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Tropane alkaloids in food

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Summary

A large number of wild and cultured plants produce secondary metabolites that are toxic to humans and animals. Through accidental or intentional mixing of these plants with normal food and feed the consumers of these products will be exposed to the toxins. In this report tropane alkaloids will be discussed. Tropane alkaloids naturally occur in numerous plant families such as Erythroxylaceae (including coca) and *Solanaceae* (including mandrake, henbane, deadly nightshade, datura, potato, tomato), *Proteaceae*, *Euphorbiaceae, Rhizophoraceae, Convolvulaceae* and *Cruciferae*. The class contains over 200 compounds, but the most common tropane alkaloids are atropine, hyoscyamine and scopolamine.

The alkaloids are often extracted, to be used as medicine, drug, poison or antidote.
Poisonings of humans by plants containing tropane alkaloids can be aggregated into different categories: unintended ingestions (contamination, mistaken identity, carry-over) and intended ingestions (overdoses). Contamination can occur when toxic plant (parts) are accidently mixed into edible plants during harvest or processing. Recently this happened in France when Datura flower buds were mixed in with canned green beans. Several cases of mistaken identity are reported where for example berries of deadly nightshade resemble edible berries like blueberry. Eating 10 berries of the deadly nightshade could already be fatal. Carry-over does not appear to be a real problem. There are only a few examples of animal products containing (low levels) of tropane alkaloids because the animals were fed with contaminated feed. Poisoning due to intended ingestions can be divided into consumption for recreational purposes (hallucinogenic effects) or medical properties (e.g. arthritis, anesthetic), homicides and suicides.

In the literature many different methods of analysis of tropane alkaloids are described. RIKILT is already using some of these methods to analyse tropane alkaloids in animal feed. These methods can be used for analysis of human food as well. Based on the incidents with both animals and humans it is to be expected that human foods potentially containing tropane alkaloids would be herbal teas, herbal preparations (e.g. traditional Chinese or Ayurvedic), blue- or black berries (either fresh of dried), edible flowers. Contamination has also been found in buckwheat (for human consumption), soybean and linseed (animal feed). These are the products that should primarily be monitored to prevent accidental exposure of humans to tropane alkaloids.

Contents

1 Tropane alkaloids in food

A large number of wild and cultured plants produce secondary metabolites that are toxic to humans and/or animals. Through accidental or intentional mixing of these plants with normal food and feed the consumers of these products may be exposed to the toxins. A lot of information is available on some of these secondary metabolites, but others are less well known. In this report tropane alkaloids in relation to human incidental or accidental exposure will be discussed. This report also aims to provide background information for EFSA and EC-SANCO, in view of the plans to draft an EFSA scientific opinion on tropane alkaloids in 2011, with the focus on human health.

1.1 Tropane alkaloids

Tropane alkaloids are a class of alkaloids and secondary metabolites that contain a tropane ring in their chemical structure. The class consists of more than 200 compounds[1]. Tropane alkaloids naturally occur in plants of the families Erythroxylaceae (including coca) and Solanaceae (including mandrake, henbane, deadly nightshade, datura, potato, tomato). Important tropane alkaloids are atropine, hyoscyamine and scopolamine. Atropine is an racemic mix of the R- an L-enantiomer of hyoscyamine. The L-hyoscyamine is the active form. These tropane alkaloids are known to prevent binding of acetylcholine to its receptor and as a result have effects on heart rate, respiration and functions in the central nervous system (anticholinergic poisoning). Scopolamine, acting as an antagonist at both peripheral and central muscarinic receptors, is thought to be the primary compound responsible for the toxic effects of these plants.

Tropane alkaloids are found in all parts of the plants, with highest concentrations in roots and seeds[2]. The proportion of each alkaloid present varies among species, time of year, location, and part of plant. As little as one-half teaspoon of *Datura* seed, equivalent to 0.1 mg of atropine per seed, has caused death from cardiopulmonary arrest. The usual route of ingestion is as a tea, although ingesting seeds or other plant parts and smoking dried leaves also are common[3].

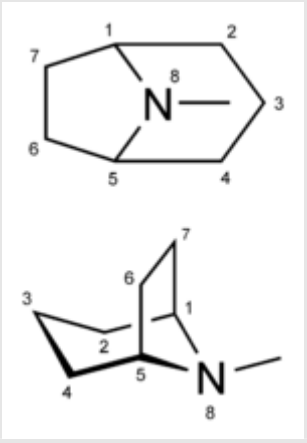
Scopolamine has three primary medical uses: treatment of nausea and motion sickness, treatment of intestinal cramping, and for ophthalmic (relating to eyes) purposes. Use as a general depressant and adjunct to narcotic painkillers is also common. The drug is less commonly used as a preanesthetic agent and uncommonly for some forms of Parkinsonism. Scopolamine is also used as an adjunct to narcotic analgesia, such as the product Twilight Sleep which contains morphine and scopolamine, some of the original formulations of Percodan and some European brands of injectable methadone, as well as use of tablets or patches to combat nausea as well as enhance the pain-killing ability of various opioids. Scopolamine can be used as an occasional sleep aid and was available in some over the counter products in the United States for this purpose until November 1990[4].

Relatively recent a novel group of tropane alkaloids was detected in deadly nightshade: calystegines[5]. These alkaloids were also detected in extracts of the roots of *Calystegia sepium* (hedge bindweed) and *Convolvulus arvensis* (field bindweed), both in the family Convolvulaceae. Calystegines are formed

partially by the same biosynthetic steps as the well-known and medicinally significant tropane alkaloids.

Other tropane alkaloids are used as stimulants, such as cocaine and cocaine-related alkaloids:

- cocaine, from *Erythroxylum coca*
- ecgonine, a precursor and metabolite of cocaine
- benzoylecgonine, a metabolite of cocaine
- hydroxytropacocaine
- methylecgonine cinnamate
- catuabines, found in the drug catuaba, from *Erythroxylum vacciniifolium*



Molecular formula $C_8H_{15}N$
IUPAC-name (1R,5S)-8-methyl-8-azabicyclo[3.2.1]octane
Other names: tropane
8-Azabicyclo(3.2.1)octane, 8-methyl-; 529-17-9
Molar mass 125.211 g/mol
SMILES CN1[C@@H]2CCC[C@H]1CC2
CAS-number 529-17-9
PubChem 637986

Figure 1: Chemical structure of tropane.

1.2 Occurrence

Tropane alkaloids are produced by numerous plant families: *Solanaceae*, *Erythroxylaceae*, *Proteaceae*, *Euphorbiaceae, Rhizophoraceae, Convolvulaceae* and *Cruciferae*. An extensive review on chemotaxonomy and geographical distribution of tropane alkaloids can be found in Griffin and Lin (2000)[6]. Since tropane alkaloids are often used for their hallucinogenic effects, a large amount of information is available on the internet. Sometimes these "unscientific" internetsites use scientific sources of information, for example on the Lycaeum Forum[7].

Often naturally occurring plants are used for extraction of the alkaloids, to be used as medicine, drug, poison or antidote[8]. The highest concentrations are usually found in seeds, but leaves and roots are used as well. For example, *Scopolia carniolica* Jacq. (Solanaceae, found at the basis of the forests in Central and South-east Europe) is used in Romania in the industrial extraction of scopolamine and atropine, alkaloids that are present in the rhizomes (*Scopoliae rhizoma*)[9]. *Brugmansia* and *Dubosia* species are collected (and sometimes cultivated) for scopolamine as well, e.g. in Australia[6]. *Erythroxylum coca* is the source of all commercial coca leaves from which cocaine is derived.

There are also studies of in vitro cultivation of the plant to protect the environment from excessive harvesting. For example the production of scopolamine and hyoscyamine in *Nicotiana tabacum* and

Hyoscyamus muticus hairy roots[10]. Other techniques involve greenhouse cultivation of plants on a liquid medium which can be made to excrete compounds of interest via their roots (http://www.international.inra.fr/partnerships/with_the_private_sector/live_from_the_labs/plant_advanced_technologies_sas) .

Table 1: Most common plants containing tropane alkaloids (images of the plants can be found in the Appendix).

Plants	Toxin	Plant parts used and sometimes mistaken for other species
Atropa belladonna (deadly nightshade, Dutch: wolfskers) Figure 3.1, Figure 3.2, Figure 3.3	scopolamine, hyoscyamine, atropine (without treatment the intake of 2 to 5 berries in children and 10 to 20 berries in adults is considered lethal[11]), calystegine[5]	berry: resembles edible berries like *Vaccinium* (e.g. bilberry, blueberry, cranberry, huckleberry) leaf: *Malva sylvestri*s (mallow, Dutch: kaasjeskruid); used in salads, soups or stuffed with bulgur or rice. root
Datura stramonium (jimsonweed, devil's weed, thornapple, tolguacha, Jamestown weed, stinkweed, datura, moonflower, Dutch: doornappel)[12] Figure 3.4, Figure 3.5	scopolamine, hyoscyamine, atropine	leaf: Jew's mallow[13,] nettle (*Utica*)[14], mallow (*Malva*)[15] *Symphytum officinale* (comfrey)[15,16] , used as tea root: burdock (*Arcticum*)[17] ; root tea used traditionally as blood purifier, diuretic, skinproblems seed: sesame flower: *Paulownia* (e.g. foxglove tree)[18] used in salads
Datura suaveolens (*Brugmansia suaveolens*, angel's trumpet)	scopolamine, hyoscyamine	leaf, flower, seed
Datura tatula, metel (Jimsonweed, thorn apple).	Seed contains ca. 0.1mg atropine/seed.[19]	leaf, flower, seed
Duboisia myoporoides (corkwood, leaves collected in New Caledonia[20]) Figure 3.6	scopolamine, atropine	leaf
Erycibe henryi Prain ("Ting Kung Ten")[21], a species of Convolvulaceae medicinal herb	tropane alkaloid	leaf, flower, seed
Hyoscyamus niger (black henbane, stinking nightshade, Dutch: bilzekruid)[12] Figure 3.7	scopolamine, hyoscyamine, atropine, calystegine	leaf, flower, seed
Latua pubiflora (Solanaceae, Chile)[22] Figure 1	scopolamine, hyoscyamine	berry, leaf

Plants	Toxin	Plant parts used and sometimes mistaken for other species
Lycium barbarum (wolfberry, matrimony vine, Duke of Argyll's tea plant, goji berry, Dutch: boksdoorn) Figure 3.11	atropine	berry
Mandragora officinarum[6,12](mandrake, Dutch: alruin) Figure 3.8	scopolamine, hyoscyamine, atropine	root, berry
Scopolia carniolica Jacq. (Dutch: klokbilzenkruid) [9,12] Figure 3.14	scopolamine, hyoscyamine, atropine	leaf, root
Hyoscyamus muticus hairy roots[10].	scopolamine, hyoscyamine	N.A.
Nicotiana tabacum hairy roots[10].	scopolamine, hyoscyamine	N.A.
*Calystegia sepium (*larger bindweed, hedge bindweed, or Rutland beauty[5,6] Figure 3.13	calystegine	leaf, root
Convolvulus arvensis (field bindweed)[5] Figure 3.12	calystegine	leaf, root
Physalis alkekengi[6]	calystegine	leaf
Physalis peruviana (Cape Goosberry, Chinese lantern plant)[6] Figure 3.10	tigloidine, secotropane alkaloids	root
Erythroxylum coca Figure 3.15	many alkaloids including cocaine	leaf

1.3 Legislation

Many of the plants containing tropane alkaloids are registered in lists with unapproved herbs such as the Dutch Decree herbal preparations (*Warenwetbesluit Kruidenpreparaten*, 2001)[23] and the Belgian "Royal Decree concerning the manufacture of and trade in foods from plants or preparations made from or containing plants" (*Koninklijk besluit betreffende de fabricage van en de handel in voedingsmiddelen die uit planten of uit plantenbereidingen samengesteld zijn of deze bevatten*, 1997)[24]. The Regulation (EC) No 1925/2006 of the European Parliament and of the Council of 20 December 2006 on the addition of vitamins and minerals and of certain other substances to foods" mentions an Annex III with "certain other substances" but no substances (potentially herbs) have been added to this Annex yet (2009).

1.4 Methods of analysis

In the literature many different methods of analysis are described: HPLC, GC, RIA, CE-MS, LC-MS/MS ([25, 1, 26, 27]). The EFSA Scientific Opinion on tropane alkaloids in feed (2008)[1] gives a detailed overview. The RIKILT uses an LC-MS/MS method for the determination of tropane alkaloids (atropine and scopolamine) in grains and in (compound) animal feeds. The analysis of tropane alkaloids has been incorporated into the method for ergot alkaloids (RIKILT SOP A1070). In this method samples are ground to 0.5 mm and homogenised. To the sample (4 g) 40 ml of a mixture of methanol/water/formic acid is added in a ratio of 60/40/0.4 (V/V/V/). After extraction (30 min) by means of a rotary tumbler an aliquot of the supernatant (2 ml) is filtered through a 30 kD ultra filter. The filtered extract is injected into the LC-MS/MS system. Quantification is performed by means of (multi-level) standard addition. The limit of detection for atropine and scopolamine is 3-5 µg/kg, the limit of quantification is 10-15 µg/kg.

One of the current activities in method development for tropane alkaloids takes place in the EU-funded project CON*ff*IDENCE. This Large Collaborative Project in the Food, Agriculture, Fisheries and Biotechnology Area of the EC's 7th Framework Programme, runs from 2008-2012 under coordination of RIKILT. The projects focus is on the development of simple, fast, multi-analyte, multi-class detection for a variety of analytes, including some tropane alkaloids. In this project, antibody-based dipstick methods are developed. For the tropane alkaloids, currently the focus is on the detection of atropine and scopolamine in animal feed. The antibodies used are specific and do not or hardly cross react with other alkaloids. It is anticipated that prototype dipsticks will be extensively tested in 2011, followed by interlaboratory validations later in 2011 and in 2012. Dipstick tests are particularly useful for field testing. The project will end in the course of 2012.

1.5 Exposure to tropane alkaloids

In an opinion of the Scientific Committee of the Panel on Contaminants in the Food Chain on Animal Nutrition on Undesirable Substances in Feed from the EFSA (2008)[1] the exposure of animals to tropane alkaloids has been described extensively. Often tropane alkaloid poisoning in animals is the result of the consumption of *Datura* plants rather than contamination of feed materials with *Datura* seeds. The consumption of fresh *Datura* plants is unlikely because the plant has a very unpleasant taste and odour, but animals do not detect the impurities in dried material like hay. Tropane alkaloids are fairly stable during drying and heat treatment of feed materials. After baking bread from wheat flour contaminated with jimsonweed seeds (*Datura stramonium*) the baked bread still contained 72 - 100% of the tropane alkaloid content of the flour[19]. Cases of *Datura* intoxication have been reported for many (farm) animals, but pigs are especially sensitive.

Plant poisonings of humans can be aggregated into different categories: unintended ingestions (contamination, mistaken identity, carry-over), intended ingestions, and poisoning due to abuse of plant material (overdoses). Bulk commercial grain, such as soybeans and wheat, may be contaminated by nongrain impurities, including jimsonweed seeds, that coexist with the crop to be harvested[19]. Unintended ingestions often occur in children or from a mix-up of plants and mushrooms in adults. Jimsonweed (or Jamestown weed) is named for a case of human poisoning in Jamestown, USA., when soldiers were poisoned by eating the plant in a salad and then suffered delirium and hallucinations.

Intended ingestions are common in homicides and suicides. Increasingly common is the abuse of plants for hallucinogenic reasons[26]. The use of cocaine for this purpose is very well known, either ingestion through chewing of coca leaves or intake of more purified forms. Cocaine will not be discussed in this report.

In a study using seeds of jimsonweed obtained from different locations in the USA an average concentration of 2.3 and 0.5 mg/g seeds of atropine and scopolamine, respectively, was detected [28]. Other sources (in [1]) indicate levels between 1 and 9 mg/g seeds. The estimated lethal dose of atropine in humans is 10 mg and 2–4 mg for scopolamine. Without treatment the intake of 2 to 5 berries of deadly nightshade in children and 10 to 20 berries in adults is considered lethal[11]) Jimson weed toxicity usually occurs within 60 minutes after ingestion and clinical symptoms may persist for 24 to 48 hours[29]. One jimsonweed seed weighs approximately 8 mg[1], which means that approximately 100 seeds are equivalent with 10 mg atropine.

Another source reports that for adults 100 mg atropine, 100 mg scopolamine or 10 mg hyoscyamine is considered a lethal dose, but for children only a few milligram is sufficient[11]. The intake of 2 to 5 berries of *Atropa belladonna* in children and 10 tot 20 berries in adults is considered lethal.

1.5.1 Carry-over

There are only a few examples of animal products containing tropane alkaloids because the animals were fed with contaminated feed. The EMEA (European Medicinal Agency)[30] reports that residues of scopolamine (butylscopolaminium bromide) in tissues and milk are rapidly depleted in cattle.

Reference	Place, date	Incident
Kovatsis et al[31]	1994	Traces of scopolamine have been detected in eggs laid by hens of a meat producing strain that for three months were fed a standard diet supplemented with 150 mg purified scopolamine and hyoscyamine/ kg feed.
EMEA[30]	1997	Residue depletion studies in horses, pigs and cattle receiving intravenous or intramuscular doses of scopolamine resulted eventually in levels below the detection limit, both in meat and milk.

1.5.2 Contamination

Different sources report cases of poisoning due to contamination of foods with plants containing tropane alkaloids.

Reference	Place, date	Incident
Perharic (2005)[32]	Slovenia, 2003	Contamination of **buckwheat** flour with seeds from *Datura stramonium*. Buckwheat flour is commonly used in preparation of traditional dishes in Slovenia. In September 2003, cases of domestic food poisoning with a typical syndrome of tropane alkaloid toxicity: dry mouth, hot red skin, blurred vision, tachycardia, urinary retention, ataxia, speech disturbance, disorientation and visual hallucinations, were identified. All victims reported ingestion of a traditional dish made of buckwheat flour a few hours prior to the onset of symptoms. Examination of whole buckwheat grain showed up to 190 *Datura stramonium* seeds/kg of grain.
Fretz et al (2007)[33]	Austria, 2006	Food poisoning due to jimsonweed mimicking *Bacillus cereus* food intoxication. **Millet-carrots** balls contained *Datura stramonium* seeds (50 seeds/kg of grain).
Bryson[17], cited by Awang (1989)[15]	USA, 1978	**Burdock** (*Arcticum*) root tea poisoning. Acute atropine-like poisoning occurred in a woman who drank a strong decoction of burdock tea.
Scholz[14], cited by Awang (1989)[15]	Austria, 1980	**Nettle** (*Urtica*) tea poisoning. The description of the case of a 57 yr old woman is given who showed the symptoms of an atropine poisoning after drinking stinging nettle tea. The analysis of the tea specimen proved bad defilements among other things, with elements of the 'belladonna' (*Atropa belladonna*). Several similar reports became known recently and it seems to be necessary to discuss checking the purity of the tea species.
Awang (1989)[15]	Toronto, 1981, 1984	**Mallow** (*Malva sylvestris*) poisoning; packages revealed berries of Atropa belladonna (deadly nightshade).
Russell et al[28]	Maryland, 2008	Family of 6 poisoned after eating stew that contained jimsonweed (*Datura stramonium*). **Stew** consisted mainly of potatoes but also included garlic, onion, tomato, curry powder, and leaves from two plants growing in the yard. One plant was confirmed to be mint. The meal preparer did not know what the other plant was, only that it grew wild in the yard.
Ramirez et al (1999)[34]	Venezuela, 1999	Fifteen persons developed atropine poisoning following consumption of **wasp honey**. Clinical signs, antidotal response and the presence of *Datura* plants near the wasp nests supported that the intoxications were caused by ingestion of atropine-contaminated honey.
CDC(1995)[35]	USA, 1994	The CDC reported 7 cases of anticholinergic poisoning in 3 families who consumed contaminated commercial **Paraguay tea** (*Ilex paraguariensis*). Probably contaminated with leaves from plants containing belladonna alkaloids.
Department of Health and Sports (2010)[36]	France, 2010	Presence of *Datura stramonium* in **canned green beans**. The Directorate General for Competition, Consumption and Fraud Control and the Directorate General of Health recommend not to eat canned beans distributed by some stores with labels "Magasin U" and "Leclerc". This recommendation follows the recent poisoning of three people, with a flower bud of *Datura stramonium* contained in the preserves.

Reference	Place, date	Incident
Galizia (1983)[37]	Great Britain, 1983	Atropine as possible contaminant of comfrey tea. Contamination with a *Datura spp* is the most likely explanation.NB Comfrey itself contains pyrrolizidine alkaloids, but no tropane alkaloids.
Routledge and Spriggs[38]	Great Britain, 1989	Atropine as possible contaminant of comfrey (*Symphytum*) tea. A 30-year-old man visited a health-food store complaining of flatulence. Comfrey tea was recommended. He put 28 g into boiling water. He had several cups of the infusion, after which he felt light-headed, agitated, and confused, and had difficulty in micturition.

1.5.3 Mistaken identity

Other intoxications occurred after leaves, roots, berries or seeds of toxic plants are mistaken for edible plants.

Reference	Place, date	Incident
CDC(1984)[39]	Canada, 1983	After a husband and wife ate a meal of hamburger prepared at home, the husband collapsed, and the wife telephoned for an ambulance to take him to a local hospital. When the ambulance arrived, the wife also became unconscious. In preparing the hamburger, the wife added what she thought was seasoning but later realized was seeds of Angels' Trumpets (*Datura suaveolens*) that had been drying above the stove for planting the next year. After removing most of the seeds from the cooked meat, the husband and wife ate one hamburger patty each.
Houghton (2004)[18]		Wrong drug supplied: tropane alkaloid poisoning occurring because *Datura metel* flowers had been supplied instead of those from *Paulownia* species (foxglove tree).
Kimura S (1995)[40] cited by Namera (2005) [25]	Japan, 1995	A 71-year-old female parboiled and ate a plant in the evening, which had been grown in her garden; she had believed it to be the Jew's mallow. About 20 min after ingestion, paresthesia appeared in the hand and then extended to her whole body. A doctor at the clinic suspected atropine poisoning, because of her clouded consciousness, mydriasis, dry mouth and palpitations. The same plant as that eaten by her was examined by a specialist and proved to be *Datura tatula*.
Chang et all (1999).[41]	Taiwan, 1999	Poisoning by Datura leaves used as edible wild vegetables.
Pereira et all (1994)[42]	Brazil, 1994	Poisoning by the use of Datura leaves in a homemade toothpaste. Toxic absorption after mucosal application is evident in 24 h of atropinism sustained by a woman who used a toothpaste mixed with the leaves and flowers of Datura sp., table salt, vinegar and an alcoholic beverage.

Reference	Place, date	Incident
Goto et al (1996)[13] cited by Namera (2005) [25]	Japan, 1996	The seeds of *Datura metel* are being sold in gardening stores; people are growing this plant in their own gardens. There were poisoning cases in which *Datura metel was* eaten by mistaking it for Jew's mallow; its root eaten for that of burdock and its seeds eaten for sesame.
Smith et al (1991)[43]	USA, 1991	A 76-year-old Caucasian male, ingested 3 teaspoons (15 mL) of a homemade wine over a 1-h period and became ill. Approximately 1.5 h later, he was taken to the emergency room of a local hospital with symptoms of respiratory distress and weakness. The plant used in making the wine was Angel's trumpet (*Datura suaveolens*), which reportedly contains varying amounts of scopolamine and atropine. A sample of the wine was collected and analyzed for these two compounds by reversed-phase HPLC chromatography using 97% methanol-3% deionized water. The filtered wine contained an estimated 29 mg scopolamine/mL, which produced a total ingested dose of 435 mg. No atropine was detected.
van der Heide (1988)[44]	Germany, 1988	A 10 year old Turkish girl was intoxicated after drinking tea prepared from dried *Datura stramonium* (thornapple) leaves. Hyoscyamine en scopolamine were found in her urine. There were no instructions on the package with dried leaves but it probably should have been used for inhalation. Thorn apple leaves used to be a component of "asthma cigarettes".[3]

1.5.4 Overdoses

Plants containing tropane alkaloids are sometimes ingested to experience its hallucinogenic effects, presumed medicinal effects or to commit suicide. The name belladonna in *Atropa belladonna* means beautiful women, and refers to the past use of this plant in European medicine to dilate the pupils in order to make a women appear more attractive.

Reference	Place, date	Incident
Wagner and Keim (2009)[2]	USA, 1993	318 cases of Datura poisoning were reported to the American Association of Poison Control Centers; the Centers for Disease Control and Prevention (CDC) reported 2 deaths.
Baselt RC, Cravey RH (1995)[45] cited by Namera (2005) [25]	USA, 1995	A pharmacy college student (male) ingested about 1 g of atropine together with alcohol; he was sent to a hospital and survived. His blood atropine concentration was 130 ng/mL.
Baselt RC, Cravey RH (1995)[45] cited by Namera (2005) [25]	USA, 1995	A 18-year-old male ingested atropine tablets (30 mg per tablet, but the number of the tablets is not known), and died. The atropine concentration in his whole blood was 200 ng/mL.

Reference	Place, date	Incident
Tiongson and Salen (1998)[46]	USA, 1998	50 *Datura stramonium* seeds caused hallucinations for 36 hours in an 18-year-old
Wagner and Keim (2009)[2]	USA, 2005	Of the 975 anticholinergic plant poisonings reported to the American Association of Poison Control Centers in 2005, there were no fatalities.
Lin et al (2002)	Taiwan, 2002	A 73-year-old male intentionally ingested a decoction made from approximately 30 g of the raw stem of a plant "Ting Kung Teng" (*Erycibe henryi* Prain) he picked from a hillside"), as recommended in traditional Chinese medicine for arthritis. Shortly, he developed a cholinergic syndrome that included dizziness, diaphoresis, chills, lacrimation, salivation, rhinorrhea, nausea, and vomiting. He was also hypothermic and hypotensive. Notable laboratory values included a normal serum cholinesterase and transiently elevated blood urea nitrogen, creatinine, and glucose. There is no previous report on the toxicity due to this herb in the literature. Active constituents of the herb include a number of tropane alkaloids, one of which possesses cholinergic rather than anticholinergic activities. A study conducted on mice, with a related herb, has demonstrated renal, hepatic, and erythrocyte toxicity.
Al-Shaikh et al (2005)[47]	Kingdom of Saudi Arabia, 2005	Acute *Datura stramonium* intoxication in a 6-year-old boy from Khamis Mushayt, KSA, who presented with restlessness, hallucinations and mydriasis 8 hours after ingesting the seeds of Datura plant.
Boumba et al (2004)[48]	Greece, 2004	A 19-y old male who intentionally ingested an unknown quantity of *Datura stramonium* seeds to experience its hallucinogenic effects was found dead. Hyoscyamine and scopolamine were detected in postmortem blood and urine. Blood concentrations of hyoscyamine and scopolamine were 1.1 and 0.2 μg/ml, respectively; in urine only hyoscyamine at 14.2 μg/ml was found. This fatality presents the highest blood concentrations ever reported and confirms that death was due to *Datura Stramonium* seed ingestion.
Koevoets and van Harten (1997)[49]	the Netherlands, 1997	A 20-year-old man presented with signs of thornapple intoxication: restlessness, disorientation, hallucinations, euphoria, and furthermore dry and red skin and symmetrical dilation of the pupils. Thornapple intoxication mimics atropine intoxication. Thorn apples (*Datura stramonium*) are seemingly becoming popular as a hallucinogenic drug.
Spina and Taddei (2007) [29]	Canada, 2007	A teenager brought a Jimson weed plant to a party after watching youths misusing the plant on a popular television show. Eight teenagers opened the seed pods, each chewing and ingesting the seeds from 2 to 3 pods (~100–300 seeds) in combination with alcohol. A 16-yearold white male and a 15-year-old female of Asian descent presented with a severe acute anticholinergic toxidrome after this ingestion, which was 1–2 hours before presentation.

2 Conclusions and recommendations

Secondary metabolites in wild and cultured plants can be toxic to humans and animals. Due to accidental or intentional mixing of these plants in food or feed the consumers of these products will be exposed to the toxins. Based on the incidents with both animals and humans described in the previous paragraphs it is to be expected that foods potentially (and unintentionally) containing tropane alkaloids would be herbal teas, herbal preparations (traditional Chinese or Ayurvedic medicins[12]), blue- or black berries (either fresh of dried), edible flowers. Contamination has also been found in buckwheat (for human consumption), soybean and linseed (animal feed). In the Netherlands buckwheat is mainly used for human consumption as flour for yeast dough (*poffertjes*, pancakes) or broken as buckwheat groats (Dutch: *boekweitgrutjes, boekweitgort*). In health food stores it is also sold as kernels. It is often recommended in diets for celiacs since it does not contain gluten. Roasted buckwheat grains are also known as 'kasha ' and have been known from the Eastern European cuisine. These are the products that should be monitored to prevent accidental exposure of humans to tropane alkaloids. Plants containing tropane alkaloids have also been used in homemade products like wine and toothpaste, but these products are not likely to be sold commercially.

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Appendix - Images of plants containing tropane alkaloids

Figure 3.1 Atropa belladonna berries.

Figure 3.2 - The leaves of Atropa belladonna.

Figure 3.3 - Atropa belladonna.

Figure 3.4 - Datura stramonium.

Figure 3.5 - Datura fruit.

Figure 3.6 - Duboisia myoporoides.

Figure 3.7 - Hyoscyamus niger.

Figure 3.8 - Mandragora officinarum berries.

Figure 3.9 - Latua pubiflora.

Figure 3.10 - Physalis peruviana fruit.

Figure 3.11 - Lycium barbarum.

Figure 3.12 - Convolvulus arvensis.

Figure 3.13 - Calystegia sepium.

Figure 3.14 - Scopolia carniolica.

Figure 3.15 - Erythroxylum coca.