thymus, and other tissues. At the doses of 15 and 25 mg/kg (0.018-0.029 mmol/kg), higher levels of α-[^{3}H]chaconine were found in the tissues and fecal and urinary excretion was decreased. The major constituent in urine and feces was presumably solanidine.

In hamsters orally administered α-[^{3}H]chaconine at a dose of 10 mg/kg (0.012 mmol/kg), 20-24% of the administered dose was excreted in the urine and 1% was excreted in the feces within 7 days (Alozie et al., 1979a; 1979b). In the urine, over half of the dose was excreted as unchanged α-chaconine within the first 24 hours (Alozie et al., 1979a). In the feces, most of the dose was excreted as the metabolite solanidine. Since less than 0.3% of the dose was excreted in the feces in the initial 72 hours, the authors concluded that α-chaconine was not poorly absorbed,

since the long duration is an above-average transit time for ingested material in the hamster gastrointestinal tract. Peak tissue concentrations were much higher following i.p. administration at the same dose (Alozie, 1978), and excretion was much lower; after 24 hours, only 18% of the administered dose was excreted in the urine and feces (Alozie et al., 1979b). Peak concentrations in the tissues were observed 12 hours after oral administration (Alozie et al., 1979b). Highest concentrations were found in the lungs, liver, spleen, skeletal muscle, kidney, and pancreas and moderate concentrations were found in the heart and brain. On a subcellular level, the highest level of α-[^{3}H]chaconine was bound in the nuclear and microsomal fractions of brain, liver, and heart tissues, but binding was also observed in the testes, kidney, and lung. Thus, the authors concluded that much of the administered dose persists in various tissues in the bound form.

9.1.2.2 α-Solanine

When α-[^{3}H]solanine was administered orally (5 mg/kg; 0.0058 mmol/kg) or i.p. (10-35 mg/kg; 0.012-0.04 mmol/kg) to male Fischer rats, the glycoalkaloid was poorly absorbed from the gastrointestinal tract and was rapidly eliminated in the urine and feces (Nishie et al., 1971). α-Solanine reached peak levels in the spleen, kidney, liver, lung, fat, heart, brain, and blood (in decreasing order) within 12 hours. Within 24 hours after administration, 78% of the dose was excreted in the urine and feces (72% in the feces). About 65% of the dose excreted in the feces was unchanged. About 72% of the portion excreted in the urine was identified as basic compounds and 6% was identified as solanidine.

After oral administration of 0.17 mg α-[^{3}H]solanine/kg (0.00020 mmol/kg) to male SPF Riv: TOX rats, plasma concentration of α-solanine peaked in less than 30 hours (Groen et al., 1993). About 3% and 86% of the dose was excreted in the urine and feces, respectively, within seven days. No detectable levels of unchanged α-solanine were present in urine.

When male SPF Riv: TOX rats were administered 0.05 mg α-[^{3}H]solanine/kg (0.000058 mmol/kg) intravenously (i.v.), the mean plasma concentration of α-solanine steadily declined over 150 hours (Groen et al., 1993). About 26% and 37% of the dose was excreted in the urine and

feces, respectively, within seven days. About 17% of the dose was excreted unchanged in the urine.

Plasma concentrations of α-solanine peaked in less than 35 hours when male SPF Charles River/Wiga Syrian golden hamsters were administered 0.17 mg α-solanine/kg (0.00020 mmol/kg) orally (Groen et al., 1993). The amount of the dose excreted within seven days in the urine and feces was 10% and 29%, respectively. No detectable unchanged α-solanine was present in urine.

When male SPF Charles River/Wiga Syrian golden hamsters were administered 0.05 mg α-solanine/kg (0.000058 mmol/kg) i.v., the concentration of α-solanine in plasma decreased over 175 hours (Groen et al., 1993). The amount of the dose excreted within seven days in the urine and feces was 28% and 23%, respectively. About 20% of the dose was excreted unchanged in the urine.

9.1.2.3 Concomitant Administration of Both Glycoalkaloids

In a study of 43 subjects from the U.K. and Sweden who maintained their usual diets, the mean serum total glycoalkaloid concentration (including α-chaconine and α-solanine) was about 2.7 times the mean serum solanidine concentrations (Harvey et al., 1985b; cited by JECFA, 1993). The authors concluded that humans metabolize α-chaconine and α-solanine to solanidine through hydrolysis of the sugar residues, which could take place in the acid environment of the stomach or at the site of absorption. The ratio may also reflect preferential absorption of the more lipophilic solanidine, or α-chaconine and α-solanine might be absorbed unchanged and metabolized within the body.

In another study by Harvey et al. (1985a), solanidine was detected in the serum of 57 normal healthy volunteers. The solanidine concentration in the serum was significantly correlated with the dietary intake of potatoes; when two subjects abstained from potatoes, serum solanidine fell markedly after two weeks.

After seven human volunteers ate a single meal of potatoes with an ingested dose of 0.6 mg/kg (0.0007 mmol/kg) α-chaconine and 0.4 mg/kg (0.0005 mmol/kg) α-solanine, both glycoalkaloids were detected in blood serum samples within 1 to 25 hours (Hellenäs et al.,

1992b). Solanidine was detected in the serum within 4 to 8 hours. On average, peak serum concentrations of α-chaconine and α-solanine were 14.4 and 7.7 ng/mL (16.9 and 8.8 nM), respectively, and were reached after 6.0 and 5.1 hours, respectively. Peak solanidine concentrations ranged from 1.0 to 4.8 ng/mL (2.5 and 12 nM) and were observed between 8 and 25 hours after eating the potato meal. The biological half-lives of α-chaconine and α-solanine were 19.1 and 10.7 hours, respectively.

Incubation of potato glycoalkaloids with rumen microorganisms *in vitro* resulted in hydrolysis of the glycoalkaloids to solanidine (King and McQueen, 1981). Much of the solanidine was then reduced to 5β-solanidan-3β-ol. No subsequent esterification processes or metabolism of the nitrogen moiety were detected.

When cows were fed a diet containing 10 or 20% tater meal (an animal feed made from potato waste products known to contain high levels of glycoalkaloids), no detectable amount of the glycoalkaloid metabolite solanidine was found in any milk samples after 60 and 150 days of lactation (Bushway et al., 1984).

9.1.3 Acute Exposure

Acute toxicity values for α-chaconine, α-solanine, and solanine hydrochloride are presented in **Tables 1**, **2**, and **3**, respectively. Acute exposure studies discussed in this section are presented in **Table 4**.

Table 1. Acute Toxicity Values for α-Chaconine

Route	Species (sex and strain)	LD_{50} or LD_{Lo}	Reference
.p.	mouse (sex and strain n.p.)	LD_{50}=27.5 mg/kg (0.032 mmol/kg)	Swinyard and Chaube (1973)
	mouse (male, Swiss-	LD_{50}=27.5 mg/kg (0.032 mmol/kg)	Nishie et al. (1975)

Route	Species (sex and strain)	LD_{50} or LD_{Lo}	Reference
	Webster)		
	mouse (male, Swiss-Webster)	LD_{50}=19.2 mg/kg (0.023 mmol/kg)	Sharma et al. (1979)
	rat (female, Wistar)	LD_{50}=84 mg/kg (0.099 mmol/kg)	Chaube and Swinyard (1976)
	rabbit (sex n.p., white New Zealand)	LD_{Lo}=50 mg/kg (0.059 mmol/kg)	Nishie et al. (1975)

Abbreviations: i.p. = intraperitoneal; n.p. = not provided

Table 2. Acute Toxicity Values for α-Solanine

Route	Species (sex and strain)	LD_{50} or LD_{Lo}	Reference
oral	rat (sex and strain n.p.)	LD_{50}=590 mg/kg (0.68 mmol/kg)	Gull et al. (1970; cited by Maga, 1980)
i.p.	mouse (male, albino)	LD_{50}=42 mg/kg (0.048 mmol/kg)	Nishie et al. (1971)
	mouse (male, Swiss-Webster)	LD_{50}=32.3 mg/kg (0.037 mmol/kg)	Patil et al. (1972); Sharma et al. (1979)
	mouse (male, Swiss-Webster)	LD_{50}=30.0 mg/kg (0.035 mmol/kg)	Nishie et al. (1975)
	rat (sex and strain n.p.)	LD_{50}=75 mg/kg (0.086 mmol/kg)	Gull et al. (1970; cited by Maga, 1980)
	rat (female, Wistar)	LD_{50}=67 mg/kg (0.077 mmol/kg)	Chaube and Swinyard (1976)
	monkey (rhesus, sex n.p.)	LD_{50}< 40 mg/kg (0.046 mmol/kg)	Swinyard and Chaube (1973)
	rabbit (sex n.p., white New Zealand)	LD_{Lo}=40 mg/kg (0.046 mmol/kg)	Nishie et al. (1975)

Abbreviations: i.p. = intraperitoneal; n.p. = not provided

Table 3. Acute Toxicity Values for Solanine Hydrochloride

Route	Species (sex and strain)	LD_{50}	Reference
i.p.	mouse (sex and strain n.p.)	42 mg/kg (0.046 mmol/kg)	Budavari (1989)

Abbreviations: i.p. = intraperitoneal; n.p. = not provided

Table 4. Acute Exposure to α-Chaconine and α-Solanine

Species, Strain, and Age	Number and Sex of Animals	Chemical Form[a] and Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
9.1.3.1 Oral Administration						
Mice (Albino, age n.p.)	10 M	solanine, purity n.p.	1000 mg/kg (1 mmol/kg)	single exposure; observation period n.p.	Nontoxic. No other experimental details were given.	Nishie et al. (1971)
Rats (Sprague-Dawley, age n.p.)	5 M	solanine, 'purified'	250 mg/kg (0.29 mmol/kg) by gavage	single exposure; 24 hour observation	Treatment did not alter activities of ALT, AST, or serum cholinesterase. The authors presumed that hepatoxicity was not induced due to poor absorption of the dose in the stomach.	Dalvi (1985)
Hamsters (SPF Charles River/Wiga Syrian, golden, 12-15 wks-old)	5 M	α-[^{3}H] solanine, purity n.p.	0.17 mg/kg (0.00020 mmol/kg)	single exposure; observation period n.p.	Caused severe damage of the duodenal wall in some animals, but the incidence ratio was n.p.	Groen et al. (1993)
Rats (strain and age n.p.)	n.p.	potatoes containing varying amounts of glycoalkaloids	n.p.	n.p.	Serum levels of calcium, phosphorous, magnesium, and hydroxyproline were decreased. The decrease had no relation to the solanine content of the potatoes (concentration n.p.). The authors stated that solanine appeared to exert a Vitamin D-like effect by increasing calcium absorption.	Yoon and Kirkowski (1979)
Rats (strain and age n.p.)	n.p.	Cara potato top homogenate	10 or 20 mL/kg by gavage (higher dose contained 1.76 mg α-chaconine/kg and 0.66 mg α-solanine/kg (0.00207 and 0.00076 mmol/kg, respectively)	single exposure; observation period n.p.	No changes in body weight were observed. No abnormalities were observed during necropsy.	Phillips et al. (1996)

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; ECG = electrocardiogram; EEG = electroencephalogram; F = female; M = male; n.p. = not provided

Table 4. Acute Exposure to α-Chaconine and α-Solanine (continued)

Species, Strain, and Age	Number and Sex of Animals	Chemical Form[a] and Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
Hamsters (Syrian, mature)	10 F (potato sprouts) 5 F (alkaloid extract)	potato sprouts or an extract of potato sprout alkaloids, crude	4,170 mg/kg potato sprouts or 330 mg/kg alkaloid extract, by gavage	single exposure; 72 hour observation	α-Chaconine and α-solanine were confirmed in significant quantities in the potato sprouts and in trace amounts in the crude alkaloidal extract. Administration of the sprout material induced 5/10 deaths within 24 hours; only one survived for the entire exposure period. Gross and microscopic lesions of the stomach and proximal small intestine were identified in all animals which died (9/10). The glandular mucosa of the stomach was thickened and hemorrhagic. The duodenum and jejunum were dilated with blood-tinged luminal contents and a red, hemorrhagic mucosa. Occasional subseral petechial hemorrhages on the cecum were observed. The one animal which survived had mild, focal areas of necrosis with hemorrhage and congestion of the gastric glandular mucosa. 3/5 hamsters administered the extract died during the 72 hour exposure period. The gross and microscopic lesions in those which died were similar to the lesions identified in those who died from administration of sprout material. The 2 surviving animals had mild congestion of the gastric glandular mucosa and epithelial necrosis.	Baker et al. (1987)
Hamsters (Syrian, adult)	10 F per group	potato sprout material	300, 400, or 500 mg/kg by gavage	single exposure; 72 hour observation	Concentrations of α-chaconine and α-solanine in the sprout material were not provided. Acetylcholinesterase activity was significantly increased in the 300 mg/kg group. In the 400 and 500 mg/kg groups, acetylcholinesterase activity was 90 and 84% of the mean activity in the control group, respectively. The incidences of death prior to 72 hours were 1/10 at 300 mg/kg, 4/10 at 400 mg/kg, and 9/10 at 500 mg/kg. Those hamsters which died prior to 72 hours had severe gastric and proximal small intestinal necrosis. In the 400 mg/kg group, 2 of the hamsters which survived for 72 hours had valvular endocarditis and infarcts. 8/10 of the hamsters dosed with 300 mg/kg had lesions, while all of the hamsters at the 400 and	Baker et al. (1988)

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; ECG = electrocardiogram; EEG = electroencephalogram; F = female; M = male; n.p. = not provided

Table 4. Acute Exposure to α-Chaconine and α-Solanine (continued)

Species, Strain, and Age	Number and Sex of Animals	Chemical Form[a] and Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
					500 mg/kg levels had lesions. The authors concluded that death was not attributed to the slight acetylcholinesterase inhibition induced by the 2 higher doses of potato sprout material. Rather, death was related to severe gastrointestinal necrosis.	

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; ECG = electrocardiogram; EEG = electroencephalogram; F = female; M = male; n.p. = not provided

Table 4. Acute Exposure to α-Chaconine and α-Solanine (continued)

Species, Strain, and Age	Number and Sex of Animals	Chemical Form[a] and Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
Hamsters (strain and age n.p.)	n.p.	potato leaves, freeze-dried, suspended in corn oil	estimated dose: 2.65 mg/kg (0.00311 mmol/kg) α-chaconine plus 0.95 mg/kg (0.0011 mmol) α-solanine by gavage	single exposure; observation period n.p.	No effect on body weight or behavior was noted. No abnormalities were observed in any tissue, including the stomach mucosa, during necropsy.	Phillips et al. (1996)
Rabbits (White New Zealand, both young and adult)	5 young and 4 adult (sex n.p.)	succulent potato plants	100% of the diet	single exposure; 17 day observation	3 of the young rabbits developed diarrhea 6 days after feeding, had torticollis and stretched legs, and went into a coma before death. All young rabbits died by day 17 post-feeding. Most had turbid urine with amorphous crystals. 1 rabbit had an increased number of erythrocytes in the blood. All of the adult rabbits lost weight, became emaciated, and had symptoms similar to those of the young rabbits; leucopenia and lymphopenia were also induced. All adult rabbits died within 16 days. Treatment of both young and adult rabbits induced marked congestion in the lung, small intestines and liver. The spleen was atrophied. Hyperemia of the brain, lung, and kidneys was observed. Edema was seen in brain and lung tissues. Liver tissues had engorged sinusoids, blood vessels, and focal proliferation of mononuclear cells adjoining to blood vessels.	Somvanshi et al. (1992)
Sheep (strain and age n.p.)	n.p.	'solanine[b]', purity n.p.	225 mg/kg (0.259 mmol/kg)	single exposure; observation period n.p.	Dose was not lethal, but produced blood dyscrasias.	Konig and Stafze (1953; cited by Dalvi and Bowie, 1983)
Sheep (strain and age n.p.)	n.p.	'solanine[b]', purity n.p.	500 mg/kg (0.6 mmol/kg)	single exposure; observation period n.p.	The dose was lethal.	Konig (1953; cited by Maga, 1980)
9.1.3.2 Intraperitoneal Injection						
Mice (Swiss-Webster, adult)	6-10 M	α-chaconine, >95% purity	12-50 mg/kg (0.014-0.06 mmol/kg)	single exposure; 7 day observation	The higher doses (n.p.) produced respiratory distress and the animals died within a few hours. Animals treated with the lower doses (n.p.) died three days after exposure. All doses caused hyperemia in the kidney. Effects	Sharma et al. (1979)

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; ECG = electrocardiogram; EEG = electroencephalogram; F = female; M = male; n.p. = not provided

Table 4. Acute Exposure to α-Chaconine and α-Solanine (continued)

Species, Strain, and Age	Number and Sex of Animals	Chemical Form[a] and Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
					were not dose-related.	

[a]The chemical form is given as the original author(s) presented it.

[b]The 'solanine' isolated prior to 1954 was actually a mixture of α-chaconine and α-solanine (Friedman and McDonald, 1997).

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; ECG = electrocardiogram; EEG = electroencephalogram; F = female; M = male; n.p. = not provided

Table 4. Acute Exposure to α-Chaconine and α-Solanine (continued)

Species, Strain, and Age	Number and Sex of Animals	Chemical Form[a] and Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
Rats (Wistar, 9-wk-old)	F (see results/ comments for numbers)	α-chaconine, pure	10-100 mg/kg (0.01-0.1 mmol/kg)	single exposure; 11 day observation	Doses of 50-100 mg/kg caused death: 50 mg/kg, 3/11; 75 mg/kg, 2/6; 85 mg/kg, 5/10; and 100 mg/kg, 4/4. Observed signs of toxicity included periorbital, nasal, and oral hemorrhage. Internally, bloody ascitic fluid and pleuritic fluid were observed.	Chaube and Swinyard (1976)
Rats (Sprague-Dawley, age n.p.)	3 M per group	α-chaconine, purity n.p.	10, 30, or 60 mg/kg (0.01, 0.04, or 0.07 mmol/kg)	single exposure; 3 hour observation	All rats showed initial signs of depression and respiratory depression. Acetylcholinesterase activity in brain homogenates was reduced dose-dependently to 79, 55, and 18% of that found in the control group. Heart acetylcholinesterase activity was reduced to 40% of the control in all treatment groups; plasma cholinesterase activity was also reduced compared to the control group. The authors concluded that α-chaconine is a fairly potent cholinesterase inhibitor.	Alozie et al. (1978; cited by JECFA, 1993)
Rats (Sprague-Dawley, age n.p.)	12 M per dose	α-chaconine, purity n.p.	3, 8, or 20 mg/kg (0.004, 0.009, or 0.02 mmol/kg)	single exposure; 3 or 12 hour observation	Treatment did not alter levels of acetylcholine, catecholamine, seratonin, or its metabolite 5-hydroxyindoleacetic acid at any dose. Norepinephrine levels decreased with increasing doses in the groups observed for 3 hours. Symptoms observed at 8 mg/kg included sedation, respiratory impairment, and constriction of abdominal muscles.	Aldous et al. (1980)
	3 M (3 lower doses); 1 M (high dose)		10, 20, 30 , or 40 mg/kg (0.01, 0.02, 0.04, or 0.05 mmol/kg)	single exposure; observed at time of exposure and 3 and 7 hours later	There was a significant increase in the proportion of low frequency activity, as observed on the EEG, following administration of 10 mg/kg. Tachycardia was observed at the 10 and 40 mg/kg levels, while bradycardia was observed at the 20 and 30 mg/kg levels.	
Rabbits (White New Zealand, age n.p.)	n.p.	α-chaconine, purity n.p.	60 mg/kg (0.07 mmol/kg)	single exposure; observed for 2.5 hours	No significant abnormal EEG patterns were initially observed. Over time, however, high voltage delta waves, cyanosis, tachycardia, and coma were observed. The respiratory rate increased in the first hour of exposure, and then decreased steadily. Terminal signs of death began with isoelectric EEG	Nishie et al. (1975)

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; ECG = electrocardiogram; EEG = electroencephalogram; F = female; M = male; n.p. = not provided

Table 4. Acute Exposure to α-Chaconine and α-Solanine (continued)

Species, Strain, and Age	Number and Sex of Animals	Chemical Form[a] and Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
					signals followed by respiratory arrest and cardiac arrest.	
Mice (Albino, age n.p.)	10 M per group	solanine, purity n.p.	5 or 10 mg/kg (0.006 or 0.01 mmol/kg)	single exposure; 5 minute observation	10 mg/kg caused a significant reduction in spontaneous motor activity. No effect was noted at 5 mg/kg.	Nishie et al. (1971)
Mice (Albino, age n.p.)	10 M per group	solanine, purity n.p.	50 mg/kg pentobarbital sodium followed by 5, 10, or 20 mg/kg (0.006, 0.01, or 0.02 mmol/kg) solanine	single exposure; observed until time of recovery of righting reflex	Only the 20 mg/kg dose produced a significant increase in pentobarbital-induced sleeping time.	Nishie et al. (1971)
Mice (Swiss-Webster, adult)	10 M per group	solanine, purity n.p.	10-50 mg/kg (0.01-0.06 mmol/kg)	single exposure; 24 hour observation	10 mg/kg elicited symptoms but no deaths, while 50 mg/kg caused death within 1-3 hours. The animals were irritated for 1 minute after administration and then became drowsy and apathetic. Breathing was increased and the animals developed diarrhea, followed by hind-leg paralysis and dyspnoea. Before death, the animals experienced a deep and prolonged state of unconsciousness.	Patil et al. (1972)
Mice (Swiss-Webster, adult)	6-10 M	α-solanine, >95% purity	12-50 mg/kg (0.01-0.06 mmol/kg)	single exposure; 7 day observation	The higher doses (actual doses n.p.) produced respiratory distress and the animals died within a few hours. Deaths of animals treated with the lower doses were distributed throughout the observation period. α-Solanine treatment caused occasional hepatic leukocytic infiltration. Effects were not dose-related.	Sharma et al. (1979)
Rats (Wistar, 9-wk-old)	F (see results/ comments for numbers)	α-solanine, purity n.p.	10-85 mg/kg (0.01-0.098 mmol/kg)	single exposure; 11 day observation	Doses of 40-85 mg/kg caused death: 40 mg/kg, 1/9; 60 mg/kg, 3/8; and 85 mg/kg, 6/6. Signs of toxicity included periorbital, nasal, and oral hemorrhage. Internally, bloody ascitic fluid and pleuritic fluid were observed.	Chaube and Swinyard (1976)
Rats (Sprague-Dawley, age n.p.)	5 M	solanine, 'purified'	20 mg/kg (0.02 mmol/kg)	single exposure; 24 hour observation	Treatment significantly increased ALT and AST levels and decreased the activities of serum cholinesterase and microsomal enzymes, including cytochrome P-450. These results indicate the hepatotoxic nature of solanine.	Dalvi (1985)

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; ECG = electrocardiogram; EEG = electroencephalogram; F = female; M = male; n.p. = not provided

Table 4. Acute Exposure to α-Chaconine and α-Solanine (continued)

Species, Strain, and Age	Number and Sex of Animals	Chemical Form[a] and Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
Rabbits (strain and age n.p.)	1 per dose (sex n.p.)	solanine, purity n.p.	10, 15, 20, or 30 mg/kg (0.01, 0.017, 0.02, or 0.03 mmol/kg)	single exposure; observation period n.p.	Rabbits administered doses below 15 mg/kg did not have EEG readings different from the controls, but did experience an increase in heart rate. Generally, the EEG changed gradually with time at doses ranging from 15-30 mg/kg. During an initial period of rapid rise in respiratory rate (1 to 1.5 hours after dosing), the EEG was slightly activated. Delta waves appeared on the EEG when the respiratory rates dropped below those of the controls (2.5 to 6 hours after dosing). Significant increases in heart rate were also induced at 20 and 30 mg/kg, but the rabbit dosed with 15 mg/kg experienced no change in heart rate. The animal administered 20 mg/kg died overnight and the animal treated with 30 mg/kg died in 6.25 hours. The heart kept beating after breathing ceased. Deep cyanosis and semiconsiousness preceded death.	Nishie et al. (1971)
Rabbits (New Zealand white, age n.p.)	At the low dose, 2 M and 1 F At the high dose, 1 F	solanine, purity n.p.	20 or 30 mg/kg (0.02 or 0.03 mmol/kg)	single exposure; observation period n.p.	No marked parasympathetic stimulation, excess secretions, or muscular twitching was observed. Rate of respiration was increased for the first 15 to 30 minutes after injection. Breathing was difficult. Animals experienced a depressive phase caused by prostration (severe exhaustion) prior to death. Depressive phase was indicated by lack of response to stimuli, partially closed eyes, disinclination to move, and muscle weakness resembling partial paralysis of the limbs. Occasional twitching or convulsions preceded death; pupils were widely dilated.	Patil et al. (1972)

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; ECG = electrocardiogram; EEG = electroencephalogram; F = female; M = male; n.p. = not provided

Table 4. Acute Exposure to α-Chaconine and α-Solanine (continued)

Species, Strain, and Age	Number and Sex of Animals	Chemical Form[a] and Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
					The rabbit given 30 mg/kg died within 50 minutes. At 20 mg/kg, 1 rabbit died in 145 minutes, one died in 24 hours, and a third survived and recovered completely. The authors noted that solanine was a weak to moderate inhibitor of both specific and non-specific cholinesterase when tested in serum and erythrocytes after dosing. Generally, there was less inhibition in the erythrocytes than in the plasma.	
Monkeys (Rhesus, age n.p.)	1 F	solanine, reference standard	20 mg/kg (0.02 mmol/kg)	2 doses given 24 hours apart; observed 2 hours after last injection	The dose caused an increase in pulse, systolic pressure, and respiratory rate, followed by death approximately 2 hours after the last injection. Hemorrhage of the nasal and periorbital cavities was noted at necropsy, in addition to hemorrhagic congestion in the lung, liver, and spleen. Accumulation of serosanguinous pleural and peritoneal fluids and mild hepatic and splenic congestion were induced.	Swinyard and Chaube (1973)
Hamsters (strain and age n.p.)	n.p.	1:1 mixture of α-chaconine and α-solanine	5, 10, 25, 50, or 100 mg/kg (0.006, 0.01, 0.029, 0.058, or 0.116 mmol/kg)	single exposure; 24 hour observation	No effect was observed at 5 and 10 mg/kg. At 25, 50, and 100 mg/kg, death occurred within 24 hours. Blood was found in and around the stomach and duodenum during necropsy, which indicates that uptake is facilitated by cell membrane disruption.	Phillips et al. (1996)
Monkeys (rhesus, age n.p.)	2 F	glycoalkaloids, purity n.p.	40 mg/kg (0.05 mmol/kg)	single exposure; 48 hour observation	Both animals died 48 hours after treatment. Prior to death, pulse, systolic pressure, and respiratory rate was increased. Hemorrhage of the nasal and periorbital cavities was noted at necropsy, in addition to hemorrhagic congestion in the lung, liver, and spleen. Accumulation of serosanguinous pleural and peritoneal fluids and mild hepatic and splenic congestion were induced.	Swinyard and Chaube (1973)
9.1.3.3 Intravenous Injection						

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; ECG = electrocardiogram; EEG = electroencephalogram; F = female; M = male; n.p. = not provided

Table 4. Acute Exposure to α-Chaconine and α-Solanine (continued)

Species, Strain, and Age	Number and Sex of Animals	Chemical Form[a] and Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
Rabbits (White New Zealand, age n.p.)	n.p.	α-chaconine, purity n.p.	1.0, 1.5, or 2.0 mg/kg (0.0012, 0.0018, or 0.0023 mmol/kg)	single exposure; observation period n.p.	Treatment with 1.0-1.5 mg/kg slightly decreased heart rate and blood pressure. 2.0 mg/kg produced short runs of ventricular extrasystoles and bigeminy within 1-7 minutes after injection.	Nishie et al. (1975)
Rabbits (strain and age n.p.)	1 (sex n.p.)	solanine, purity n.p.	10 mg/kg (0.01 mmol/kg)	single exposure; observation period n.p.	Death was induced within 2 minutes. Respiration and EEG signals stopped simultaneously.	Nishie et al. (1971)
	n.p.		pentobarbital followed by 2 or 3 mg/kg solanine (0.002 or 0.003 mmol/kg)		At 2 mg/kg, solanine induced a transient increase in respiratory rate, ventricular extrasystoles, and a lowering of blood pressure. 3 mg/kg caused a 30-second cessation of respiration 2.5 min. after injection.	
Rabbits (White New Zealand, age n.p.)	n.p.	solanine, purity n.p.	1.0, 1.5, or 2.0 mg/kg (0.0011, 0.0017, or 0.0023 mmol/kg)	single exposure; observation period n.p.	Treatment with 1.0-1.5 mg/kg slightly decreased heart rate and blood pressure. The 2.0 mg/kg dose produced short runs of ventricular extrasystoles and bigeminy within 1-7 minutes after injection.	Nishie et al. (1975)

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; ECG = electrocardiogram; EEG = electroencephalogram; F = female; M = male; n.p. = not provided

Table 4. Acute Exposure to α-Chaconine and α-Solanine (continued)

Species, Strain, and Age	Number and Sex of Animals	Chemical Form[a] and Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
Dog (strain and age n.p.)	1 M	solanine, purity n.p.	pentobarbital sodium followed by 5 doses of 6 mg/kg (0.007 mmol/kg) solanine administered 10 min. apart	see dose for exposure; observation period n.p.	Quick serum cholinesterase inhibition was followed by a rapid recovery. Erythrocyte cholinesterase inhibition was not observed.	Patil et al. (1972)
Sheep (strain and age n.p.)	n.p.	'solanine[b]', purity n.p.	17 or 50 mg/kg (0.020 or 0.06 mmol/kg)	single exposure; observation period n.p.	17 mg/kg was poisonous and 50 mg/kg was lethal. No other experimental details were provided.	Konig (1953; cited by Maga, 1980)

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; ECG = electrocardiogram; EEG = electroencephalogram; F = female; M = male; n.p. = not provided

[a]The chemical form is given as the original author(s) presented it.

[b]The 'solanine' isolated prior to 1954 was actually a mixture of α-chaconine and α-solanine (Friedman and McDonald, 1997).

Abbreviations: ALT = alanine aminotransferase; AST = aspartate aminotransferase; ECG = electrocardiogram; EEG = electroencephalogram; F = female; M = male; n.p. = not provided

9.1.3.1 Oral Administration

α-Solanine

An oral solanine dose of 1000 mg/kg (1 mmol/kg) to male albino mice was not lethal (Nishie et al., 1971). No other experimental details were provided.

Solanine, administered at 250 mg/kg (0.29 mmol/kg) by gavage, did not induce hepatotoxicity in male Sprague-Dawley rats, as measured by a change in the activities of alanine aminotransferase (ALT), aspartate aminotransferase (AST), or serum cholinesterase (Dalvi, 1985). The authors presumed that hepatotoxicity was not induced because the dose was poorly absorbed in the stomach.

A 0.17 mg/kg (0.00020 mmol/kg) dose of α-[^{3}H]solanine caused severe damage in the duodenal wall of male SPF Charles River/Wiga Syrian golden hamsters (incidence ratio not provided) (Groen et al., 1993).

Mixtures of α-Chaconine and α-Solanine

In rats (strain n.p.), serum levels of calcium, phosphorus, magnesium, and hydroxyproline decreased with oral administration of potatoes, but the decrease had no relation to glycoalkaloid content (Yoon and Kirkowski, 1979). Solanine appeared to exert an effect similar to that of vitamin D (i.e., increased calcium absorption).

Administration of 10 or 20 mL/kg Cara potato top homogenate by gavage to rats (sex and strain not provided) did not effect body weight or necropsy results (Phillips et al., 1996). The 20 mL/kg dose contained 1.76 mg α-chaconine/kg (0.00207 mmol/kg) and 0.66 mg α-solanine/kg (0.00076 mmol/kg).

When female Syrian hamsters were fed potato sprouts (4,170 mg/kg) in the diet, half of the animals (5/10) died within 24 hours and only 1 survived to the end of the 72-hour observation period (Baker et al., 1987). Similarly, administration of an extract of potato sprout alkaloids (330 mg/kg) induced 3/5 deaths. All animals that died had gastric and intestinal mucosal necrosis of the

stomach and proximal small intestine. α-Chaconine and α-solanine were present in significant quantities in the potato sprouts and in trace amounts in the alkaloid extract.

In another study by Baker et al. (1988), 300, 400 or 500 mg/kg potato sprout material induced death in 1/10, 4/10 and 9/10 female Syrian hamsters, respectively, within 72 hours. Severe gastric and proximal small intestinal necrosis was observed in all animals that died. Additionally, the 400 mg/kg dose induced valvular endocarditis and infarcts in 2 surviving hamsters. The mean acetylcholinesterase activity was increased compared to the controls at the 300 mg/kg dose, and decreased to 90 and 84% of the controls at the 400 and 500 mg/kg doses, respectively. The authors noted that the slight inhibition of acetylcholinesterase activity at the two higher doses did not induce death, but rather, death was attributed to severe gastrointestinal necrosis. Concentrations of α-chaconine and α-solanine in the sprout material were not provided.

Administration of freeze-dried potato leaves suspended in corn oil to hamsters by gavage (sex and strain not provided) did not affect body weight or behavior (Phillips et al., 1996). No abnormalities were observed in any tissue, including the stomach, during necropsy. The estimated doses of α-chaconine and α-solanine were 2.65 mg/kg (0.00311 mmol/kg) and 0.95 mg/kg (0.0011 mmol/kg), respectively.

When succulent potato plants were fed to young white New Zealand rabbits (sex not provided), 3/5 developed diarrhea, and had torticollis and stretched legs; all died within 17 days after treatment (Somvanshi et al.,1992). When adult rabbits were administered the same diet, the animals lost weight, became emaciated, and had symptoms similar to those of young rabbits, with all adult rabbits dying within 16 days after treatment. In both young and adult rabbits, treatment induced marked congestion of the lung, small intestines, and liver and atrophy of the spleen. Hyperemia of the brain, lung and kidneys was also induced, as was edema in brain and lung tissues. Liver tissues had engorged sinusoids, blood vessels, and focal proliferation of mononuclear cells adjoining to blood vessels. Concentrations of α-chaconine and α-solanine in the potato plants were not provided.

A glycoalkaloid dose of 225 mg/kg (0.259 mmol/kg) induced blood dyscrasias in sheep (sex and strain not provided) (Konig and Stafze, 1953; cited by Dalvi and Bowie, 1983), and a dose of 500 mg/kg (0.6 mmol/kg) was lethal (Konig, 1953; cited by Maga, 1980).

9.1.3.2 Intraperitoneal Injection

α-Chaconine

Intraperitoneal doses of α-chaconine (12-50 mg/kg; 0.014-0.06 mmol/kg) administered i.p. to male Swiss-Webster mice induced hyperemia in kidney tissue (Sharma et al., 1979). Mice administered the higher doses (not provided) exhibited respiratory distress and died within a few hours. The lower doses (not provided) induced death 3 days after treatment.

Toxic effects including periorbital, nasal, and oral hemorrhage were noted when female Wistar rats were administered α-chaconine i.p. at doses of 10 to 100 mg/kg (0.01 to 0.12 mmol/kg) (Chaube and Swinyard, 1976). Internal signs of toxicity included bloody ascitic and pleuritic fluid. Doses of 50, 75, 85, and 100 mg/kg (0.06, 0.088, 0.010, and 0.012 mmol/kg) induced death in 27,33, 50, and 100% of the rats, respectively; doses less than 50 mg/kg were not lethal.

Male Sprague-Dawley rats administered α-chaconine at doses of 10, 30, or 60 mg/kg (0.01, 0.04, or 0.07 mmol/kg) showed initial signs of nervous system depression and respiratory depression (Alozie et al., 1978; cited by JECFA, 1993). Brain acetylcholinesterase activity was reduced in a dose-dependent manner to 79, 55, and 18 % of that of the control group, respectively. Heart acetylcholinesterase activity was reduced to 40% of that of the control group at all treatment levels, and plasma cholinesterase activity was also reduced. Thus, the authors concluded that α-chaconine is a fairly potent cholinesterase inhibitor.

Levels of acetylcholine, catecholamine, serotonin, and its metabolite 5-hydroxyindoleacetic acid were not altered by i.p. administration of α-chaconine at 3, 8, or 20 mg/kg (0.004, 0.009, or 0.02 mmol/kg) to male Sprague-Dawley rats (Aldous et al., 1980). Norepinephrine levels decreased with increasing doses in animals observed at 3 hours after

dosing, but not when observed at 12 hours after dosing. Symptoms induced by 8 mg/kg included sedation, respiratory impairment, and constriction of abdominal muscles.

An electroencephalogram (EEG) showed a significant increase in the proportion of low-frequency activity following i.p. administration of 10 mg/kg (0.01 mmol/kg) of α-chaconine to male Sprague-Dawley rats (Aldous et al., 1980). Doses of 10 and 40 mg/kg (0.01 and 0.05 mmol/kg) induced an increase in heart rate, while doses of 20 and 30 mg/kg (0.02 and 0.04 mmol/kg) induced a decrease .

α-Chaconine (60 mg/kg; 0.07 mmol/kg), administered i.p to white New Zealand rabbits (sex not provided), was lethal, inducing high voltage delta brain waves over time, as observed on an EEG (Nishie et al., 1975). The brain waves were accompanied by cyanosis, increased heart rate, and coma. Respiratory rate increased in the first hour after administration and then steadily decreased. Terminal signs of death began with isoelectric EEG signals, followed by respiratory and cardiac arrest.

α-Solanine

In male albino mice, solanine at 10 mg/kg (0.01 mmol/kg) i.p. caused a significant reduction in spontaneous motor activity, but 5 mg/kg (0.006 mmol/kg) had no effect (Nishie et al., 1971).

When pentobarbital sodium (50 mg/kg) followed by solanine at 5, 10, or 20 mg/kg (0.006, 0.012, or 0.023 mmol/kg) was administered i.p. to male albino mice, only the highest dose caused a significant increase in pentobarbital-induced sleeping time (Nishie et al., 1971).

When male Swiss-Webster mice were administered solanine at doses ranging from 10 to 50 mg/kg (0.01-0.06 mg/kg) i.p., the animals were observably irritated for 1 minute following dosing, and then became drowsy and apathetic (Patil et al., 1972). Breathing rate was increased, and the animals developed diarrhea followed by hind-leg paralysis and dyspnea. The 50 mg/kg dose induced death within 1 to 3 hours, preceded by a deep and prolonged state of unconsciousness; no deaths were observed at the 10 mg/kg dose. Incidences of death for the intermediate doses were not provided.

α-Solanine, administered at doses of 12 to 50 mg/kg (0.01-0.06 mmol/kg) i.p., caused occasional hepatic leukocytic infiltration in male Swiss-Webster mice (Sharma et al., 1979). The response was not dose-related. Animals administered the higher doses (not provided) exhibited respiratory distress and died within a few hours. Deaths of animals administered the lower doses (not provided) were equally distributed over the 7-day observation period.

As was observed with α-chaconine administration, α-solanine (10 to 85 mg/kg; 0.01 to 0.098 mmol/kg) induced hemorrhaging of the periorbital, nasal, and oral cavities, and internally, bloody ascitic and pleuritic fluid in female Wistar rats (Chaube and Swinyard, 1976). Doses of 40, 60, and 85 mg/kg (0.046, 0.069, and 0.098 mmol/kg) induced death in 11, 38, and 100% of the rats, respectively; doses less than 40 mg/kg were not lethal.

A 20 mg/kg dose of solanine induced hepatotoxic effects in male Sprague-Dawley rats; i.e. the dose significantly increased AST and ALT and decreased the activities of serum cholinesterase and microsomal enzymes, including cytochrome P-450 (Dalvi, 1985).

When rabbits (sex and strain not provided) were administered solanine at doses of 10, 15, 20, or 30 mg/kg (0.01, 0.017, 0.02, or 0.03), brain waves changed gradually over time at doses of 15 mg/kg and greater, while 10 mg/kg did not alter brain wave activity (Nishie et al., 1971). At doses of 15 mg/kg and greater, the animals experienced an initial rapid increase in respiration 1 to 1.5 hours after dosing, accompanied by slightly activated brain waves. Once the respiratory rate had decreased to a level below that of the controls (2.5 to 6 hours after dosing), delta brain waves were observed on an EEG. All doses except the 15 mg/kg dose induced an increase in heart rate. The animals treated with the 20 and 30 mg/kg died overnight or in 6.25 hours, respectively. The heart kept beating after breathing ceased and deep cyanosis and semiconciousness preceded death.

Solanine (20 or 30 mg/kg; 0.02 or 0.03 mmol/kg) increased the rate of respiration for the initial 15 to 30 minutes after dosing in male and female white New Zealand rabbits, making breathing difficult (Patil et al., 1972). Following this initial period, the rabbits went into a depressive phase, indicated by a lack of response to stimuli, partially closed eyes, disinclination to move, and muscle weakness resembling partial paralysis of the limbs; this depressive phase

was caused by severe exhaustion. Two out of 3 rabbits administered the 20 mg/kg dose and the only rabbit administered the 30 mg/kg dose died. Occasional twitching or convulsions preceded death, and the pupils were widely dilated. The authors noted that solanine was a weak to moderate inhibitor of both specific and non-specific cholinesterase in serum and erythrocytes.

A solanine dose of 20 mg/kg (0.02 mmol/kg) induced an increase in pulse, systolic pressure, and respiratory rate in one female Rhesus monkey that died 2 hours after dosing (Swinyard and Chaube, 1973). Hemorrhage of the nasal and periorbital cavities and hemorrhagic congestion in the lung, liver, and spleen were noted at necropsy. Accumulation of serosanguinous pleural and peritoneal fluids and mild hepatic and splenic congestion was also induced.

Mixtures of α-Chaconine and α-Solanine

No effects were noted with i.p. administration of 5 or 10 mg/kg (0.006 or 0.01 mmol/kg) of a 1:1 mixture of α-chaconine and α-solanine to hamsters (sex and strain not provided) (Phillips et al., 1996). At doses of 25, 50, or 100 mg/kg (0.029, 0.058, or 0.116 mmol/kg), however, the mixture caused death within 24 hours. Blood was found in and around the stomach and duodenum during necropsy, indicating that glycoalkaloid uptake is facilitated by cell membrane disruption.

A glycoalkaloid dose of 40 mg/kg, administered to female Rhesus monkeys, induced an increase in pulse, systolic pressure, and respiratory rate and caused death within 48 hours (Swinyard and Chaube, 1973). The dose induced hemorrhage of the nasal and periorbital cavities in addition to hemorrhagic congestion in the lung, liver, and spleen. An accumulation of serosanguinous pleural and peritoneal fluids and mild hepatic and splenic congestion were also induced. The concentration of α-chaconine and α-solanine in the glycoalkaloid dose was not provided.

9.1.3.3 Intravenous Injection

α-Chaconine

α-Chaconine (1.0 or 1.5 mg/kg; 0.0012 or 0.0018 mmol/kg) i.v. slightly decreased heart rate and blood pressure in white New Zealand rabbits (sex not provided), while 2.0 mg/kg (0.0023 mmol/kg) increased heart rate within 1 to 7 minutes after injection (Nishie et al., 1975).

α-Solanine

One rabbit (sex and strain not provided) died within 2 minutes after receiving an i.v. injection of solanine at 10 mg/kg (0.01 mmol/kg); brain waves and respiration stopped simultaneously (Nishie et al., 1971).

Rabbits (sex and strain not provided) pretreated with pentobarbital before i.v. injection of solanine at 2 mg/kg (0.002 mmol/kg) had transient increases in respiratory rate and ventricular extrasystoles, and a decrease in blood pressure (Nishie et al., 1971). With administration of a solanine dose of 3 mg/kg (0.003 mmol/kg) after pentobarbital pretreatment, rabbits experienced a 30-second cessation of respiration 2.5 minutes after the solanine injection.

As was observed with i.v. administration of α-chaconine to white New Zealand rabbits (sex not provided), α-solanine slightly decreased heart rate and blood pressure at doses of 1.0 or 1.5 mg/kg (0.0011 or 0.0017 mmol/kg) and induced an increase in heart rate within 1 to 7 minutes after injection with 2.0 mg/kg (0.0023 mmol/kg) (Nishie et al., 1975).

Rapid serum cholinesterase inhibition was observed in a male dog (strain not provided) given pentobarbital sodium followed by 5 doses of 6 mg solanine/kg body weight (0.007 mmol/kg) i.v. at 10-minute intervals, (Patil et al., 1972). The inhibition was followed by a rapid recovery of serum cholinesterase. Erythrocyte cholinesterase was not inhibited.

Mixtures of α-Chaconine and α-Solanine

Intravenous administration of glycoalkaloids at 17 mg/kg (0.020 mmol/kg) was toxic to sheep (sex and strain not provided), while 50 mg/kg (0.06 mmol/kg) was lethal (Konig, 1953; cited by Maga, 1980). No other experimental details were provided.

9.1.4 Short-Term and Subchronic Exposure

The studies discussed in this section are also summarized in **Table 5**.

9.1.4.1 Oral Administration

Female Swiss-Webster mice fed 2.4 mmol α-chaconine or α-solanine per kg diet for 7 days had decreased body and liver weights (Friedman et al., 1996). α-Chaconine administration also reduced the percentage of liver weight per body weight. The authors attributed the decreased liver weights to hepatotoxicity of the two glycoalkaloids.

α-Solanine (5 mM administered in the drinking water for 14 days) inhibited calcium transport in the duodenum of male and female Wistar albino rats (Michalska et al., 1985). The ability to absorb calcium was reduced to 33% of that absorbed in the controls.

Feeding a diet containing 40% potato berries for 14 days induced 100% mortality in Swiss-Webster mice, but diets containing 1-20% potato berries or 1-40% potatoes were not fatal (Friedman, 1992). Weight gain was significantly reduced only in the groups fed 20 or 40% potato berries. The average glycoalkaloid contents were 0.45 mg/g potato berry and 0.064 mg/g potato.

Administration of 2.5% freeze-dried potato tops in the diet for 12 days to mice or rats (sex and strain not provided) did not induce adverse effects (Phillips et al., 1996). The stomach lining of the rats was examined histologically, but no abnormalities were found.

Table 5. Short-Term and Subchronic Exposure to α-Chaconine and α-Solanine

Species, Strain, and Age	Number and Sex of Animals	Chemical Form[a] and Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
9.1.4.1 Oral Administration						
Mice (Swiss-Webster, 8-wks-old)	8 F per group	α-chaconine isolated from potato sprouts	2.4 mmol/kg in the diet	7 day exposure; observation period n.p.	Significant decreases in body weight, liver weight, and the percent liver weight/body weight were observed. The authors suggest that the decreased liver weights were due to hepatotoxicity.	Friedman et al. (1996)
		α-solanine isolated from potato sprouts			Significant decreases in body weight and liver weight were observed. The authors suggest that the decreased liver weight was due to hepatotoxicity.	
Rats (Wistar albino, 5-6 wks old)	12, M and F	α-solanine, chromatographically pure	5 mM in the water	14 day exposure; observation period n.p.	Inhibited calcium transport in the duodenum. The ability to absorb calcium was 1/3 of that for the control group.	Michalska et al. (1985)
Mice (Swiss-Webster, age n.p.)	5 per group (sex n.p.)	Freeze-dried potato berries containing 45 mg glycoalkaloids/ 100 g potato berry or potatoes containing 6.4 mg glycoalkaloids/ 100 g potato	1, 5, 10, 20, or 40% ad libitum in the diet	14 day exposure; no additional observation period	The group fed 40% potato berries had 100% mortality, while all other groups had no mortality. Weight gain was significantly reduced only in the groups fed 20 or 40% potato berries.	Friedman (1992)
Mice (strain and age n.p.)	n.p.	Potato tops, freeze-dried	2.5% in the diet α-chaconine and α solanine intake: 0.88 mg/kg/day (0.001 mmol/kg/day) and 0.38 mg/kg/ day (0.00044 mmol/kg/day), respectively	12 day exposure; observation period n.p.	No adverse effects were observed.	Phillips et al. (1996)
Rats (strain and age n.p.)					No adverse effects, including abnormalities of the stomach lining, were observed.	
Hamsters (strain and age n.p.)	n.p.	potato tops, freeze-dried	12.4 g/day, average food consumption α-chaconine and α solanine intake: 28.2 mg/kg/day (0.033 mmol/kg/day) and 10.1 mg/kg/ day (0.011 mmol/kg/day), respectively	1 week exposure; observation period n.p.	No effect on body weight or behavior or abnormal findings at necropsy were observed.	

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: F = female; M = male; n.p. = not provided; RBC = red blood cell

Table 5. Short-Term and Subchronic Exposure to α-Chaconine and α-Solanine

Species, Strain, and Age	Number and Sex of Animals	Chemical Form[a] and Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
		1:1 α-chaconine: α-solanine mixture, purity n.p.	5, 10, 20, or 50 mg/kg/day (0.0058, 0.012, 0.023, or 0.058 mmol/kg/day) by gavage	3 day exposure; observation period n.p.	No ill-effects were observed at any dose. At necropsy, there was no evidence of damage in any tissue, including the stomach.	

Table 5. Short-Term and Subchronic Exposure to α-Chaconine and α-Solanine (continued)

Species, Strain, and Age	Number and Sex of Animals	Chemical Form[a] and Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
Rabbits (strain and age n.p.)	4 (sex n.p.)	potatoes containing 7.4 mg glycoalkaloids/ 100 g potato	estimated glycoalkaloid intake: 20-23 mg/kg/day (0.023-0.027 mmol/kg/day)	up to 20 day exposure; observation period n.p.	No ill-effects were observed.	Azim et al. (1983; cited by JECFA, 1993)
		greened potatoes containing 20.4 mg glycoalkaloids/ 100 g potato	estimated glycoalkaloid intake: 49-53 mg/kg/day (0.057-0.062 mmol/kg/day) in the diet		After 4-6 days, the animals became dull and inactive. After 10 days, the animals had symptoms of diarrhea, hair loss, and weight loss followed by watering eyes, body rigidity, and dullness. Protein digestibility was decreased by 45% from day 1. One animal died within 10 to 20 days.	
Rabbits (strain and age n.p.)	5 (sex n.p.)	potatoes containing 29.75 mg glycoalkaloids/ 100 g potato	estimated glycoalkaloid intake : 73.9 to 75.0 mg/kg/day (0.086-0.087 mmol/kg/day) in the diet	45 day exposure; observation period n.p.	The rabbits developed hemolytic anemia. RBC counts decreased by 27.5%. Hemoglobin concentrations also decreased. The authors stated that the metabolite solanidine increased the permeability and fragility of RBC membranes.	Azim et al. (1984; cited by JECFA, 1993)
Monkeys (Rhesus, age n.p.)	4 F	B5141 potatoes coated with molasses and rolled in powdered monkey chow	estimated α-chaconine and α-solanine intake: 2.31-3.05 mg/kg/day (0.0027-0.0036 mmol/kg/day) and 0.77-1.01 mg/kg/day (0.00089-0.0012 mmol/kg/ day), respectively	25 consecutive day exposure over a 42-day observation period	No toxic effects were observed.	Swinyard and Chaube (1973)
9.1.4.2 Intraperitoneal Injection						

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: F = female; M = male; n.p. = not provided; RBC = red blood cell

Table 5. Short-Term and Subchronic Exposure to α-Chaconine and α-Solanine (continued)

Species, Strain, and Age	Number and Sex of Animals	Chemical Form[a] and Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
Rats (Wistar, 9-wks-old)	5-11 F per dose	α-chaconine, purity n.p.	5, 10, or 20 mg/kg/day (0.0058, 0.012, or 0.023 mmol/ kg/day) for 8 days, or 40 mg/kg/day (0.05 mmol/kg/ day) for 2 days	see dose for exposure period; observed for 9 days after final dose	Lethality was observed at 20 and 40 mg/kg/day. External signs of toxicity included bloody ascitic fluid recovered from all animals that died and 47% of those that survived the 20 or 40 mg/kg/day doses. Occasional visceral adhesions and congestive hepatosplenomegalies were observed. Histologically, moderate congestion of the lung, spleen, and liver was observed.	Chaube and Swinyard (1976)
		α-solanine, purity n.p.			Lethality was observed only in the 40 mg/kg/day dose group. External and histological signs of toxicity were the same as those listed above.	
Rats (Sprague-Dawley, age n.p.)	At least 3 M	solanine, purity n.p.	10 mg/kg/day (0.012 mmol/kg/ day) suspended in corn oil followed by pentobarbital	3 day exposure; observation period n.p.	Pretreatment with solanine increased pentobarbital-induced sleeping time by 275% over the controls. It also reduced benzphetamine *N*-demethylase and aniline hydroxylase activity, and cytochrome P-450 content. These results suggest that solanine is an inhibitor of microsomal enzymes.	Dalvi and Peeples (1981)
			10 mg/kg/day (0.012 mmol/kg/ day) suspended in corn oil simultaneously with 75 mg/kg/ day phenobarbital sodium		No effect on the process of hepatic microsomal enzyme induction was observed. Solanine did not show that it is an inhibitor of microsomal enzymes.	
Rats (Wistar, mature)	F (number n.p.)	glycoalkaloids, purity n.p.	40 mg/kg/day (0.05 mmol/kg/day)	8 day exposure; observed for 8 days post-exposure	The females were pregnant. All animals died and necropsy revealed orbital, nasal, and oral hemorrhage. The peritoneal cavities contained serosanguinous fluid.	Swinyard and Chaube (1973)
Rats (Wistar, 9-wks-old)	4 F	α-chaconine and α-solanine, purity n.p.	10 mg/kg/day (0.012 mmol/kg/day) α-chaconine plus 5 mg/kg/day (0.0058 mmol/kg/day) α-solanine	8 day exposure; observed for 9 days after final dose	Treatment did not induce lethality.	Chaube and Swinyard (1976)

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: F = female; M = male; n.p. = not provided; RBC = red blood cell

The calculated intake of α-chaconine and α-solanine was 0.88 and 0.38 mg/kg/day (0.001 and 0.00044 mmol/kg/day), respectively.

When hamsters (sex and strain not provided) were fed freeze-dried potato tops in the diet for 1 week, no effects on body weight or behavior were observed (Phillips et al., 1996). No abnormal findings were found during necropsy. The estimated intake of α-chaconine and α-solanine was 28.2 and 10.1 mg/kg/day (0.033 and 0.011 mmol/kg/day), respectively.

Administration of a 1:1 mixture of α-chaconine and α-solanine to hamsters (sex and strain not provided) by gavage for 3 days did not induce ill-effects at doses ranging from 5 to50 mg/kg (0.0058-0.058 mmol/kg/day) (Phillips et al., 1996). No evidence of damage to any tissues, including the stomach, was found during necropsy.

No ill effects were observed in rabbits (sex and strain not provided) fed potatoes in the diet (Azim et al., 1983; cited by JECFA, 1993). The estimated glycoalkaloid intake was 20-23 mg/kg/day (0.023-0.027 mmol/kg/day). However, when rabbits were administered greened potatoes for up to 20 days, the animals became dull and inactive after 4 to 6 days. After 10 days, the animals experienced diarrhea, hair loss, and weight loss followed by watering eyes, body rigidity, and dullness. Treatment decreased protein digestibility by 45% starting on day 1 of administration, and one animal died within 10 to 20 days. The estimated glycoalkaloid intake was 49-53 mg/kg/day (0.057-0.062 mmol/kg/day).

Feeding potatoes to rabbits (sex and strain not provided) for 45 days induced hemolytic anemia, decreasing the red blood cell (RBC) count by 27.5% (Azim et al., 1984; cited by JECFA, 1993). The metabolite solanidine is hypothesized to have increased the permeability and fragility of RBC membranes. The estimated glycoalkaloid intake was 73.9 to 75.0 mg/kg/day (0.086-0.087 mmol/kg/day).

No toxic effects were observed when B5141 potatoes were fed in the diet for 25 consecutive days to female Rhesus monkeys (Swinyard and Chaube, 1973). The estimated α-chaconine and α-solanine intakes were 2.31 to 3.05 mg/kg/day (0.0027-0.0036 mmol/kg/day) and 0.77 to 1.01 mg/kg/day (0.00089-0.0012 mmol/kg/day), respectively.

9.1.4.2 Intraperitoneal Injection

When i.p. α-chaconine doses of 5, 10, or 20 mg/kg/day (0.0058, 0.012, or 0.023 mmol/kg/day) for 8 days or 40 mg/kg/day (0.05 mmol/kg/day) for 2 days were administered to female Wistar rats, lethality was observed in the 20 and 40 mg/kg/day dose groups (Chaube and Swinyard, 1976). When the same doses of α-solanine were administered, lethality was induced only at the 40 mg/kg/day dose. External signs of toxicity following dosing with either α-chaconine or α-solanine included bloody ascitic fluid recovered from all animals that died and 47% of those that survived, and occasional visceral adhesions and congestive hepatosplenomegalies. Moderate congestion of the lung, spleen, and liver was also observed.

Intraperitoneal administration of solanine at 10 mg/kg/day (0.012 mmol/kg/day) for 3 days, followed by pentobarbital, to male Sprague-Dawley rats increased the pentobarbital-induced sleeping time by 275% over the controls (Dalvi and Peeples, 1981). It also increased the activities of benzphetamine *N*-demethylase and aniline hydroxylase and the content of cytochrome P-450. These results suggest that solanine is an inhibitor of microsomal enzymes. However, when the same dose was administered simultaneously with phenobarbital sodium, the process of hepatic microsomal induction was not altered. Therefore, solanine failed to show decisively that it is an inhibitor of microsomal enzymes.

A glycoalkaloid dose of 40 mg/kg/day (0.005 mmol/kg/day) for 8 days was lethal to pregnant Wistar rats and induced orbital, nasal, and oral hemorrhage (Swinyard and Chaube, 1973). Serosanguinous fluid was present in the peritoneal cavities.

Simultaneous administration of α-chaconine (10 mg/kg/day; 0.012 mmol/kg/day) and α-solanine (5 mg/kg/day; 0.0058 mmol/kg/day) for 8 days to female Wistar rats did not induce lethality (Chaube and Swinyard, 1976).

9.1.5 Chronic Exposure

No data were found for α-chaconine, α-solanine, or related alkaloids or hydrolysis products.

9.2 Embryotoxicity and Teratogenicity

The studies discussed in this section are also summarized in **Table 6**.

9.2.1 Oral Administration

α-Chaconine

Administration of α-chaconine at 1.5 mg/kg/day (0.002 mmol/kg/day) to pregnant Wistar rats on days 6 through 15 of gestation did not induce teratogenic or embryolethal effects (Ruddick et al., 1974). Similarly, no maternal toxicity or fetal abnormalities were induced by a single α-chaconine dose of 50 mg/kg (0.06 mmol/kg) administered to female Wistar rats on day 9 of gestation (Waalkens-Berendsen et al., 1992).

A single α-chaconine dose of 200 mg/kg (0.23 mmol/kg) to pregnant Syrian hamsters on day 8 of gestation induced maternal toxicity (incidence ratio not provided) and death of all fetuses in 12% of the litters (Renwick, 1982). Seven out of eight live litters had at least one embryo with malformations of the central nervous system (CNS) (i.e., exencephaly and cranial bleb).

Table 6. Embryotoxicity and Teratogenicity of α-Chaconine and α-Solanine

Species, Strain, Age	Number and Sex of Animals	Chemical Form[a], Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
9.2.1 Oral Administration						
Rats (Wistar, mature)	4 F	α-chaconine, purity n.p.	1.5 mg/kg/day (0.002 mmol/kg/day) by gavage	exposed on days 6 to 15 of gestation; observed to day 22 of gestation	No teratogenic or embryolethal effects were observed.	Ruddick et al. (1974)
Rats (Wistar, mature)	F (number n.p.)	α-chaconine, purity n.p.	50 mg/kg (0.06 mmol/kg) by gavage	single exposure on day 9 of gestation; observed to day 21 of gestation	No signs of maternal toxicity were observed. In the fetuses, no exencephaly, micrognatia, or skeletal abnormalities were observed.	Waalkens-Berendsen et al. (1992)
Hamsters (Syrian, mature)	F (number n.p.)	α-chaconine, purity n.p.	200 mg/kg (0.23 mmol/kg) by gavage	single exposure on day 8 of gestation; observation period n.p.	6 cases (percentage n.p.) of maternal toxicity and 12% embryotoxicity were observed. 7/8 live litters had at least one CNS-malformed embryo (exencephaly and cranial bleb).	Renwick (1982)
Hamsters (Syrian, mature)	F (number n.p.)	α-chaconine, purity n.p.	150, 165 or 180 mg/kg (0.18, 0.19, or 0.21 mmol/kg) by gavage	single exposure on day 8 of gestation; 15 day observation	Number of hamster dam deaths was increased at the 165 and 180 mg/kg doses as compared to controls. Dam deaths at 150 mg/kg were n.p. The number of malformed litters was dose-related. Percentage of malformed litters was negligible at the low dose, 63% at the middle dose, and 88% at the high dose. Teratogenic malformations were restricted to those of the neural tube, mostly cranial bleb and exenchephaly.	Renwick et al. (1984)
Hamsters (Syrian, mature)	F (number n.p.)	22*R*, 25*S*-α-chaconine, pure	160-200 mg/kg (0.19-0.23 mmol/kg) by gavage	single exposure on day 8 of gestation; observation period n.p.	The incidence of malformations (craniofacial defects) was 20%. Based on teratogenicity data from administered doses of α-chaconine, α-solanine, and solanidine, the authors concluded that dam toxicity is not responsible for the teratogenicity of α-chaconine and α-solanine.	Gaffield et al. (1992)
Hamsters (Syrian, mature)	F (number n.p.)	α-chaconine, 'pure'	0.21 or 0.29 mmol/kg by gavage	single exposure on day 8 of gestation; observed to day 15 of gestation	Fetal abnormalities observed at the 0.21 mmol/kg dose were not statistically significant, but the one litter from a dam dosed with 0.29 mmol/kg had a statistically significant number of abnormal fetuses. Abnormalities included exencephaly, encephalocele, and anophthalmia.	Gaffield and Keeler (1996)

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: CNS = central nervous system; F = female; M = male; n.p. = not provided

Table 6. Embryotoxicity and Teratogenicity of α-Chaconine and α-Solanine (continued)

Species, Strain, Age	Number and Sex of Animals	Chemical Form[a], Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
Rats (Holzman, approx. 4-months-old)	F (number n.p.)	solanine, purity n.p.	30 or 40 mg/kg/day (0.03 or 0.05 mmol/kg/day) in the basal diet	Exposed through gestation and weaning; observation period n.p.	An increased number of litters in which all pups died was observed with administration of both doses compared to controls: control, 1/ll; 30 mg/kg solanine, 6/10; 40 mg/kg solanine, 5/10. Percentage of pups weaned was decreased at both doses compared to controls: control, 82.6%; 30 mg/kg solanine, 31.0%; 40 mg/kg solanine, 31.1%.	Kline et al. (1961)
Rats (Wistar, mature)	9 F per group	α-solanine, purity n.p.	0.3, 1.0, or 3.0 mg/kg/day (0.0003, 0.001, or 0.003 mmol/kg/day) by gavage	exposed on days 6 to 15 of gestation; observed to day 22 of gestation	At the 0.3 mg/kg/day dose, one fetus had twisted pelvic limbs and an absent tail. At the 3 mg/kg/day dose, one fetus had craniorachischisis and exopthalmos. These effects did not appear to be treatment-related.	Ruddick et al. (1974)
			6 mg/kg/day (0.007 mmol/kg) by gavage	exposed on days 7 to 10 of gestation; observed to day 22 of gestation	No evidence of teratogenicity was observed.	
	3-4 F per group		2, 10, or 25 mg/kg/day (0.002, 0.01, or 0.03 mmol/kg/day) by gavage	exposed on days 8 to 11 of gestation; observed to day 22 of gestation		
Rats (Wistar, mature)	F (number n.p.)	α-solanine, purity n.p.	50 mg/kg (0.06 mmol/kg) by gavage	single exposure on day 9 of gestation; observed to day 21 of gestation	No signs of maternal toxicity were found. No exencephaly, micrognatia, or skeletal abnormalities were observed in the fetuses.	Waalkens-Berendsen et al. (1992)
Hamsters (Syrian, mature)	F, number n.p.	α-solanine, purity n.p.	217 mg/kg (0.25 mmol/kg) by gavage	single exposure on day 8 of gestation; observation period n.p.	3 cases (percent incidence n.p.) of maternal toxicity and 41% embryotoxicity were observed. 20/34 live litters had at least one CNS-malformed embryo (exencephaly, cranial bleb, and other unspecified abnormalities).	Renwick (1982)

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: CNS = central nervous system; F = female; M = male; n.p. = not provided

Table 6. Embryotoxicity and Teratogenicity of α-Chaconine and α-Solanine (continued)

Species, Strain, Age	Number and Sex of Animals	Chemical Form[a], Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
Hamsters (Syrian, mature)	F (number n.p.)	α-solanine, purity n.p.	200 mg/kg (0.23 mmol/kg) by gavage (other doses were administered, but n.p.)	single exposure on day 8 of gestation; 15 day observation	Number of hamster dam deaths was increased as compared to controls. The number of malformed litters was dose-related. Teratogenic malformations were restricted to those of the neural tube, mostly cranial bleb and exenchephaly. α-Chaconine produced the same results at a 21% lower dose than α-solanine.	Renwick et al. (1984)
Hamsters (Syrian, mature)	F (number n.p.)	22*R*, 25*S*-α-solanine, 'pure'	200-288 mg/kg (0.23-0.33 mmol/kg/day) by gavage	single exposure on day 8 of gestation; observation period n.p.	The incidence of malformations (craniofacial defects) was 20%. Based on teratogenicity data from administered doses of α-chaconine, α-solanine, and solanidine, the authors concluded that dam toxicity is not responsible for the teratogenicity of α-chaconine and α-solanine.	Gaffield et al. (1992)
Hamsters (Syrian, mature)	F (number n.p.)	22*R*,25*S*α-solanine, 'pure'	0.28 mmol/kg by gavage	single exposure on day 8 of gestation; observed to day 15 of gestation	21% (5/24) of the litters had fetuses with abnormalities, including exencephaly, encephalocele, and anophthalmia.	Gaffield and Keeler (1996)
Rats (Wistar, mature)	14 F	cooked and freeze-dried visibly blighted tubers, as 73% of the diet	19,700 mg/kg/day in the diet (mean consumption)	exposed on day 1 to 22 of gestation; no additional observation period	The content of the glycoalkaloids in the diet was not determined. No evidence of maternal toxicity, fetal toxicity, or teratogenicity was observed.	Ruddick et al. (1974)
Hamsters (strain n.p., mature)	12-15 F per group	freeze-dried potato concentrate	50% freeze-dried, unblighted potato concentrate (diet 1), 50% *Phytophthora infestans* infected freeze-dried, blighted potato concentrate (diet 2), or 50% *Alternaria solani* infected freeze-dried, blighted potato concentrate (diet 3)	exposed on day 5 to 10 of gestation; observed to day 15 of gestation	The content of the glycoalkaloids in the diet was not determined. Feed consumption, maternal body weight gain, litter size, number of resorptions, and fetal weight were not affected by any of the treatments. The most frequent gross anomaly (hemorrhagic necrosis of the central nervous system) was not treatment related: diet 1, 1/114; diet 2, 3/153; and diet 3, 0/135.	Sharma et al. (1978; cited by JECFA, 1993)

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: CNS = central nervous system; F = female; M = male; n.p. = not provided

Table 6. Embryotoxicity and Teratogenicity of α-Chaconine and α-Solanine (continued)

Species, Strain, Age	Number and Sex of Animals	Chemical Form[a], Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
Hamsters (Simonsen, mature)	F (number n.p.)	potato sprout material	2.7-6.3 g/kg (a glycoalkaloid dose of 94.5-346.5 mg/kg [0.11-0.40 mmol/kg]) in the diet	single exposure on day 7 or 8 of gestation; observed to day 15 of gestation	Sprout material was both teratogenic and embryolethal. The number of resorptions was dramatically increased when compared to the controls. Types of malformations included cranial bleb, exencephaly, microphthalmia, and spina bifida; incidence varied with different potato strains.	Keeler et al. (1978)
Hamsters (Simonsen, mature)	F (number n.p.)	potato peel or tuber material, sprouted or unsprouted	potato peel: 10-20 g/kg (a glycoalkaloid dose of 20-40 mg/kg [0.023-0.047 mmol/kg]) in the diet potato tuber: 10-20 g/kg (a glycoalkaloid dose of 0.3-0.6 mg/kg [0.0003-0.0007 mmol/kg]) in the diet	single exposure on day 7 or 8 of gestation; observed to day 15 of gestation	No significant embryolethal or teratogenic effects were observed.	Keeler et al. (1978)
Rabbits (New Zealand, mature)	2-6 F	freeze-dried potato concentrate	50% freeze-dried, unblighted potato concentrate (diet 1), 50% *Phytophthora infestans* infected freeze-dried, blighted potato concentrate (diet 2), or 50% *Alternaria solani* infected freeze-dried, blighted potato concentrate (diet 3)	exposed through gestation; observation period n.p.	The content of the glycoalkaloids in the diet was not determined. No effects were observed from treatment with diet 1 (0/9 abnormal fetuses). 3/21 fetuses from mothers fed diet 2 had incomplete closure of the caudal vertebral column. 2/21 were very small and had shortened appendages. 2/28 of the fetuses from mothers fed diet 3 had incomplete closure of the caudal vertebral column, 1/28 had a very small brain and the cranial cavity was filled with fluid, and 2/28 were abnormally small. The authors noted that feeding blighted potatoes to pregnant rabbits produces a low incidence of the caudal vertebral column malformation. However, the conclusion should be taken with caution due to a small size of the control group which does not allow for the determination of spontaneous rates of this malformation.	Sharma et al. (1978; cited by JECFA, 1993)

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: CNS = central nervous system; F = female; M = male; n.p. = not provided

Table 6. Embryotoxicity and Teratogenicity of α-Chaconine and α-Solanine (continued)

Species, Strain, Age	Number and Sex of Animals	Chemical Form[a], Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
Swine (Miniature, mature)	2 F per group	freeze-dried potato concentrate	50% freeze-dried, unblighted potato concentrate (diet 1), 50% *Phytophthora infestans* infected freeze-dried, blighted potato concentrate (diet 2), or 50% *Alternaria solani* infected freeze-dried, blighted potato concentrate (diet 3)	exposed through the 1st half of gestation (about 57 days); observed to the end of gestation (day n.p.)	The content of the glycoalkaloids in the diet was not determined. Diet 3 depressed weight gain in the maternal swine. 1 fetus out of 15 from the swine fed diet 2 had anencephaly with extensive internal hydrocephaly. No other fetuses were affected. The authors concluded that feeding potatoes blighted with *P. infestans* may cause anencephaly in miniature swine, but that definitive conclusions cannot be drawn due to the small sample size.	Sharma et al. (1978; cited by JECFA, 1993)
Marmosets (*Callithrix jacchus*, 5-yrs-old)	6 F	freeze-dried potato concentrate, blighted	4.7 g/kg/day in the diet (a glycoalkaloid dose of 0.9 mg/kg/day [0.001 mmol/kg/day])	50 day exposure, on either days 0-50 or 20-70 of gestation; observed to day 80-120 of gestation	4/11 fetuses had cranial osseous defects. There was a replacement of bone by a collagenous membrane in the occipital area. The lateral ventricle of the brain was enlarged. The authors concluded that the results are suggestive of the teratogenicity of blighted potatoes.	Poswillo et al. (1972; 1973; cited by JECFA, 1993)
	7 F	freeze-dried potato concentrate, blemished	4.7 g/kg/day in the diet (a glycoalkaloid dose of 0.78 mg/kg/day [0.0009 mmol/kg/day])	exposed through gestation (length n.p.); newborns were observed at regular intervals up to 6 months.	Behavior anomalies of 3 sets of twins included continuous clinging to parents or siblings and prolonged weaning time. The significance of these behavior responses was not determined. No anatomical abnormalities were observed.	Poswillo et al. (1973; cited by JECFA, 1993)
	6 F	freeze-dried potato concentrate of unblemished potatoes	4.7 g/kg/day in the diet (a glycoalkaloid dose of 0.56 mg/kg/day [0.0007 mmol/kg/day])		No anatomical or behavioral abnormalities were observed.	
	5 F	freeze-dried potato concentrate of potatoes infected with *Erwinia carotovera*	4.7 g/kg/day in the diet (a glycoalkaloid dose of 0.07 mg/kg/day [0.00008 mmol/kg/day])	exposed for 90 to 110 days; no additional observation period	All marmosets had previously produced normal offspring, and dosing began 10 days postpartum of the previous litter. Females were sacrificed between days 90 and 110 of gestation. Fetuses were examined grossly and radiographically for abnormalities. No anatomical abnormalities were observed.	
9.2.2 Intraperitoneal Injection						

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: CNS = central nervous system; F = female; M = male; n.p. = not provided

Table 6. Embryotoxicity and Teratogenicity of α-Chaconine and α-Solanine (continued)

Species, Strain, Age	Number and Sex of Animals	Chemical Form[a], Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
Rats (Wistar, 9-wk-old)	4-7 F per group	α-chaconine, purity n.p.	2.5, 5, 10, or 20 mg/kg/day (0.003, 0.006, 0.01, or 0.02 mmol/kg/day) on days 5-12 of gestation, or 40 mg/kg/day (0.05 mmol/kg/day) on days 5-6 of gestation	see dose for exposure period; observed to day 21 of gestation	10, 20, and 40 mg/kg/day were lethal to maternal rats. Additionally, intense endometrial inflammatory reactions were encountered in the uterus at the sites of fetal resorption. Significant fetal growth retardation and embryolethality were observed at 5 mg/kg/day and higher. One incidence of irregular or fused ribs in a fetus was observed at 5 mg/kg.	Chaube and Swinyard (1976)
Mice (strain n.p., mature)	F (number n.p.)	α-solanine, purity n.p.	n.p.	single exposure on day 8, 9, or later in gestational period; observation period n.p.	α-Solanine markedly increased embryonic mortality following treatment on day 8 or 9 of gestation, but not later in gestation. Decidual swellings that were collected following dosing showed signs of destruction of mesenchymal cells, which interferes with allantois outgrowth and precedes embryo resorption.	Pierro et al. (1976)
Mice (ASH/CS1, adult)	16 or 20 F per group	solanine, commercially extracted	20 mg/kg/day (0.02 mmol/kg/day) on day 7, on days 7-10, or on days 7-11 of gestation	see dose for exposure period; observed to day 17 of gestation	The greatest embryotoxicity (defined as induced abortions) occurred in the group receiving treatment for 5 days. Treatment did not significantly increase the number of resorptions and no malformations were observed among the viable fetuses.	Bell et al. (1976)
Rats (Wistar, mature)	F (number n.p.)	solanine, purity n.p.	5 or 10 mg/kg/day (0.006 or 0.01 mmol/kg/day)	exposed on days 7-17 of gestation; observed to day 21 of gestation	No maternal toxicity was observed. There was no fetal mortality at the low dose and 7% fetal mortality at the high dose. No neural tube defects were observed, but a high incidence of minor abnormalities (mild hydronephrosis, hydroureter, and ribs showing knobby protuberances on the posterior third of their length) was induced.	Swinyard and Chaube (1973)
				exposed on days 5-12 of gestation; observed to day 21 of gestation	Findings matched those for administration on days 7-17 of gestation (above) except that there was 14% fetal mortality at the high dose.	
Rats (Wistar, 9-wks-old)	6-8 F per group	α-solanine, purity n.p.	5, 10, or 20 mg/kg/day (0.006, 0.01, or 0.02 mmol/kg/day) on days 5-12 of gestation, or 40 mg/kg/day (0.05 mmol/kg/day) on days 5-6 of gestation	see dose for exposure period; observed to day 21 of gestation	No maternal deaths were induced, but intense endometrial inflammatory reactions were encountered in the uterus at the sites of fetal resorption. Significant embryolethality was observed at 5 mg/kg/day and higher. Fetal growth retardation was observed at 20 and 40 mg/kg. Irregular or fused ribs were induced in fetuses at all doses.	Chaube and Swinyard (1976)

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: CNS = central nervous system; F = female; M = male; n.p. = not provided

Table 6. Embryotoxicity and Teratogenicity of α-Chaconine and α-Solanine (continued)

Species, Strain, Age	Number and Sex of Animals	Chemical Form[a], Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
Rabbits (New Zealand White, mature)	3 F	solanine, reference standard	5 mg/kg (0.006 mmol/kg/day)	single exposure on day 0-8 of gestation; observed to day 22 of gestation	1 rabbit that delivered prematurely had 2 normal, living fetuses, 2 dead fetuses with retarded growth, 2 extensively resorbed fetuses, and 4 totally resorbed fetuses. The 2 rabbits carrying pregnancy to the time of necropsy had a total of 13 normal, living fetuses; the rate of resorption was 18%.	Swinyard and Chaube (1973)
Rats (Wistar, mature)	F (number n.p.)	glycoalkaloids, purity n.p.	10 or 20 mg/kg/day (0.01 or 0.02 mmol/kg/day)	exposed on days 5-12 of gestation; observed to day 21 of gestation	No maternal lethality was observed at either dose. Fetal mortality was 50 and 100% at 10 and 20 mg/kg, respectively. No neural tube defects were observed, but a high incidence of minor abnormalities (mild hydronephrosis, hydroureter, and ribs showing knobby protuberances on the posterior third of their length) was induced. At 10 mg/kg, the total glycoalkaloid dose was 7 times more toxic than the same dose of solanine.	
Rats (Wistar, 9-wks-old)	6F per group	α-chaconine and α-solanine, purity n.p.	10 mg/kg/day (0.01 mmol/kg/day) α-chaconine and 5 mg/kg/day (0.006 mmol/kg/day) α-solanine on days 5-12 of gestation	see dose for exposure period; observed to day 21 of gestation	The combined dose was not lethal to maternal or fetal rats. 6.7% of the fetal rats had irregular or fused ribs.	Chaube and Swinyard (1976)
9.2.3 Intravenous Injection						
Rats (Sprague-Dawley, mature)	13 F	α-chaconine, purity n.p.	1.7 mg/kg/day (0.002 mmol/kg/day)	exposed on days 6-13 of gestation; observed to day 19 of gestation	The average maternal blood serum concentration of α-chaconine was 340 ng/mL, which is more than 20 times greater than the average peak serum level reported for human volunteers after ingesting potatoes with a total glycoalkaloid content at the upper safe limit. No signs of maternal toxicity were observed. Of the 143 fetuses in the treatment group, none had external malformations (soft tissue anomalies were not investigated). When treatment and control groups were compared, no statistical differences in number of resorptions or dead fetuses were observed, nor were there significant differences in fetal body weight per litter.	Hellenäs et al. (1992a)
9.2.4 Injection into the Yolk Sac						

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: CNS = central nervous system; F = female; M = male; n.p. = not provided

Table 6. Embryotoxicity and Teratogenicity of α-Chaconine and α-Solanine (continued)

Species, Strain, Age	Number and Sex of Animals	Chemical Form[a], Purity	Dose	Exposure/ Observation Period	Results/Comments	Reference
Chicken eggs, (strain n.p., fertile)	n.p.	α-chaconine, purity n.p.	0.5-1.5 mg/kg (0.00059-0.0018 mmol/ kg) before incubation or 12, 20, or 30 mg/kg (0.014, 0.023, or 0.035 mmol/kg) after 96 hours of incubation	single exposure; observation period n.p.	All doses except 0.5 mg/kg caused a reduction in hatchability. The mean body weights of hatched chicks were not significantly different from the controls at any dose. The incidence of congenital malformations (phocomelia, one-leggedness, absence of claws, and microcephaly) was not statistically significant.	Nishie et al. (1975)
Chicken eggs (Foghorn, fertile)	41-88 per group	solanine, purity n.p.	10, 19, or 25 mg/kg (0.01, 0.02, or 0.03 mmol/kg) on day 4 of incubation	single exposure; observed for 22 days	No statistically significant increase in abnormal chicks was observed. 25 mg/kg reduced hatchability by 29%.	Nishie et al. (1971)
Chicken eggs (strain n.p., fertile)	n.p.	α-solanine, purity n.p.	0.5-1.5 mg/kg (0.00058-0.0017 mmol/ kg) before incubation or 19 mg/kg (0.022 mmol/ kg) after 96 hours of incubation	single exposure; observation period n.p.	The low doses (0.5-1.5 mg/kg) had no effect on hatchability, but 19 mg/kg reduced hatchability. The mean body weights of hatched chicks were not significantly different from the controls at any dose. The incidence of congenital malformations (unfeathered skin in the retroinguinal area, unilateral anophthalmia) was not statistically significant.	Nishie et al., 1975)
Chicken eggs (white Leghorn, fertile)	18-179 per group	solanine or mixed glycoalkaloids from potatoes infected with *P. infestans*	0.015, 0.13, 0.17, 0.26, or 1.5 mg/egg (0.00002, 0.00015, 0.0002, 0.0003, or 0.0017 mmol/egg) solanine or 0.26 mg/egg (0.0003 mmol/egg) glycoalkaloids from blighted potatoes, injected between 0 and 26 hours of incubation	single exposure; observed for 72 hours of incubation	With the 1.5 mg/egg solanine treatment, most embryos died at the early stages of development. In the other dose groups (including the glycoalkaloid dose from blighted potatoes), the percent of dead embryos was decreased, but the incidence (15-29%) of abnormalities was increased. Abnormalities included rumplessness (absence of the tail below the wing bud) and trunklessness (absence of a trunk below the wing bud). Fluid- or blood-filled vesicles in the lower trunk or tail region was also observed.	Mun et al. (1975)
Chicken eggs (white Leghorn, 2-4 days old)	6 per group	ethanol extract from potatoes infected with *P. infestans,* extract from healthy potatoes, or solanine, 'pure'	0.3 mg/egg (0.0003 mmol/egg)	subgerminal injections on day 2 of incubation; intraamniotic injection on days 3 and 4 of incubation	Equivalent doses of three treatments had the same effects. The dose interfered with the caudal morphogenetic system at the somite stages. Injections on the 3rd and 4th days led to malformations including cranioschisis, celosoma, and cardiac septal defects.	Jelínek et al. (1976)

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: CNS = central nervous system; F = female; M = male; n.p. = not provided

A dose-dependent increase in the number of litters with malformed pups was found with administration of a single α-chaconine dose of 150, 165, or 180 mg/kg (day 8 of gestation) to pregnant Syrian hamsters; the percentage of litters with malformed pups was negligible at the low dose (percentage not provided), 63% at the middle dose, and 88% at the high dose (Renwick et al., 1984). Malformations were restricted to those of the neural tube, mostly cranial bleb and exencephaly. The number of maternal deaths was increased at the 2 higher doses; information on maternal deaths at the low dose was not provided.

The incidence of malformations (i.e. craniofacial defects) was 20% with administration of α-chaconine at doses ranging from 160 to 200 mg/kg (0.19-0.23 mmol/kg) to pregnant Syrian hamsters (Gaffield et al., 1992).

Fetal abnormalities induced by dosing pregnant Syrian hamsters with α-chaconine were statistically significant at a dose of 0.29 mmol/kg, but not at a dose of 0.21 mmol/kg (Gaffield and Keeler, 1996). Abnormalities included exencephaly, encephalocele, and anophthalmia.

α-Solanine

When solanine was administered at 30 or 40 mg/kg/day (0.03 or 0.05 mmol/kg) to pregnant Holtzman rats through gestation and weaning, an increase in the number of litters in which all the pups died was observed (Kline et al., 1961). Additionally, the percentage of pups surviving past weaning was reduced from 82.6% in the control group to 31% at both doses.

Fetal abnormalities were observed with administration of α-solanine (0.3, 1.0, or 3.0 mg/kg/day; 0.0003, 0.001, or 0.003 mmol/kg/day) to pregnant Wistar rats on days 6 to 15 of gestation, but the effects did not appear to be treatment related (Ruddick et al., 1974). At the 0.3 mg/kg/day dose, one fetus had twisted pelvic limbs and an absent tail and at the 3.0 mg/kg/day dose, one fetus had craniorachischisis and exophthalmos.

Administration of the following α-solanine doses to pregnant Wistar rats did not induce teratogenic effects: 6 mg/kg/day (0.007 mmol/kg/day) on days 7 to 10 of gestation; 2, 10, or 25 mg/kg/day (0.002, 0.01, or 0.03 mmol/kg/day) on days 8 to 11 of gestation (Ruddick et al., 1974); or 50 mg/kg (0.06 mmol/kg) on day 9 of gestation (Waalkens-Berendsen et al., 1992).

Maternal toxicity (incidence ratio not provided) and 41% embryotoxicity were induced with administration of α-solanine at 217 mg/kg (0.25 mmol/kg) to pregnant Syrian hamsters (Renwick, 1982). Twenty out of 34 live litters (59%) had at least one fetus with a malformation of the central nervous system (CNS) (i.e., exencephaly, cranial bleb, and other unspecified abnormalities).

When α-solanine (200 mg/kg [0.23 mmol/kg] and other, unspecified, doses) was administered to pregnant Syrian hamsters, the number of malformed litters was dose-related (Renwick et al., 1984). Malformations were restricted to neural tube defects, mostly cranial bleb and exencephaly. Additionally, the maternal lethality was increased compared to the controls.

The incidence of malformed fetuses from pregnant Syrian hamsters was 20% with administration of α-solanine at 200-288 mg/kg (0.23-0.33 mmol/kg) (Gaffield et al, 1992). Similarly, 0.28 mmol/kg of α-solanine induced malformations in 21% of the litters (Gaffield and Keeler, 1996). Abnormalities included exencephaly, encephalocele, and anophthalmia.

Mixtures of α-Chaconine and α-Solanine

Administration of cooked and freeze-dried visibly blighted tubers as 73% of the diet (glycoalkaloid content not provided) did not induce maternal toxicity in pregnant Wistar rats, nor did it induce fetal toxicity or teratogenicity in the offspring (Ruddick et al., 1974).

Maternal and fetal toxicity were not induced when pregnant hamsters (strain not provided) were administered the three following diets: 50% freeze-dried, unblighted potato concentrate; 50% *Phytophthora infestans*-infected freeze-dried, blighted potato concentrate; or 50% *Alternaria solani*-infected freeze-dried, blighted potato concentrate (Sharma et al., 1978; cited by JECFA, 1993). The most frequent gross anomaly, hemorrhagic necrosis of the CNS, was not treatment-related.

Feeding potato sprouts to pregnant Simonsen hamsters on day 7 or 8 of gestation was both embryolethal, dramatically increasing the number of resorptions, and teratogenic, inducing cranial bleb, exencephaly, microphthalmia, and spina bifida (Keeler et al., 1978). The glycoalkaloid dose found in the sprout material ranged from 94.5 to 346.5 mg/kg (0.11-0.40

mmol/kg). However, when potato peel or tuber material (sprouted or unsprouted) providing lower glycoalkaloid doses (20-40 mg/kg [0.0023-0.047 mmol/kg] or 0.3-0.6 mg/kg [0.0003-0.0007 mmol/kg], respectively) were fed on day 7 or 8 of gestation, no embryolethal or teratogenic effects were observed.

When pregnant New Zealand rabbits were fed freeze-dried potato concentrate as 50% of the diet, teratogenicity was not induced (Sharma et al., 1978; cited by JECFA, 1993). However, feeding *P. infestans*- or *A. solani*-infected freeze-dried, blighted potato concentrate as 50% of the diet induced a low incidence of caudal vertebral column malformation. The authors urged caution in interpretation of the results because a small control group size was used, which did not allow for determination of the spontaneous rates of the malformation. When the same diets were fed to miniature swine, the *A. solani*-infested diet depressed maternal weight gain and 1/15 fetuses from the swine that were fed the *P. infestans*-infected diet had anencephaly with extensive internal hydrocephaly; however, investigators used a small sample size. The glycoalkaloid content of the diets was not provided, but blighted potatoes are known to have higher glycoalkaloid contents than unblighted potatoes (Renwick, 1972).

The fetuses of marmosets (*Callithrix jacchus*) fed blighted freeze-dried potato concentrate had cranial osseus defects (4/11) when the diet provided a glycoalkaloid dose of 0.9 mg/kg/day (0.001 mmol/kg/day) for 50 days (Poswillo et al., 1972; 1973; both cited by JECFA, 1993). When the same diet provided a glycoalkaloid dose of 0.78 mg/kg/day (0.0009 mmol/kg/day) through gestation, behavioral anomalies, but not anatomical abnormalities, were induced. These included continuous clinging to the parents or siblings and prolonged weaning; the biological significance of the behaviors was not determined. When the glycoalkaloid doses were 0.56 mg/kg/day (0.0007 mmol/kg/day) through gestation or 0.07 mg/kg/day (0.00008 mmol/kg/day) for 90 to 100 days, no anatomical or behavioral abnormalities were induced.

9.2.2 Intraperitoneal Injection

α-Chaconine

When pregnant Wistar rats were dosed i.p. with α-chaconine at doses of 2.5, 5, 10, or 20 mg/kg/day (0.003, 0.006, 0.01, or 0.02 mmol/kg/day) on days 5-12 of gestation or 40 mg/kg/day (0.05 mmol/kg/day) on days 5-6 of gestation, significant fetal growth retardation and embryolethality were induced at all doses except the lowest dose (Chaube and Swinyard, 1976). A single incidence of teratogenicity (i.e. irregular or fused ribs) was observed at the 5 mg/kg/day dose. Doses of 10 mg/kg/day or greater were lethal to maternal rats, and also induced intense endometrial inflammatory reactions in the uterus at the sites of fetal resorption.

α-Solanine

When administered on day 8 or 9 of gestation to pregnant mice (strain not provided), α-solanine (dose not provided) was embryolethal (Pierro et al., 1976). Decidual swellings showed signs of destruction of mesenchymal cells, which interferes with allantois outgrowth and precedes embryo resorption. When α-solanine was administered later in the gestational cycle, however, no increase in embryo deaths was observed.

Embryolethality or teratogenicity were not induced when pregnant ASH/CS1 mice were administered solanine at 20 mg/kg/day (0.02 mmol/kg/day) on day 7 of gestation, on days 7 to 10 of gestation, or on days 7 to 11 of gestation (Bell et al., 1976). The greatest toxicity (measured as the number of induced abortions) occurred in the group dosed for 5 days.

Treatment of pregnant Wistar rats with solanine (5 or 10 mg/kg/day; 0.006 or 0.01 mmol/kg/day) on days 7 through 17 of gestation induced 7% embryolethality at the 10 mg/kg/day dose (Swinyard and Chaube, 1973). Similarly, when the same doses were administered on days 5 through 12 of gestation, 14% embryolethality was induced at the 10 mg/kg/day dose. No maternal toxicity was observed at any dose, nor were there any neural tube defects. However, a high incidence of minor abnormalities was observed at all doses, including mild hydronephrosis, hydroureter, and ribs showing knobby protuberances on the posterior third of their length.

When pregnant Wistar rats were dosed with α-solanine at 5, 10, or 20 mg/kg/day (0.006, 0.01, or 0.02 mmol/kg/day) on days 5 through 12 of gestation or 40 mg/kg/day (0.05 mmol/kg/day) on days 5 and 6 of gestation, all doses were embryolethal (Chaube and Swinyard, 1976) and irregular and fused ribs were induced in fetuses from mothers administered all doses. Fetal growth retardation was observed at the 20 and 40 mg/kg/day doses. Maternal lethality was not observed, but intense endometrial inflammatory reactions were encountered in the uterus at the sites of fetal resorption.

In pregnant rabbits administered a single solanine (5 mg/kg; 0.006 mmol/kg/day) dose within the first eight days of gestation, one rabbit that delivered prematurely had 2 normal, living fetuses, 2 dead fetuses with retarded growth, 2 extensively resorbed fetuses, and 4 totally resorbed fetuses (Swinyard and Chaube, 1973). Of the two rabbits carrying pregnancy to the time of necropsy (day 22 of gestation, normally considered as term), the rate of resorption was 18% and no teratogenic effects were observed.

Mixtures of α-Chaconine and α-Solanine

Fetal mortality was 50 and 100% after administration of glycoalkaloids (10 or 20 mg/kg/day [0.01 or 0.02 mmol/kg/day], respectively) to pregnant Wistar rats on days 5 through 12 of gestation (Swinyard and Chaube, 1973). A high incidence of minor abnormalities was observed, but none were neural tube defects. Malformations included mild hydronephrosis, hydroureter, and ribs showing knobby protuberances on the posterior third of their length. The 10 mg/kg/day glycoalkaloid dose was 7 times more toxic than the same dose of solanine.

A combined dose of α-chaconine (10 mg/kg/day; 0.01 mmol/kg/day) and α-solanine (5 mg/kg/day; 0.006 mmol/kg/day) was not lethal to pregnant Wistar rats or their fetuses when administered on days 5 through 12 of gestation (Chaube and Swinyard, 1976). However, nearly 7% of the fetal rats had irregular or fused ribs.

9.2.3 Intravenous Injection

No signs of maternal toxicity were observed with i.v. α-chaconine administration of 1.7 mg/kg/day (0.002 mmol/kg/day) to pregnant Sprague-Dawley rats on days 6 through 13 of gestation (Hellenäs et al., 1992a). There were also no signs of embryotoxicity or teratogenicity.

9.2.4 Injection into the Yolk Sac

α-Chaconine reduced hatchability when injected into chicken eggs (strain not provided) at doses of 1.0 or 1.5 mg/kg (0.0012-0.0018 mmol/kg) before incubation or 12, 20, or 30 mg/kg (0.014, 0.023, or 0.035 mmol/kg) after 96 hours of incubation (Nishie et al., 1975). No change in body weight of hatched chicks was observed and the one incidence of congenital malformation was not statistically significant.

Solanine injection into Foghorn chicken eggs reduced hatchability by 29% when administered at a dose of 25 mg/kg (0.03 mmol/kg) on day 4 of incubation, but doses of 10 or 19 mg/kg (0.01 or 0.02 mmol/kg) had no effect (Nishie et al., 1971). No statistically significant increase in abnormal chicks was observed at any dose. Similarly, a solanine dose of 19 mg/kg (0.022 mmol/kg) after 96 hour of incubation reduced hatchability in chicken eggs (strain not provided), while doses of 0.5-1.5 mg/kg (0.0058-0.017 mmol/kg) had no effect (Nishie et al., 1975). No statistically significant changes in chick body weights or teratogenic effects were observed.

When white Leghorn chicken eggs were injected with solanine at a dose of 1.5 mg/egg (0.0017 mmol/egg), most embryos died (Mun et al., 1975). At doses ranging from 0.015 to 0.26 mg/egg (0.00002-0.0003 mmol/egg), the percent lethality was reduced and the incidence of abnormalities was increased by 15 to 29% of that of the controls. Abnormalities included rumplessness (absence of the tail below the wing bud) and trunklessness (absence of the trunk below the wing bud). Vesicles filled with fluid or blood were also observed in the lower trunk or tail region. The incidence of malformations from administration of glycoalkaloids from potatoes infected with *P. infestans* (0.26 mg/kg; 0.0003 mmol/egg) was in the range of those found with solanine administration and the types of abnormalities were also similar.

When 0.3 mg/egg of solanine or glycoalkaloid extracts (ethanol extract from healthy potatoes or potatoes infected with *P. infestans*) were injected into the amniotic fluid of white Leghorn chicken eggs on day 3 or 4 of incubation, malformations including cranioschisis, celosoma, and cardiac septal defects were induced (Jelínek et al., 1976). In addition to the injections on days 3 and 4 or incubation, subgerminal injections on day 2 of incubation interfered with the caudal morphogenetic system at the somite stages.

9.3 Carcinogenicity

No data were found for α-chaconine, α-solanine, or related alkaloids or hydrolysis products.

9.4 Genotoxicity

These studies are also summarized in **Table 7**.

Table 7. Genotoxicity of α-Chaconine and α-Solanine

Test System	Biological Endpoint	S9 Metabolic Activation	Chemical Form[a], Purity	Dose	Endpoint Response	Comments	Reference
9.4.1 Prokaryotic Systems							
Salmonella typhimurium strains TA98 and TA100	*his* gene mutations	+/-	α-chaconine, purity n.p.	70, 140, 290, 580, 1200, or 2300 µmol/plate	negative in TA98, with metabolic activation, and in TA100, with and without metabolic activation weak positive response in TA98 without S9 when data pooled from duplicate tests was evaluated	2300 µmol/plate was toxic to TA100 without S9. The maximum mutagenic index for TA98 (-S9) was 1.9.	Friedman and Henika (1992)
S. typhimurium strains TA98 and TA100	*his* gene mutations	+/-	α-solanine, pure or an extract from potatoes (lowest dose)	7.5 or 10-50 µg/plate (0.0087 or 0.012-0.058 µmol/plate)	negative	50 µg/plate was toxic to strain TA100 without S9.	Ness et al. (1984)
S. typhimurium strains TA98 and TA100	*his* gene mutations	+/-	α-solanine, purity n.p.	70, 140, 290, 580, 1200, or 2300 µmol/plate	weak positive response in TA100 with S9 in one of two tests, but pooled data from duplicate tests gave a negative response negative in TA100 without S9 and TA98 with and without S9	2300 µmol/plate was toxic to TA100 without S9.	Friedman and Henika (1992)
Escherichia coli strain Q13	Binding of DNA to *E. coli* cells	+/-	d-solanine (presumed misnomer for solanine)	25 or 250 µM	negative	Radiolabeled DNA isolated from *E. coli* was incubated with *E. coli* cells in suspension, with and without metabolic activation and lysozyme, for up to one hour at 37°C. At the end of the treatment period, the cells were pelleted by centrifugation, and the amount of radioactive label	Kubinski et al. (1981)

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: n.p. = not provided

Table 7. Genotoxicity of α-Chaconine and α-Solanine

Test System	Biological Endpoint	S9 Metabolic Activation	Chemical Form[a], Purity	Dose	Endpoint Response	Comments	Reference
						in the cell sediment was determined by scintillation counting.	

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: n.p. = not provided

Table 7. Genotoxicity of α-Chaconine and α-Solanine (continued)

Test System	Biological Endpoint	S9 Metabolic Activation	Chemical Form[a], Purity	Dose	Endpoint Response	Comments	Reference
9.4.2 *In vivo* Mammalian Systems							
female Swiss-Webster mice	Covalent binding to hepatic DNA or RNA	n.p.	α-[^{3}H]chaconine, purity n.p.	10 mg/kg (0.012 mmol/kg) orally	negative	Animals sacrificed at 3, 6, 14, 72, and 120 hours after dosing, and hepatic DNA/RNA were isolated.	Sharma et al. (1983)
weanling male Swiss-Webster mice	micronucleated polychromatic erythrocytes in peripheral blood	n.p.	α-chaconine, purity n.p.	10, 20, or 45 mmol/kg i.p.	negative	Mortality (5/8) within 72 hours was induced at the 45 mmol/kg dose.	Friedman and Henika (1992)
fetuses from timed-pregnant Swiss-Webster mice				5 or 10 mmol/kg i.p. administered on day 15 or 16 of gestation		48-Hour fetal mortality incidences were 2/63 and 12/65 at the 5 and 10 mmol/kg doses, respectively.	
weanling male Swiss-Webster mice			α-solanine, purity n.p.	20, 45, or 90 mmol/kg i.p.		Mortality (2/8) within 72 hours was induced at the 90 mmol/kg dose.	
fetuses from timed-pregnant Swiss-Webster mice				10 or 20 mmol/kg i.p. administered on day 15 or of gestation		Mortality (8/55) within 48 hours was induced at the 20 mmol/kg dose.	

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: n.p. = not provided

9.4.1 Prokaryotic Systems

α-Chaconine was not mutagenic at concentrations of 70-2300 µmol/plate (60-2000 mg/plate) in *Salmonella typhimurium* strains TA98, with metabolic activation, or in TA100, with and without metabolic activation (Friedman and Henika, 1992). A weakly mutagenic response was reported for strain TA98 without S9 based on the evaluation of data pooled from duplicate tests. The maximum mutagenic index was 1.9.

When tested at concentrations ranging from 7.5 to 50 µg/plate (0.0087-0.058 µmol/plate) (Ness et al., 1984) or at concentrations ranging from 70 to 2300 µmol/plate (61-2000 mg/plate) (Friedman and Henika, 1992), α-solanine was not mutagenic in *S. typhimurium* strains TA98 and TA100, with or without metabolic activation.

In the DNA-Cell-Binding assay, d-solanine (presumed misnomer for solanine) at 25 or 250 µM, did not increase the binding of ^{32}P-DNA to *Escherichia coli* Q13 cells (Kubinski et al., 1981). In this assay, radiolabeled DNA isolated from *E. coli* was incubated with *E. coli* cells in suspension, with and without metabolic activation and lysozyme, for up to one hour at 37°C. At the end of the treatment period, the cells were pelleted by centrifugation, and the amount of radioactive label in the cell sediment was determined by scintillation counting.

9.4.2 *In vivo* Mammalian Systems

α-[^{3}H]Chaconine, administered orally at 10 mg/kg (0.012 mmol/kg) to female Swiss-Webster mice, did not covalently bind to DNA or RNA isolated from the livers of mice sacrificed at 3, 6, 14, 72, and 120 hours after dosing (Sharma et al., 1983).

In a micronucleus tests using blood from both weanling mice and in utero-treated fetuses, α-chaconine and α-solanine were negative for the induction of micronucleated polychromatic erythrocytes (Friedman and Henika, 1992). α-Chaconine was administered i.p. to weanling male Swiss-Webster mice and pregnant female Swiss-Webster mice (on day 15 or 16 of gestation) at concentrations of 10 to 45 and 5 to 10 mmol/kg, respectively; α-solanine was administered at concentrations of 20 to 90 and 10 to 20 mmol/kg, respectively.

9.5 Immunotoxicity

This study is also summarized in **Table 8**.

Potato plants containing 0.06% glycoalkaloids induced dermatitis in Indian buffaloes when the plants were consumed in the diet (Somvanshi et al., 1992). Lesions were induced most frequently on the legs and teats and less frequently on the hindquarters and base of the tail. The skin was thickened, edematous, cracked, and dried. Teats were red, raw, and ulcerated on the surface. The buffaloes were lame in advanced cases.

9.6 Anti-immunotoxicity

These studies are also summarized in **Table 9**.

Table 8. Immunotoxicity of α-Chaconine and α-Solanine

Test System or Species, Strain, and Age of Animal	Chemical Form[a], Purity	Dose	Endpoint Response	Comments	Reference
Buffalo (Indian, age n.p.)	potato plants containing 0.06% glycoalkaloids	dose n.p.; eaten as a part of the diet	12/16 buffaloes were affected by potato plant-induced dermatitis.	Lesions were induced most frequently on the legs and teats and less frequently on the hindquarters and the base of the tail. The skin was thickened, edematous, cracked and dried. Teats were red and had a raw, ulcerated surface. In advanced cases, the buffaloes were lame and tried to lick leg lesions.	Somvanshi et al. (1992)

Table 9. Anti-Immunotoxicity of α-Solanine

Test System or Species, Strain, and Age of Animal	Chemical Form[a], Purity	Dose	Endpoint Response	Comments	Reference
Guinea pig (strain and age n.p.)	solanine hydrochloride, purity n.p.	25 mg/kg (0.028 mmol/kg) i.v., t.d.s., every other day (length of exposure n.p.)	Provided antitoxic immunity to lethal doses (40 mg/kg) of solanine hydrochloride.		Golubeva et al. (1977)
	solanine hydrochloride, purity n.p.	0.1 mg/kg (0.00011 mmol/kg) i.v. 48-72 hours before horse serum injection	Inhibited sensitivity to horse serum; desensitizing confirmed by leukocytolytic reaction indexes.	Solanine hydrochloride acts as both a desensitizing and an immunogenic factor in the antiallergic effect mechanism.	

[a]The chemical form is given as the original author(s) presented it.

Abbreviations: i.v. = intravenous injection; n.p. = not provided; t.d.s. = three times daily

When solanine hydrochloride was administered i.v. to guinea pigs (sex and strain not provided) at doses of 25 mg/kg (0.028 mmol/kg) three times daily every other day (length of exposure not provided), the dose provided antitoxic immunity to lethal doses of solanine hydrochloride (40 mg/kg; 0.044 mmol/kg) (Golubeva et al., 1977).

Similarly, a 0.1 mg/kg (0.0001 mmol/kg) dose of solanine hydrochloride administered i.v. 48 to 72 hours before horse serum injection inhibited the sensitivity of guinea pigs (sex and strain not provided) to the horse serum (Golubeva, 1977). The desensitizing was confirmed by leukocytolytic reaction indexes. The author stated that solanine hydrochloride acts as both a desensitizing and an immunogenic factor in the antiallergic effect mechanism.

9.7 Other Data

9.7.1 Anticholinergic Activity

In thoracic superficial muscle isolated from the grass frog, solanine did not impede synaptic transmissions *in vitro*, but it reduced the number of acetylcholine molecules in the muscle portions (Khashayev and Troshko, 1981).

9.7.2 *In Vitro* Studies of Anticholinesterase Activity

The glycoalkaloid poisoning symptoms associated with the central nervous system, such as rapid and weak pulse, rapid and shallow breathing, delirium, and coma are caused by inhibition of cholinesterase activity (Friedman and McDonald, 1997).

α-Chaconine inhibited purified bovine erythrocyte acetylcholinesterase and horse serum cholinesterase *in vitro* (Alozie, 1978). At a concentration of 16,000 μM, α-chaconine inhibited subcellular acetylcholinesterase activity in nuclear-free rat brain homogenate as follows: whole homogenate, 43%; nuclear fraction, 55%; mitochondria 35%; and microsomes, 33%.

α-Chaconine (33.8 μM) and α-solanine (33.4 μM) inhibited the activity of freeze-dried buffered eel cholinesterase *in vitro* by 26.8 and 26.3%, respectively (Bushway et al., 1987).

Using acetylcholinesterase from human and bovine erythrocytes, α-chaconine and α-solanine were equally effective inhibitors *in vitro*, with concentrations of 100 µM causing 85% inhibition of human and bovine enzymes (Roddick, 1989).

An *in vitro* study revealed that α-chaconine caused 41.2% inhibition of human cholinesterase (Duan, 1994; cited by Friedman and McDonald, 1997). Under similar conditions, α-solanine caused 52.1% inhibition.

At concentrations of 2.88 µM, α-chaconine and α-solanine inhibited human plasma butyrylcholinesterase by 70 and 50%, respectively (Nigg et al., 1996). When a concentration of 10 µM α-chaconine or α-solanine was incubated with human serum or plasma, butyrylcholinesterase inhibition was reversible.

α-Chaconine and α-solanine inhibited human pseudocholinesterase activity when the glycoalkaloid levels matched those expected after eating a potato meal (Nigg, 1997). The inhibition was reversible.

9.7.3 Antiviral Activity

α-Chaconine (0.1 and 0.01% w/v) inactivated Herpes simplex virus Type I *in vitro* (Thorne et al., 1985). The inactivation of the virus resulted from the insertion of the glycones into the viral envelope via cell membrane disruption.

9.7.4 Cell Membrane Disruption *In Vitro*

The glycoalkaloid poisoning symptoms such as burning sensation in the mouth, nausea, vomiting, abdominal cramps, diarrhea, internal hemorrhaging, fluid build-up, and production of stomach lesions are attributed to cell membrane disruption (Friedman and McDonald, 1997).

α-Chaconine caused lysis of liposomes, erythrocytes, beet cells, and protoplasts, but similar levels of α-solanine had little effect (Roddick and Drysdale, 1984; Roddick and Rijnenberg, 1986; Roddick et al., 1992; all cited by Friedman and McDonald, 1997; Roddick and Rijnenberg, 1987; Roddick et al., 1988). A 1:1 α-chaconine:α-solanine mixture produced pronounced synergistic effects (Roddick and Rijnenberg, 1987; Roddick et al., 1988).

α-Solanine, when added to everted intestine duodenum sacs of Wistar albino rats *in vitro*, noncompetitively inhibited active calcium transport (Michalska et al., 1985).

At a concentration of 4000 µM, α-chaconine and α-solanine significantly reduced the transmural potential difference in the mucosa of the Wistar rat small intestine, *in vitro* (Gee et al., 1989).

α-Chaconine rapidly and markedly increased the membrane potential (i.e. the integrity of the membranes) in frog embryos *in vitro* (Blankemeyer et al., 1992). α-Solanine similarly increased the membrane potential, but to a lesser extent. Increases in membrane potential by α-chaconine and α-solanine were 1600% and 400%, respectively, compared to that of the control. In a subsequent experiment, Blankemeyer and Friedman (1997) found that the membrane potential depolarization could be reversed by folic acid.

In an *in vitro* test of effects on membranes composed of egg yolk phosphatidylcholine with or without sterols present as a component, α-chaconine and α-solanine were found to interact strongly with sterol-containing membranes (Keukens et al., 1992). A transient disruption of the bilayer, allowing for cell leakage, results from a rearrangement of the membrane by the formation of a network of sterol-glycoalkaloid complexes. α-Chaconine was more potent in cell disruption than α-solanine.

α-Chaconine and α-solanine, at concentrations 10 µg/mL (12 µM), decreased the transepithelial active transport of sodium in frog skin cells *in vitro* by 30 and 16%, respectively (Blankemeyer et al., 1995).

In vitro, α-chaconine and α-solanine rapidly induced complete hemolysis in human erythrocytes with cell membranes that contained approximately 50% cholesterol (Keukens et al., 1996). Both compounds caused 6-carboxyfluorescein (CF) leakage in CF-loaded right side out resealed erythrocyte ghosts. α-Chaconine was more potent than α-solanine in causing hemolysis and leakage. α-Chaconine also selectively decreased gap-junctional intercellular communication in Caco-2 cells.

Following exposure to α-chaconine plus α-solanine, rat and human intestinal mucosal epithelial cells exhibited a change in membrane integrity *in vitro* (Gee et al., 1996). One change

noted was leakage of the enzyme lactate dehyrogenase. A synergistic effect between the two glycoalkaloids was observed.

An equimolar mixture of α-chaconine and α-solanine induced lysis of human, rat, and hamster blood cells *in vitro* (Phillips et al., 1996). Concentrations causing 50% lysis in the three cell types were 12.5, 13.5, and 12.0 µg/mL (14, 16, and 14 µM), respectively.

9.7.5 Cholinergic Activity

When varying doses of solanine were tested for effects on the amplitude of contractions in isolated guinea pig ileum strips, concentrations of 50 and 100 µg/mL (58 and 115 µM) were comparable in effect to concentrations of 0.005 and 0.01 µg/mL (0.003 and 0.07 µM) acetylcholine, respectively (Nishie et al., 1971). In a later study, α-chaconine and α-solanine were found to be 570 and 520 times weaker, respectively, than acetylcholine in their ability to induce contractions in strips of isolated guinea pig ileum (Nishie et al., 1975).

9.7.6 Cytotoxicity

α-Chaconine and α-solanine were cytotoxic to Chinese hamster ovary cells *in vitro*; concentrations causing 50% inhibition of cell growth were estimated as 3.55 µg/mL (4.1 µM) and 13.8 µg/mL (16 µM), respectively (Phillips et al., 1996). Cells were damaged within 2 to 3 minutes of exposure to concentrations ranging from 2.5 µg/mL to 20 µg/mL (3-23 µM). Additionally, a mixture of the two glycoalkaloids was more cytotoxic than either compound alone, suggesting a synergistic action.

9.7.7 Effect on Cardiac Activity

At the concentrations tested, α-chaconine (10 µg/mL [12 µM]) and α-solanine (7 and 10 µg/mL [8 and 12 µM]) induced positive inotropic effects on electrically stimulated isolated frog ventricle (Nishie et al., 1971; 1975). Effects of the two glycoalkaloids were essentially the same (Nishie et al., 1975; 1976).

Addition of 80 µg/mL (92 µM) α-solanine to beating heart cell cultures from Zucker rats caused cessation of beating within a few minutes (Bergers and Alink, 1980). At a concentration of 40 µg/mL (46 µM), α-solanine caused a pronounced positive chronotropic effect, which lasted for at least 2 hours.

9.7.8 Effects on the Mitotic Cell Cycle

α-Solanine, at concentrations of 4.1 to 33.3 µg/mL (4.7-38.4 µM), stimulated the growth of cultured human fibroblasts by shortening the G_1 cell cycle phase (Kirk and Mittwoch, 1975). In contrast, α-solanine at 66.6 µg/mL (76.7 µM) markedly inhibited fibroblast cell growth, and an abnormal accumulation of cells in the G_2 phase was observed.

9.7.9 Effect on Ornithine Decarboxylase Activity

Administration of 7.5, 15, and 30 mg/kg (0.0086, 0.017, and 0.35 mmol/kg) α-solanine by i.p. injection to Sprague Dawley rats caused a dose-dependent increase in ornithine decarboxylase (ODC) activity 4 hours after treatment (Caldwell et al., 1991). At a dose of 17 mM/kg, α-chaconine induced higher levels of ODC activity than α-solanine.

9.7.10 Glycemic Effects

Solanine injected i.p. exhibited hyperglycemic activity in intact Wistar rats and hypoglycemic activity in adrenalectomized rats (Satoh, 1967). It was hypothesized that the hyperglycemic effect was mediated through stimulation of the adrenals.

10.0 STRUCTURE-ACTIVITY RELATIONSHIPS

10.1 Alkaloid Moiety Relationships

The cardiotonic activity of the glycoalkaloids on isolated frog heart is determined by the nature of the aglycone and the number of sugars, but not by the kinds of sugars or their stereochemical configuration (Nishie et al., 1976). The cardiotonic potencies of Solanaceae

glycoalkaloids containing solanidine or dihydrosolanidine are as follows: α-chaconine = α-solanine > demissine = commersonine > β-chaconine > solanidine.

The teratogenic activity of solanidine [(22*S*,25*R*)-solanid-5en-3β-ol] was comparable to that of highly teratogenic jervine alkaloids (Brown and Keeler, 1978). The investigators concluded that the teratogenic activity resulted from the unhindered nitrogen nonbonding electron pair, which was accessible to the α steroid face. Synthetic solanidine epimers [(22*S*, 25*S*)-5α-solanidan-3β-ol and (22*R*, 25*S*) -5α-solanidan-3β-ol] were not teratogenic, but did increase resorption.

Gaffield and Keeler (1993) found that hamster teratogenicity may be closely related to the presence or absence of the 5-6 double bond on the steroidal alkaloid and that this double bond may be more important than the molecular configuration at C-22 and the placement of the nitrogen atom in regard to the plane of the steroid.

10.2 Sugar Moiety Relationships

The biological activity of the glycoalkaloids is influenced by both the nature and the number of sugars composing the carbohydrate moiety attached to the 3-OH position of the aglycone (Rayburn et al., 1994; Friedman and McDonald, 1997), and the stereochemical orientation of the chaconine diglycosides (Rayburn et al., 1994). Embryotoxicity generally decreased with stepwise removal of sugar units from the chacotriose and solatriose side chains (Rayburn et al., 1994; Friedman and McDonald, 1997).

Based on a similar incidence of teratogenicity for α-chaconine and α-solanine, the authors stated that the oligosaccharide is not required to facilitate passage of a teratogen to the fetus (Gaffield et al., 1992). In contrast to the glycoalkaloids, solanidine was not toxic to hamsters, which indicated that the lytic activity provided by the carbohydrate is necessary for lesion formation.

Sterol-mediated glycoalkaloid-induced cell membrane disruption is specific for the type of glycoalkaloid and sterol (Keukens et al., 1992). The order of potency of the glycoalkaloids was α-tomatine > α-chaconine > α-solanine. In another experiment using model systems to monitor

cell membrane disruption, sugar-sugar interactions were evident by the highly synergistic effect between α-chaconine and α-solanine, the leaking enhancement effect of the glycolipids, and the almost complete loss of activity after deleting one or more monosaccharides from the glycoalkaloids (Keukens et al., 1995).

11.0 ONLINE DATABASES AND SECONDARY REFERENCES

11.1 Online Databases

Chemical Information System Files

SANSS
TSCATS (Toxic Substances Control Act Test Submissions)
DIALOG Files

FRIP (Federal Research in Progress)
Kirk-Othmer Encyclopedia of Chem. Technol.

National Library of Medicine Databases

DART
EMIC and EMICBACK (Environmental Mutagen Information Center)

STN International Files

BIOSIS
CANCERLIT
CAPLUS
CHEMLIST
EMBASE
HSDB
MEDLINE
REGISTRY
RTECS
TOXLINE

TOXLINE includes the following subfiles:

Toxicity Bibliography	TOXBIB
International Labor Office	CIS
Hazardous Materials Technical Center	HMTC
Environmental Mutagen Information Center File	EMIC
Environmental Teratology Information Center File (continued after 1989 by DART)	ETIC
Toxicology Document and Data Depository	NTIS
Toxicological Research Projects	CRISP
NIOSHTIC7	NIOSH
Pesticides Abstracts	PESTAB
Poisonous Plants Bibliography	PPBIB
Aneuploidy	ANEUPL
Epidemiology Information System	EPIDEM
Toxic Substances Control Act Test Submissions	TSCATS
Toxicological Aspects of Environmental Health	BIOSIS
International Pharmaceutical Abstracts	IPA
Federal Research in Progress	FEDRIP
Developmental and Reproductive Toxicology	DART

Databases Available on the Internet

Phytochemeco Database (Agricultural Research Service)

In-House Databases

Current Contents on Diskette
The Merck Index, 1996, 12th ed., on CD-ROM

11.2 Secondary References

The Merck Index, 12th ed., Budavari, S. Ed. Merck & Co., Inc., Whitehall, NJ. Listed in Section 12 as Budavari (1996).

12.0 REFERENCES[a]

21 CFR 250.12. Special requirements for specific human drugs. Subpart A, drugs regarded as misbranded.

Achterberg, C. L., D. M. Clauson, J. A. Blease, and E. S. Barden. 1979. [Title not provided]. Am. Potato J. 56:145. (Cited by Jadhav et al., 1981).

Ahmed, S. S. and K. Müller. 1978. [Title not provided]. Lebensm. Wiss. Technol. 11:144. (Cited by Jadhav et al., 1981).

Aldous, C. N., R. P. Sharma, and D. K. Salunkhe. 1980. Effects of alpha-chaconine on brain biogenic amines, electroencephalogram, cardiac rates, and respiratory response in rats. J. Food. Saf. 2(1):20-33.

Alfa, J. and E. Heyl. 1923. Potatoes of the 1922 harvest with an unusually high solanine content. Z. Nahr. Genussm. 46:306-309. (Cited by Beier, 1990).

Allen, E. H. and J. Kúc. 1968. α-Solanine and α-chaconine as fungitoxic compounds in extracts of Irish potato tubers. Phytopathology 58:776-781. (Cited by Matthew et al., 1983, and Beier, 1990).

Alozie, S. O. 1978. Toxicological and biochemical investigations of alpha-chaconine in potato (Solanum tuberosum L.) tubers: Physiologic disposition and tissue binding, and inhibition of tissue cholinesterases and isoenzymes. Diss. Abstr. Int. B 38(12, pt. 1):5854.

Alozie, S. O., R. P. Sharma, and D. K. Salunkhe. 1978. Inhibition of rat cholinesterase isoenzymes *in vitro* and *in vivo* by the potato alkaloid, α-chaconine. J. Food Biochem. 2:259-276. (Cited by JECFA, 1993).

Alozie, S. O., R. P. Sharma, and D. K. Salunkhe. 1979a. Excretion of α-chaconine-^{3}H, a steroidal glycoalkaloid from Solanum tuberosum L. and its metabolites in hamsters. Pharmacol. Res. Commun. 11(6):483-490.

Alozie, S. O., R. P. Sharma, and D. K. Salunkhe. 1979b. Physiological disposition, subcellular distribution, and tissue binding of α-chaconine (^{3}H). J. Food Saf. 1(4):257-273.

Anonymous. 1984. Solanine food poisoning associated with a school lunch program—Alberta. Canada Diseases Weekly Report, Health and Welfare Canada 10-18:71. (Cited by Hopkins, 1995).

Azim, A., H. A. Shaikh, and R. Ahmad. 1983. Toxic effects of high glycoalkaloid feeding on the protein digestibility and growth of rabbits. J. Pharm. Univ. Karachi 2:15-24. (Cited by JECFA, 1993).

Azim, A., H. A. Shaikh, and R. Ahmad. 1984. Toxic effects of high glycoalkaloid feeding on the red blood cell counts and haemoglobin concentration of rabbit blood. J. Pharm. Univ. Karachi 3:43-49. (Cited by JECFA, 1993).

[a]Sources cited by other authors are listed as completely as possible using the information provided. Inclusive page numbers are not always provided for these sources.

Baker, D., R. Keeler, and W. Gaffield. 1987. Lesions of potato sprout and extracted potato sprout alkaloid toxicity in Syrian hamsters. Clin. Toxicol. 25(3):199-208.

Baker, D. C., R. F. Keeler, and W. P. Gaffield. 1988. Mechanism of death in Syrian hamsters gavaged potato sprout material. Toxicol. Pathol. 16(3):333-339.

Beckstrom-Sternberg, S.M. and J. A. Duke. 1997. Plants containing α-chaconine and α-solanine. Phytochemeco Database produced by USDA Agricultural Research Service, Internet URL: http://sun.ars-grin.gov/cgi-bin/duke/ethnobot.pl.

Beier, R. C. 1990. Natural pesticides and bioactive components in foods. Rev. Environ. Contam. Toxicol. 113:47-137.

Bell, D. P., J. G. Gibson, A. M. McCarroll, and G. A. McClean. 1976. Embryotoxicity of solanine and aspirin in mice. J. Reprod. Fert. 46:257-259.

Benito, E. et al. [other authors not provided]. 1990. [Title not provided]. Int. J. Cancer 45:69. (Cited by Hopkins, 1995).

Benito, E. et al. [other authors not provided]. 1993. [Title not provided]. Int. J. Cancer 55:213. (Cited by Hopkins, 1995).

Bentley, M. D., D. E. Leonard, and R. J. Bushway. 1984. Solanum alkaloids as larval feeding deterrents for spruce budworm *Choristoneura-fumiferana* Lepidoptera Tortricidae. Ann. Entomol. Soc. Am. 77(4):401-403.

Bergers, W. W. A. and G. M. Alink. 1980. Toxic effect of the glycoalkaloids solanine and tomatine on cultured neonatal rat heart cells. Toxicol. Lett. 6:29-32.

Bidoli, E. et al. [other authors not provided]. 1992. [Title not provided]. Int. J. Cancer 50:223. (Cited by Hopkins, 1995).

Blankemeyer, J. T. and M. Friedman. 1997. A novel role for folic acid: Amelioration of the lethal effect of plant glycoalkaloids on embryos and correlation of amelioration with membrane potential. FASEB J. 11(3):A179. Abstr.

Blankemeyer, J. T., B. K. Stringer, J. R. Rayburn, J. A. Bantle, and M. Friedman. 1992. Effect of potato glycoalkaloids, α-chaconine and α-solanine, on membrane potential of frog embryos. J. Agric. Food Chem. 40:2022-2025.

Blankemeyer, J. T., R. Atherton, and M. Friedman. 1995. Effect of potato glycoalkaloids α-chaconine and α-solanine on sodium active transport in frog skin. J. Agric. Food Chem. 43:636-639.

Boeing, H. et al. [other authors not provided]. 1993. [Title not provided]. Int. J. Cancer 53:561. (Cited by Hopkins, 1995).

Boll, P. M. 1962. [Title not provided]. Acta Chem. Scand. 16:1819. (Cited by Jadhav et al., 1981).

Bomer, A. and H. Mattis. 1924. *Der Solaningehalt der Kartoffeln*. [Solanine content of potatoes.] Z. Unters. Nahr. Genussm. Gebrauchsgegenstände 47:97. (Cited by Maga, 1980).

Brain, K. R. and T. D. Turner. 1971. Toxic fruits in frozen peas. J. Assoc. Public Anal. 9:100-101. (Cited by Morris and Lee, 1984).

Brebion, G., R. Cabridenc, and B. Huriet. 1967. Effect of seasonal effluent supply from the agricultural industry on the operation of sewage purification plants. Eau 54(3):107-116. Abstract from CAPLUS 1967:457081.

Brown, D. and R. F. Keeler. 1978. Structure-activity relation of steroid teratogens. 3. Solanidan epimers. J. Agric. Food Chem. 26(3):566-569.

Brown, L. M. et al. [other authors not provided]. 1988. [Title not provided]. J. Natl. Cancer Inst. 80:1620. (Cited by Hopkins, 1995).

Budavari, S. Ed. 1989. Solanine Hydrochloride. In: The Merck Index. 11th ed., Merck & Co., Inc., Whitehall, NJ.

Budavari, S. Ed. 1996. Solanine. In: The Merck Index. 12th ed., Merck & Co., Inc., Whitehall, NJ.

Bushway, R. J. and R. Ponnampalam. 1981. α-Chaconine and α-solanine content of potato products and their stability during several modes of cooking. J. Agric. Food Chem. 29(4):814-817.

Bushway, A. A., A. W. Bushway, P. R. Belyea, and R. J. Bushway. 1980a. The proximate composition and glycoalkaloid content of three potato meals. Am. Potato J. 57(4):167-171.

Bushway, R. J., E. S. Barden, A. W. Bushway, and A. A. Bushway. 1980b. [Title not provided]. Am. Potato J. 57:175. (Cited by Jadhav et al., 1981).

Bushway, R. J., J. L. Bureau, and D. F. McGann. 1983. alpha-Chaconine and alpha-solanine content of potato peels and potato peel products. J. Food Sci. 48(1):84-86.

Bushway, R. J., D. F. McGann, and A. A. Bushway. 1984. Gas chromatographic method for the determination of solanidine and its application to a study of feed-milk transfer in the cow. J. Agric. Food Chem. 32:548-551.

Bushway, A. A., J. L. Bureau, D. Bergeron, M. R. Stickney, and R. J. Bushway. 1985. The nutrient and glycoalkaloid content of a new potato meal. Am. Potato J. 62(6):301-306.

Bushway, R. J., S. A. Savage, and B. S. Ferguson. 1987. Inhibition of acetyl cholinesterase by solanaceous glycoalkaloids and alkaloids. Am. Potato J. 64(8):409-414.

Cadle, L. S., D. A. Stelzig, K. L. Harper, and R. J. Young. 1978. [Title not provided]. J. Agric. Food Chem. 26:1453. (Cited by Jadhav et al., 1981).

Caldwell, K. A., O. K. Grosjean, P. R. Henika, and M. Friedman. 1991. Hepatic ornithine decarboxylase induction by potato glycoalkaloids in rats. Food Chem. Toxicol. 29(8):531-535.

Ceha, L. J., C. Presperin, E. Young, M. Allswede, and T. Erickson. 1997. Anticholinergic toxicity from nightshade berry poisoning responsive to physostigmine. J. Emergency Med. 15(1):65-69.

Centonze, S. et al. [other authors not provided]. 1994. [Title not provided]. Nutr. Cancer 21:233. (Cited by Hopkins, 1995).

Chaube, S. and C. A. Swinyard. 1976. Teratological and toxicological studies of alkaloidal and phenolic compounds from *Solanum Tuberosum L*. Toxicol. Appl. Pharmacol. 36:227-237.

CHEMCATS (Chemical Catalogs Online) [database online]. 1995. Chemical Abstracts Service; 1998 [production date 1995 Jul 28]. Suppliers of chaconine, solanine, and solanidine; Accession Nos. 96:132328, 96:70305, and 97:37786. Available from: STN International.

Dalvi, R. R. 1985. Comparative assessment of the effect of solanine administered orally and intraperitoneally on hepatic dysfunction in male rats. Nippon Juigaku Zasshi [Japanese Journal of Veterinary Science] 47(4):657-659.

Dalvi, R. R. and W. C. Bowie. 1983. Toxicology of solanine: An overview. Vet. Hum. Toxicol. 25(1):13-15.

Dalvi, R. R. and A. Peeples. 1981. In vivo effect of toxic alkaloids on drug metabolism. J. Pharm. Pharmacol. 33:51-53.

Demirer, T. et al. [other authors not provided]. 1990. [Title not provided]. Cancer 65:2344. (Cited by Hopkins, 1995).

Dorland's Illustrated Medical Dictionary. 1994. 28th ed. W. B. Saunders Co., Philadelphia.

Duan, G. M. 1994. Inhibition of potato glycoalkaloids to human blood cholinesterase. Chin. Biochem. J. 10:575-578. (Cited by Friedman and McDonald, 1997).

Elwood, J. M. 1976. Anencephalus, spina bifida, and potato blight in Canada. Can. J. Public Health 67:122-126.

Famighetti, R. Ed. 1995. Grain, hay, potato, cotton, soybean, tobacco production, by state, 1994. In: The World Almanac and Book of Facts: 1996. Funk and Wagnalls Corp., Mahwah, NJ. p. 141.

Fitzpatrick, T. J., S. F. Herb, S. F. Osman, and J. A. McDermott. 1977. [Title not provided]. Am. Potato J. 54:539. (Cited by Jadhav et al., 1981).

Fitzpatrick, T. J., J. D. Mackenzie, and P. Gregory. 1978. [Title not provided]. Am. Potato J. 55:247. (Cited by Jadhav et al., 1981).

Franceschi, S. et al. [other authors not provided]. 1989. [Title not provided]. Int. J. Epidemiol. 18:578. (Cited by Hopkins, 1995).

Friedman, M. 1992. Composition and safety evaluation of potato berries, potato and tomato seeds, potatoes, and potato alkaloids. In: M. J. Comstock (Ed.) Food Safety Assessment, ACS Symposium Series 484. pp. 429-462.

Friedman, M. and L. Dao. 1992. Distribution of glycoalkaloids in potato plants and commercial potato products. J. Agric. Food Chem. 40:419-423.

Friedman, M. and P. R. Henika. 1992. Absence of genotoxicity of potato alkaloids α-chaconine, α-solanine and solanidine in the Ames Salmonella and adult and foetal erythrocyte micronucleus assays. Food Chem. Toxicol. 30(8):689-694.

Friedman, M. and G. M. McDonald. 1997. Potato glycoalkaloids: Chemistry, analysis, safety, and plant physiology. Crit. Rev. Plant Sci. 16(1):55-132.

Friedman, M., P. R. Henika, and B. E. Mackey. 1996. Feeding of potato, tomato and eggplant alkaloids affects food consumption and body and liver weights in mice. J. Nutr. 126(4):989-999.

Gaffield, W. and R. F. Keeler. 1993. Implication of C-5, C-6 unsaturation as a key structural factor in steroidal alkaloid-induced mammalian teratogenesis. Experientia 49(10):922-924.

Gaffield, W. and R. F. Keeler. 1996. Induction of terata in hamsters by solanidane alkaloids derived from *Solanum tuberosum*. Chem. Res. Toxicol. 9:426-433.

Gaffield, W., R. R. Keeler, D. C. Baker, and A. E. Stafford. 1992. Studies on the *Solanum tuberosum* sprout teratogen. In: L. F. James, T. L. Wierenga, B. J. Sigler, and J. A. Johnson (Eds.), Poisonous Plants: Proceedings of the Third International Symposium. 1st ed. Iowa State University Press, IA. pp. 418-422.

Gee, J. M., K. R. Price, C. L. Ridout, I. T. Johnson, and G. R. Fenwick. 1989. Effects of some purified saponins on transmural potential difference in mammalian small intestine. Toxicol. *in Vitro* 3(2):85-90.

Gee, J. M., G. M. Wortley, I. T. Johnson, K. R. Price, A. A. J. J. L. Rutten, G. F. Houben, and A. H. Penninks. 1996. Effects of saponins and glycoalkaloids on the permeability and viability of mammalian intestinal cells and on the integrity of tissue preparations *in vitro*. Toxicol. *in Vitro* 10(2):117-128.

Golubeva, S. N., V. B. Bureva, and L. M. Andronova. 1977. Effect of solanine hydrochloride on sensitization of guinea pigs under experimental conditions. Zh. Ushn., Nos. Gorl. Bolezn. 4:64-68. CAPLUS Abstract No. 88:424.

Gonmori, K., H. Meguro, Y.-Q. Lu, N. Yoshioka, K. Hori, and S. Kikkawa. 1993. The risk of solanine poisoning in a folk remedy and solanine production in potato. Res. Pract. Forensic Med. 36:91-95.

Gonzalez, T. A., M. Vance, and C. J. Umberger. 1954. Legal Medicine Pathology and Toxicology. Appleton-Century-Crofts, New York. p. 868. (Cited by Maga, 1980).

Gosselin, R. E., H. C. Hodge, R. P. Smith, and M. N. Gleason. 1976. Section 730, Solanine. In: Clinical Toxicology of Commercial Products, 4th ed. Baltimore, Williams and Wilkins. pp. 163-164.

Graham, S. et al. [other authors not provided]. 1972. [Title not provided]. Cancer 30:927. (Cited by Hopkins, 1995).

Griebel, C. 1924. *Zum Solaningehalt der Kartoffeln 1922-Er Ernte*. [Solanine content of potatoes of the 1922 crop.] Z. Nahr. Genussm. Gebrauchsgegenstände 47:436-438. (Cited by Maga, 1980 and Beier, 1990).

Groen, K., D. P. K. H. Pereboom-de Fauw, P. Besamusca, P. K. Beekhof, G. J. A. Speijers, and H. J. G. M. Derks. 1993. Bioavailability and disposition of ^{3}H-solanine in rat and hamster. Xenobiotica 23(9):995-1005.

Gull, D. D., F. M. Isenberg, and H. H. Bryan. 1970. Alkaloid toxicology of *Solanum tuberosum*. Hortic. Sci. 5:316. (Cited by Maga, 1980).

Hansen, A. A. 1925. [Title not provided]. Science 61:340. (Cited by Jadhav et al., 1981).

Hansen, A. A. 1928. Potato poisoning. North Am. Vet. 9(7):31-34.

Hansson, L.-E. et al. [other authors not provided]. 1993. [Title not provided]. Int. J. Cancer 55:181. (Cited by Hopkins, 1995).

Harris, F. W. and T. Cockburn. 1918. Alleged poisoning by potatoes. Am. J. Pharm. 90:722-726.

Harvey, M. H., M. McMillan, M. R. A. Morgan, and H. W.-S. Chan. 1985a. Solanidine is present in sera of healthy individuals and in amounts dependent on their dietary potato consumption. Hum. Toxicol. 4:187-194.

Harvey, M. H, B. A. Morris, M. McMillan, and V. Marks. 1985b. Measurement of potato steroidal alkaloids in human serum and saliva by radioimmunoassay. Hum. Toxicol. 4:503-512. (Cited by JECFA, 1993).

Harvey, M. H., B. A. Morris, M. McMillan, and V. Marks. 1986. Potato steroidal alkaloids and neural tube defects: Serum concentrations fail to demonstrate a causal relation. Hum. Toxicol. 5:249-253.

Hellenäs, K.-E., E. Cekan, P. Slanina, and K. Bergmann. 1992a. Studies of embryotoxicity and the incidence of external malformations after continuous intravenous infusion of α-chaconine in pregnant rats. Pharmacol. Toxicol. 70:381-383.

Hellenäs, K.-E., A. Nyman, P. Slanina, L. Lööf, and J. Gabrielsson. 1992b. Determination of potato glycoalkaloids and their aglycone in blood serum by high-performance liquid chromatography: Application to pharmacokinetic studies in humans. J. Chromatogr. 573:69-78.

Hopkins, J. 1995. The glycoalkaloids: Naturally of interest (but a hot potato?). Food Chem. Toxicol. 33(4):323-339.

Hoskins, F. H. Ed. 1994. Food toxicants, naturally occurring. In: Kirk-Othmer Encyclopedia of Chemical Technology, 4th ed., Vol. 11. John Wiley and Sons, New York. pp. 897-916.

Hu, J. et al. [other authors not provided]. 1988. [Title not provided]. Int. J. Cancer 41:331. (Cited by Hopkins, 1995).

Iscovich, J. M. et al. [other authors not provided]. 1989. [Title not provided]. Int. J. Cancer 44:770. (Cited by Hopkins, 1995).

Iscovich, J. M. et al. [other authors not provided]. 1992. [Title not provided]. Int. J. Cancer 51:851. (Cited by Hopkins, 1995).

Jadhav, S. J. and D. K. Salunkhe. 1975. Formation and control of chlorophyll and glycoalkaloids in tubers of *Solanum tuberosum* L. and evaluation of glycoalkaloid toxicity. Adv. Food Res. 21:307. (Cited by Maga, 1980).

Jadhav, S. J., R. P. Sharma, and D. K. Salunkhe. 1981. Naturally occurring toxic alkaloids in foods. Crit. Rev. Toxicol. 9(1):21-104.

JECFA (Joint FAO/WHO Expert Committee on Food Additives). 1993. Toxicological evaluation of certain food additives and naturally occurring toxicants. WHO Food Additives Series, Vol. 30. World Health Organization, Geneva.

Jelínek, R., V. Kyzlink, and C. Blattny, Jr. 1976. An evaluation of the embryotoxic effects of blighted potatoes on chicken embryos. Teratology 14(3):335-342.

Keeler, R. F., S. Young, D. Brown, G. F. Stallknecht, and D. Douglas. 1978. Congenital deformities produced in hamsters by potato sprouts. Teratology 17:327-334.

Keukens, E. A. J., T. de Vrije, C. H. J. P. Fabrie, R. A. Demel, W. M. F. Jongen, and B. de Kruijff. 1992. Dual specificity of sterol-mediated glycoalkaloid induced membrane disruption. Biochim. Biophys. Acta 1110:127-136.

Keukens, E. A. J., T. de Vrije, C. van den Boom, P. de Waard, H. H. Plasman, F. Thiel, V. Chupin, W. M. F. Jongen, and B. de Kruijff. 1995. Molecular basis of glycoalkaloid induced membrane disruption. Biochim. Biophys. Acta 1240:216-228.

Keukens, E. A. J., T. de Vrije, L. A. M. Jansen, H. de Boer, M. Janssen, A. I. P. M. de Kroon, W. M. F. Jongen, and B. de Kruijff. 1996. Glycoalkaloids selectively permeabilize cholesterol containing biomembranes. Biochim. Biophys. Acta 1279:243-250.

Khashayev, Z. Kh.-M. and Ye. V. Troshko. 1981. Study of the effect of solanine on synaptic transmission. Biophysics 26(1):138-139.

King, R. R. and R. E. McQueen. 1981. Transformations of potato glycoalkaloids by rumen microorganisms. J. Agric. Food Chem. 29:1101-1103.

Kirk, D. and U. Mittwoch. 1975. Changes in the mitotic cell cycle induced by α-solanine. Humangenetik 26:105-111.

Kline, B. E., H. von Elbe, N. A. Dahle, and S. M. Kupchan. 1961. Toxic effects of potato sprouts and of solanine fed to pregnant rats. Proc. Soc. Exp. Biol. Med. 107:807-809.

Konig, H. 1953. Investigations concerning the action of solanine in cattle and sheep in connection with feeding potato foliage. Schweiz. Arch. Tierheilkol. 95:97. (Cited by Maga, 1980).

Konig, H. and A. Stafze. 1953. *Beitrage zur Wirkung des Solanins auf Blutbild und Batalase beim Snaf.* [Action of solanine on hematopoiesis and catalase.] Deut. Tierärztl. Wochenschr. 60:150-153. (Cited by Maga, 1980 and Dalvi and Bowie, 1983).

Kubinski, H., G. E. Gutzke, and Z. O. Kubinski. 1981. DNA-cell-binding (DCB) assay for suspected carcinogens and mutagens. Mutat. Res. 89:95-136.

Kubo, I. and K. Fukuhara. 1996. Steroidal glycoalkaloids in Andean potatoes. Adv. Exp. Med. Biol. 405:405-417.

Kyzlink, V., K. Mikova, and R. Jelínek. 1981. Tomatine, solanine, and embryotoxicity of unripe tomatoes. Sb. Vys. Sk. Chem.-Technol. Praze, Potraviny (E51):69-83. CA Abstract No. 96:18838.

Lagolo, F. M., F. F. Filo, and E. W. Menezes. 1991. [Title not provided]. Food Technol. 45(9):119. (Cited by Hoskins, 1994).

La Vecchia, C. et al. [other authors not provided]. 1987. [Title not provided]. Int. J. Cancer 40:484. (Cited by Hopkins, 1995).

Levi, F. et al. [other authors not provided]. 1993a. [Title not provided]. Nutr. Cancer 19:327. (Cited by Hopkins, 1995).

Levi, F. et al. [other authors not provided]. 1993b. [Title not provided]. Cancer 71:3575. (Cited by Hopkins, 1995).

Locci, R. and J. Kúc. 1967. Steroid alkaloids as compounds produced by potato tubers under stress. Phytopathology 57:1272-1273. (Cited by Beier, 1990).

Maga, J. A. 1980. Potato glycoalkaloids. Crit. Rev. Food Sci. Nutr. 12(4):371-405.

Matthew, J. A., M. R. A. Morgan, R. McNerney, W. W.-S. Chan, and D. T. Coxon. 1983. Determination of solanidine in human plasma by radioimmunoassay. Food Chem. Toxicol. 21(5):637-640.

McCollum, G. D. and S. L. Sinden. 1979. [Title not provided]. Am. Potato J. 56:95. (Cited by Jadhav et al., 1981).

McKee, R. K. 1955. Host-parasitic relationships in the dry-rot disease of potatoes. Ann. Appl. Biol. 43:147-148. (Cited by Beier, 1990).

McMillan, M. and J. C. Thompson. 1979. An outbreak of suspected solanine poisoning in schoolboys. Q. J. Med. 48(190):227-243.

Meyer, G. 1895. Über Vergiftungen Durch Kartoffeln. I. *Über den Gehalt der Kartoffeln an Solanin und Uber Die Bildung Desselben Wahrend der Keimung*. [Poisoning by potato. I. Content of solanine in potatoes and its formation during germination.] Arch. Exp. Pathol. Pharmakol. 36:361. (Cited by Maga, 1980).

Michalska, L., G. Nagel, E. Swiniarski, and M. M. Úydowo. 1985. The effect of α-solanine on the active calcium transport in rat intestine. Gen. Pharmacol. 16(1):69-70.

Mondy, N. I. and G. Gosselin. 1988. Effect of peeling on total phenols, total glycoalkaloids, discoloration and flavor of cooked potatoes. J. Food Sci. 53:756-759. (Cited by Beier, 1990).

Morris, S. C. and T. H. Lee. 1984. The toxicity and teratogenicity of Solanaceae glycoalkaloids, particularly those of the potato (*Solanum tuberosum*): A review. Food Technol. Aust. 36(3):118-124.

Mun, A. M., E. S. Barden, J. M. Wilson, and J. M. Hogan. 1975. Teratogenic effects in early chick embryos of solanine and glycoalkaloids from potatoes infected with late-blight, *Phytophthora infestans*. Teratology 11(1):73-78.

Ness, E., P. E. Joner, and H. K. Dahle. 1984. α-Solanine tested for mutagenicity with Ames test. Acta Vet. Scand. 25:145-147.

Nevin, N. C. and J. D. Merrett. 1975. [Title not provided]. Br. J. Prev. Soc. Med. 29:111. (Cited by Hopkins, 1995).

NIEHS (National Institute of Environmental Health Sciences). 1997a. Information profile for NIEHS nominations on chemicals to the national toxicology program for α-chaconine.

NIEHS. 1997b. Information profile for NIEHS nominations on chemicals to the national toxicology program for α-solanine.

Nigg, H. N. 1997. Natural products chemistry as a resource for biorational methods of insect control. From Federal Research in Progress, DIALOG file 265:FEDRIP. Identifying No. 0168150; FLA-LAL-03370.

Nigg, H. N., L. E. Ramos, E. M. Graham, J. Sterling, S. Brown, and J. A. Cornell. 1996. Inhibition of human plasma and serum butyrylcholinesterase (EC 3.1.1.8) by α-chaconine and α-solanine. Fundam. Appl. Toxicol. 33:272-281.

Nishie, K., M. R. Gumbmann, and A. C. Keyl. 1971. Pharmacology of solanine. Toxicol. Appl. Pharmacol. 19:81-92.

Nishie, K., W. P. Norred, and A. P. Swain. 1975. Pharmacology and toxicology of chaconine and tomatine. Res. Commun. Chem. Pathol. Pharmacol. 12(4):657-668.

Nishie, K., T. J. Fitzpatrick, A. P. Swain, and A. C. Keyl. 1976. Positive inotropic action of Solanaceae glycoalkaloids. Res. Commun. Chem. Pathol. Pharmacol. 15(3):601-607.

Norred, W. P., K. Nishie, and S. F. Osman. 1976. Excretion, distribution, and metabolic fate of ^{3}H-α-chaconine. Res. Commun. Chem. Pathol. Pharmacol. 13(2):161-171.

Oettingen, Von, W. F. 1952. Poisoning. Harper (Hoeber), New York. p. 426. (Cited by Maga, 1980).

Oslage, H. F. 1956. *Uber das Solanin in der Kartoffel und Seine Wirkung auf das Tier*. [Solanine in the potato and its action on the animal.] Kartoffelbau 7:204. (Cited by Maga, 1980).

Osman, S. F., S. F. Herb, T. J. Fitzpatrick, and S. L. Sinden. 1976. [Title not provided]. Phytochemistry 15:1065. (Cited by Jadhav et al., 1981).

Paseshnichenko, V. A. and A. R. Guseva. 1956a. [Title not provided]. Biokhimiya 21:585. (Cited by Jadhav et al., 1981).

Paseshnichenko, V. and A. R. Guseva. 1956b. Quantitative determination of potato glycoalkaloids and their preparative separation. Biochem. USSR 21:606. (Cited by Matthew et al., 1983).

Patil, B. C., R. P. Sharma, D. K. Salunkhe, and K. Salunkhe. 1972. Short paper: Evaluation of solanine toxicity. Food Cosmet. Toxicol. 10:395-398.

Peters, R. K. et al. [other authors not provided]. 1992. [Title not provided]. Cancer Causes Control 3:457. (Cited by Hopkins, 1995).

Pfuhl, E. 1899. *Über eine Massenerkrankung durch Vergiftung mit stark solaninhaltigen Kartoffeln*. [Regarding an outbreak of illness due to poisoning by solanine in potatoes.] Deutsch. Med. Wochenschr. 25:753-754. (Cited by JECFA, 1993).

Phillips, B. J., J. A. Hughes, J. C. Phillips, D. G. Walters, D. Anderson, and C. S. M. Tahourdin. 1996. A study of the toxic hazard that might be associated with the consumption of green potato tops. Food Chem. Toxicol. 34:439-448.

Pierro, L. J., J. S. Haines, and J. Bakanauskas. 1976. Embryo resorption and development of the chorioallantoic placenta of the mouse. Am. Zool. 16(2):187. Abstr.

Poswillo, D. E., D. Sopher, and S. J. Mitchell. 1972. Experimental induction of fetal malformation with "blighted" potato: A preliminary report. Nature 239:462-464. (Cited by JECFA, 1993).

Poswillo, D. E., D. Sopher, S. J. Mitchell, D. T. Coxon, R. F. Curtis, and K. R. Price. 1973. Investigations into the teratogenic potential of imperfect potatoes. Teratology 8:339-347. (Cited by JECFA, 1993).

Ramon, J. M. et al. [other authors not provided]. 1993. [Title not provided]. Cancer 71:1731. (Cited by Hopkins, 1995).

Rayburn, J. R., J. A. Bantle, and M. Friedman. 1994. Role of carbohydrate side chains of potato glycoalkaloids in developmental toxicity. J. Agric. Food Chem. 42:1511-1515.

Renwick, J. H. 1972. Hypothesis: Anencephaly and spina bifida are usually preventable by avoidance of a specific but unidentified substance present in certain potato tubers. Br. J. Prev. Soc. Med. 26:67-88.

Renwick, J. H. 1982. Food and malformation. Practitioner 226:1947-1953.

Renwick, J. H., A. M. Possamai, and M. R. Munday. 1974. Potatoes and spina bifida. Proc. R. Soc. Med. 67:360-364.

Renwick, J. H., W. D. B. Clarinbold, M. E. Earthy, J. D. Few, and A. C. S. McLean. 1984. Neural-tube defects produced in Syrian hamsters by potato glycoalkaloids. Teratology 30:371-381.

Roddick, J. G. 1989. The acetylcholinesterase-inhibitory activity of steroidal glycoalkaloids and their aglycones. Phytochemistry 28(10):2631-2634.

Roddick, J. G. and R. B. Drysdale. 1984. Destabilization of liposome membranes by the steroidal glycoalkaloid α-tomatine. Phytochemistry 23:543-547. (Cited by Friedman and McDonald, 1997).

Roddick, J. G. and A. L. Rijnenberg. 1986. Effect of steroidal glycoalkaloids of potato on the permeability of liposome membranes. Physiol. Plant. 68:436-440. (Cited by Friedman and McDonald, 1997).

Roddick, J. G. and A. L. Rijnenberg. 1987. Synergistic interaction between the potato glycoalkaloids α-solanine and α-chaconine in relation to lysis of phospholipid/sterol liposomes. Phytochemistry 26(5):1325-1328.

Roddick, R. G., A. L. Rijnenberg, and S. F. Osman. 1988. Synergistic interaction between potato glycoalkaloids α-solanine and α-chaconine in relation to destabilization of cell membranes: Ecological implications. J. Chem. Ecol. 14(3):889-902.

Roddick, J. G., A. L. Rijnenberg, and M. Weissenberg. 1992. Alterations to the permeability of liposome membranes by the solasodine-based glycoalkaloids solasonine and solamargine. Phytochemistry 31:1951-1954. (Cited by Friedman and McDonald, 1997).

Ron, E. et al. [other authors not provided]. 1987. [Title not provided]. J. Natl. Cancer Inst. 79:1. (Cited by Hopkins, 1995).

Rothe, J. C. 1918. Illness following the eating of potatoes containing solanine. Z. Hyg. 88:1. (Cited by Maga, 1980, and Jadhav et al., 1981).

Ruddick, J. A., J. Harwig, and P. M. Scott. 1974. Nonteratogenicity in rats of blighted potatoes and compounds contained in them. Teratology 9(2):165-168.

Ruhl, R. 1951. *Beitrag zur pathologie und toxikologie des solanins*. [Pathology and toxicology of solanine]. Arch. Pharm. Weinheim Ger. 284:67-74. (Cited by Maga, 1980, and Sinden and Deahl, 1994).

Sankaranarayanan, R. et al. [other authors not provided]. 1994. [Title not provided]. Int. J. Cancer 58:644. (Cited by Hopkins, 1995).

Satoh, T. 1967. Glycemic effects of solanine in rats. Jpn. J. Pharmacol. 17:652-658.

Schilling, J. and M. Zobel. 1966. [Title not provided]. Pharmazie 21:103. (Cited by Jadhav et al., 1981).

Sharma, R. P., C. C. Willhite, M. T. Wu, and D. K. Salunkhe. 1978. Teratogenic potential of blighted potato concentrate in rabbits, hamsters, and miniature swine. Teratology 18:55-61. (Cited by JECFA, 1993).

Sharma, R. P., C. C. Willhite, J. L. Shupe, and D. K. Salunkhe. 1979. Acute toxicity and histopathological effects of certain glycoalkaloids and extracts of Alternaria solani or Phytophthora infestans in mice. Toxicol. Lett. 3:349-355.

Sharma, R. P., M. J. Taylor, and D. R. Bourcier. 1983. Subcellular distribution of α-chaconine in mouse hepatocytes. Drug Chem. Toxicol. 6:219-234.

Sinden, S. L. 1972. Effect of light and mechanical injury on the glycoalkaloid content of greening resistant potato tubers. Am. Potato J. 49: 368. (Cited by Beier, 1990).

Sinden, S. L. and K. L. Deahl. 1994. Alkaloids. In: Y. H. Hui, J. R. Gorham, K. D. Murrell, and D. O. Cliver (Eds.) Foodborne Disease Handbook, Vol. 3. Marcel Dekker, Inc., NY. pp. 227-259.

Sinden, S. L. and R. E. Webb. 1972. Effect of variety and location on the glycoalkaloid content of potatoes. Am. Potato J. 49:334-338. (Cited by Beier, 1990).

Sinden, S. L., L. L. Sanford, and S. F. Osman. 1980. Glycoalkaloids and resistance to the Colorado potato beetle in *Solanum chacoense* bitter. Am. Potato J. 57:331. (Cited by Matthew et al., 1983).

Sizer, C. H., J. A. Maga, and C. J. Craven. 1980. Total glycoalkaloids in potatoes and potato chips. J. Agric. Food Chem. 28:578-579.

Slanina, P. 1990. Solanine (glycoalkaloids) in potatoes: Toxicological Evaluation. Food. Chem. Toxicol. 28(11):759-761.

Smith, O. 1977. Chemical composition of the potato. In: Potatoes: Production, Storing, Processing, 2nd ed. AVI Publishing Co., Wesport, CT. pp. 59-109. (Cited by Beier, 1990).

Smith, R. A. 1994. Poisonous plants. In: Y. H. Hui (Ed.) Foodborne Disease Handbook. Marcel Dekker, Inc., NY. pp. 187-218.

Steinmetz, K. A. and J. D. Potter. 1993. [Title not provided]. Int. J. Cancer 53:711. (Cited by Hopkins, 1995).

Stofberg, J. and F. Grundschober. 1984. Consumption ratio and food predominance of flavoring materials—Second cumulative series. Perfum. Flavor. 9(4):53-83.

Somvanshi, R., J. C. Biswas, and M. S. Sastry. 1992. Potato plant (*Solanum tuberosum*) induced dermatitis in Indian buffaloes. Indian J. Anim. Sci. 62(7):639-641.

Swinyard, C. A. and S. Chaube. 1973. Are potatoes teratogenic for experimental animals? Teratology 8(3):349-357.

Taijima, K. and S. Tominaga. 1985. [Title not provided]. Jpn. J. Cancer Res. 76:705. (Cited by Hopkins, 1995).

Takagi, K., M. Toyoda, Y. Fujiyama, and Y. Saito. 1990. Effect of cooking on the contents of alpha chaconine and alpha solanine in potatoes. J. Food Hyg. Soc. Jpn. 31(1):67-73.

Tally, E. A. 1975. [Title not provided]. Am. Potato J. 56:145. (Cited by Jadhav et al., 1981).

Teat, D. W. and M. D. Ellis. 1981. Toxic indoor plants. U.S. Pharm. 6:38-39.

Terbruggen, A. 1936. *Todliche Solaninvergiftung Zugleich ein Beitrag zur Bedeutung der Akuten Hirnschwelung bei Verringerter Schadelkapizitat*. [Deadly solanine poisoning and a report on the meaning of acute brain swelling with decreased skull capacity.] Beitr. Pathol. Anat. Allg. Pathol. 97:391. (Cited by Maga, 1980).

Thorne, H. V., G. F. Clarke, and R. Skuce. 1985. The inactivation of herpes simplex virus by some Solanaceae glycoalkaloids. Antiviral Res. 5:335-343.

Trichopoulos, D. et al. [other authors not provided]. 1985. [Title not provided]. Int. J. Cancer 36:291. (Cited by Hopkins, 1995).

Tuyns, A. J. et al. [other authors not provided]. 1988. [Title not provided]. Nutr. Cancer 11:189. (Cited by Hopkins, 1995).

USDA Economic Research Service. 1983. [Title not provided]. TVS-227 and TVS-229. (Cited by Stofberg and Grundschober, 1984).

De Vincenzi, M., E. Mancini, and M. R. Dessi. 1996. Monographs on botanical flavouring substances used in foods. Part V. Fitotherapia 67(3):241-251.

Waalkens-Berendsen, D. H., A. E. Smits-van Prooije, H. B. W. M. Koëter, W. R. Leeman, and A. Dijkstra. 1992. Potential teratogenic effects of some glycoalkaloids. Teratology 46(3):31A.

Willard, M. 1993. Potato processing: Past, present, and future. Am. Potato J. 70:405-418. (Cited by Friedman and McDonald, 1997).

Willimott, S. C. 1933. An investigation of solanine poisoning. Analyst (London) 58:431. (Cited by Maga, 1980).

Wilson, G. S. 1959. A small outbreak of solanine poisoning. Mon. Bull. Med. Res. Counc. 18:207. (Cited by Maga, 1980 and Hopkins, 1995).

Wilson, A. M., D. F. McGann, and R. J. Bushway. 1983. Effect of growth-location and length of storage on glycoalkaloid content of roadside-stand potatoes as stored by consumers. J. Food Prot. 46(2):119-121.

Wolf, M. J., and B. M. Duggar. 1946. Estimation and physiological role of solanine in the potato. J. Agric. Res. 73:1-32. (Cited by Maga, 1980, and Beier, 1990).

Wood, F. A. and D. A. Young. 1974. TGA in potatoes. Publ. No. 1533, Canada Dept. of Agric. (Cited by Beier, 1990).

Wu, M. T. and D. K. Salunke. 1977. [Title not provided]. J. Food Sci. 42:1413. (Cited by Jadhav et al., 1981).

Yoon, D.-J. and L. Kirkowski. 1979. Effects of dietary solanaceous potatoes on the serum, calcium, phosphorus, magnesium, and hydroxyproline levels of rats. Hanguk Ch'uksan Hakhoe Chi 21(4):401-406. CAPLUS Abstract No. 1979:569593.

Zaletskaya, B. G., L. A. Golynskaya, and V. N. Zaletskii. 1977. Changes in the contents of glycoalkaloids during the manufacture and storage of dried potato puree. Konservn. Ovoshchesush. Proms. 1:13-14. (Cited by Morris and Lee, 1984).

Zeigler, R. G. et al. [other authors not provided]. 1981. [Title not provided]. J. Natl. Cancer Inst. 67:1199. (Cited by Hopkins, 1995).

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