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Review

Scopolamine in racing horses: Trace identifications associated with dietary or environmental exposure

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ABSTRACT

Scopolamine (L-hyoscine) identifications, often in small-number clusters, have been reported worldwide in performance horses over the last 30 years. Scopolamine is an Association of Racing Commissioners International (ARCI) class 3, penalty class B, substance with potential to affect performance. As such, scopolamine identification(s) in race or performance horses can result in significant penalties for the connections of the horse(s). Reviewed here is the worldwide distribution of scopolamine containing plants (primarily *Datura* spp.), with estimates of their potential toxicity to horses through dietary and/or environmental exposure. Also reviewed are the basic pharmacology of scopolamine and its precursor, urinary concentrations following feedstuff exposure, and the probable pharmacological/forensic significance of such findings.

Based on an overview of the world literature on scopolamine, the expected characteristics of inadvertent environmental exposure are also presented with a view to making clear the potential of scopolamine identifications, with or without atropine, as a direct and expected outcome of both the worldwide distribution of scopolamine-containing plants and the sensitivity of modern equine drug testing. It is of particular interest that only 2/30 reported post-event equine identifications of scopolamine have been associated with atropine, suggesting that failure to identify atropine is not a biomarker of pharmaceutical administration of scopolamine. Available quantitative information associated with scopolamine identifications is consistent with the 75 ng/mL regulatory threshold for scopolamine currently used in Louisiana racing in the USA and the 30 ng/mL reporting threshold in effect in European racing.

Introduction

Scopolamine (L-hyoscine), a tropane or 'belladonna alkaloid,' has been sporadically identified in racing horses worldwide since the advent about 30 years ago of low ng/mL equine drug testing. Since then, trace identifications of scopolamine and other environmental and dietary substances such as caffeine (Budhraja et al., 2007), benzoylecgonine (Camargo et al., 2006), and morphine (Camargo et al., 2005) have become increasingly common (Sams, 1997) and usually at much less than pharmacologically effective concentrations (Tobin et al., 2012). Furthermore, scopolamine identifications often occur in small number clusters, consistent with a local environmental source, in this case the *Datura stramonium* (Jimson weed). Equine ingestion of environmental toxins from plants is not uncommon. For instance, we cite an often fatal example, the pyrrolizidine alkaloids found in ragwort around the world and in the North-Western United States (USDA, 2009).

In this review, we summarize the chemistry, pharmacokinetics, pharmacodynamics, and toxicology of scopolamine (not to be confused with n-butylscopolamine, a structurally related synthetic, therapeutic drug), and document the worldwide distribution and occurrence of scopolamine containing plants. We then survey the scientific and world literature on its appearance outside of equestrian racing and sport to make clear its global or ubiquitous cultural presence and toxicological and pharmacological impact. Finally, we review the specifics of as many reported identifications as possible in racing and performance horses in the context of their worldwide occurrence, with the goal of developing useful guidelines for assessing the forensic significance of low concentration scopolamine identifications in post-event samples from performance horses.

Scopolamine and atropine, the belladonna alkaloids

The two principal pharmacologically significant alkaloids of the family *Solanaceae*, genus *Datura*, are scopolamine (L-hyoscine) and atropine (see Fig. 1). These alkaloids are toxic secondary

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Table 1
Names for *Datura* plants in old world cultures, demonstrating the long-recognized, essentially worldwide distribution of *Datura*.

Common name	Language
Bunjdeshtee	Persian
Chosen-asagau	Japanese
Da Dhu Ra, Tibetan	Tibetan
Datur-a	Mongolian
Datura, Dhattura, Dhatura	Sanskrit
Datura, Engletrompet	Danish
Devil's Trumpet, Flower of Ceylon	Santali
Dhetoora, Kala Dhutura	Hindi
Dhutro	Bengali
Dotter	Dutch
Goozgiah	Persian
Jousmathel, Tatorah	Arabic
Kachubong	Philippines
Karo Omatay	Tamil
Kechubong	Egyptian
Kechubong	Malayan
Kechubong	Bali
Man-t'o-lo, Nao–yang-hua, Shan-ch'ieh-erh	Chinese
Menj	Arabic/Yemen
Mnanaha	Swahili
Mondzo	Tsonga

metabolites present in several very successful and widely distributed genera of plants of the family *Solanaceae*, their toxicity serving to discourage herbivore grazing. However, their actions also include several useful pharmacological effects. The human history and cultural impact of plants of the *Solanaceae* family long antedates modern pharmacology and toxicology, with the term *Datura* itself having ancient Indo-European roots (Table 1). Theophrastus wrote about the hallucinogenic effects ('insanity') caused by *Datura stramonium* as early as circa 300 BCE (Scarborough, 1978).

Among the common names for various species of *Datura* are Thorn Apple (from the appearance of its spiked seed pod; Fig. 3), Devil's Trumpet, Angel's Trumpet, and Desert Trumpet (from the shape of its bloom; Fig. 2), and in the US, Jimson weed, *Datura stramonium*. Although its ubiquity makes it difficult to trace its linage, American Jimson weed is thought to be native to India. Jimson weed, named after Jamestown, the first English settlement in the Americas, was presumably imported from England by the settlers as a medicinal herb, the British having originally imported it from Constantinople (Friedman and Levin, 1989). Since then *Datura* has spread across the US and is widely known as a weed that grows in close proximity with food crops such as corn, sunflower seeds, soybean seeds, millet, and linseed (Rwiza, 1991; Piva and Piva, 1995; Lehoczky and Reisinger, 2003; Beres et al., 2005). Indeed, one author (CGH), since his youth, is personally familiar with 'Jimson weed' as a plant commonly found on Central Kentucky farms (Figs. 2 and 3).

As plant toxins, atropine and scopolamine are both orally bioavailable. Of the two, scopolamine enters the central nervous system (CNS) more readily and produces psychological effects, which makes plants containing scopolamine attractive for human recreational and social use. Atropine does not as easily enter the CNS. However, there is no direct comparison of the two alkaloids in the literature in terms of oral bioavailability in the horse, and there is conflicting information about the oral bioavailability of scopolamine in man. A review article by Renner et al. (2005) suggested low oral bioavailability of scopolamine due to the very low (2.6%) urinary detection of the parent drug. These authors reported that the peak plasma concentration occurs at 0.5 h following oral administration of scopolamine and since only 2.6% of the parent drug is excreted in urine, a first-pass metabolism has been suggested to occur after oral administration.

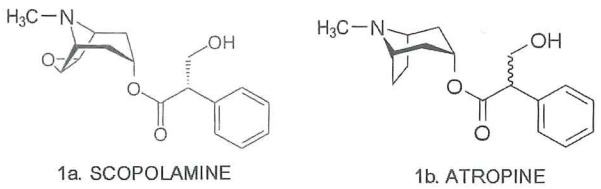

Fig. 1. The primary tropane or belladonna alkaloids found in *Datura*: scopolamine, p*K*a 7.75, and atropine, p*K*a 9.50.

Datura plants are known in most if not all human cultures as pharmacologically active agents (Tables 1 and 2). Their pharmacological and therapeutic uses are well understood in terms of the technical capabilities of each culture and, based on the number of toxic events reported in the literature, there is an ongoing significant risk of consequences up to and including overdose, toxicity, and death for both humans and animals (including horses) in most if not all areas of the world.

Datura and scopolamine toxicity in animals and man

Livestock and herbivores

Live *Datura* plants (Figs. 2 and 3) are generally unpalatable to livestock. Problems with exposure or toxicity therefore usually occur when the plant or its seeds are harvested and incorporated into hay or other animal feed where it is readily consumed. Toxicity is commonly due to the ingestion of *Datura* seeds, which, due to the widespread occurrence of the weed in close proximity with animal feed crops, are often contaminants in grains and feed. The seeds of Jimson weed contain atropine in a concentration of 1.69–2.71 mg/g and scopolamine in a concentration of 0.36–0.69 mg/g (Friedman and Levin, 1989). Ingestion of seeds by food animals usually results in chronic or subclinical toxic effects but acute poisoning is rarely seen from exposure to Jimson weed contaminants in feedstuffs (Piva and Piva, 1995). A study by Galey et al. (1996) reported that ingestion of 6.5 g of *Datura* plant material by horses resulted in peak urine concentrations of scopolamine approaching 100 ng/mL with no clinical symptoms.

Studies have been undertaken to assess the toxicological effects of *Datura* seeds in animal food (Kovatsis et al., 1993) and the relative toxicity of *Datura* alkaloids in farm animals has been reported (Day and Dilworth, 1984; Piva and Piva, 1995). Several studies have been performed to determine an acceptable level of *Datura* contamination in animal feed and it was concluded that a total alkaloid concentration as high as 75 mg/kg feed can be safely administered to egg-laying hens (Kovatsis et al., 1994). In trials, the threshold limit in pigs (20–60 kg liveweight) was 1.5 mg alkaloids/kg of feed (1.21 mg alkaloids/kg liveweight) (Worthington et al., 1981; Nelson et al., 1982; Piva et al., 1997). In Hong Kong, the maximum permitted alkaloid content in the feed of racing horses is 30 ng/g for scopolamine, and 100 ng/g for atropine.[1]

Accidental human exposure

Accidental ingestion by humans of toxic quantities of *Datura* is common and widespread not only in the US (Krenzelok and Mrvos, 2011) but worldwide, with contaminated food sources being the most common route of exposure. Cases involving contaminated food have included: Venezuela, wasp honey (Ramirez et al., 1999); Tanzania, millet seed made into porridge (Rwiza, 1991); Slovenia, buckwheat flour (Perharic et al., 2013); Japan, eggplant

[1] Personal communication from a feed company representative, 2013.

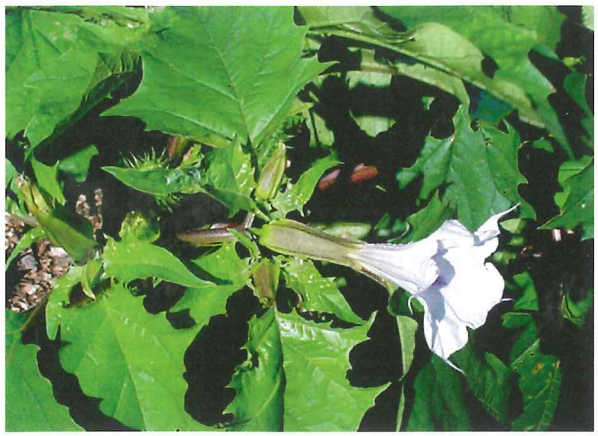

Fig. 2. Jimson weed (*Datura stramonium*), pictured in September in Kentucky.

grown grafted onto a Devil's Trumpet (Oshiro et al., 2008); Greece, *Datura* accidentally harvested with wild vegetables (Papoutsis et al., 2010). In India, where *Datura* preparations are used as a homeopathic medication, between 1950 and 1965 there were 2778 human deaths associated with *Datura* (Preissel and Preissel, 2002). China also has numerous cases of herbal medicine-induced poisoning (Cheng et al., 2013). In the USA a family ingested a potato stew in which they had included ingredients from their yard, including Jimson weed (MMWR, 2010). Other examples of *Datura* related human toxicity are presented in Table 2.

The above reports of *Datura* toxicity are examples of cases that have reached the world scientific literature because they are 'acute' toxicity cases and, as such, are associated with high plasma and urinary concentrations of tropane alkaloids. Given this circumstance, we must assume that the worldwide incidence of unreported accidental human scopolamine exposures producing trace urinary concentrations, such as those concentrations reported in horses, must occur at a frequency at least hundreds of times that of the reported acute toxicity cases.

Intentional human exposure

Due to its hallucinogenic effects, *Datura* has long been used by humans as a ceremonial, sacramental, medicinal, and recreational substance. This widespread use of the plant has resulted in many cases of accidental toxicity and acute poisoning by scopolamine and atropine (MMWR, 1995; Oerther et al., 2010). Symptoms of toxicity include hallucinations, mydriasis, motoric restlessness, excessive talkativeness, convulsive sobbing, sexual excitement, and combative behavior and autoaggressive tendencies (Al-Shaikh and Sablay, 2005; Marneros et al., 2006). The *British Medical Journal* (Chambers and Lawrence, 1858) reported that three boys, aged 7–8, ingested Thorn Apple seeds after having been told they were wine-making ingredients. They recovered in several hours after experiencing convulsions and coma. Similarly, a 76-year-old man suffered acute respiratory distress due to scopolamine poisoning after ingesting a small quantity of 'Moonflower wine' made from Angel's Trumpet (*Datura suaveolens*) (Smith et al., 1992).

The behavioral effects of *Datura* poisoning can be dramatic, as in the case of the young German man who drank Angel Trumpet tea, and while under its influence amputated both his tongue and penis (Marneros et al., 2006). In Zabrze, Poland, 18 boys between the ages 15–17 with *Datura stramonium* toxicity were treated in the years 1999–2001 (Torbus et al., 2002). Guharoy and Barajas (1991) report on four cases of poisoning due to ingestion and smoking of Jimson weed by California teenagers. The flowers of *Datura arborea* (Angel's Trumpet) were eaten by a group of seven Australians resulting in hallucinations with one of the affected persons drowning in shallow water (Hayman, 1985). In another California case, a 15-year-old boy was brought to the hospital emergency room with hallucinations. During examination, the patient reached into the air as if trying to catch a nonexistent object. The patient later stated that he and friends had intentionally consumed Jimson weed (Chan, 2002).

Non-racing equine exposure to *Datura* and scopolamine

Due to the ubiquitous nature of *Datura*, the horse, like all wild and domesticated herbivores, is subject to occasional ingestion of scopolamine containing plants. In the USA, the principal plant of interest is Jimson weed (*Datura stramonium*), considered to be one of the principal toxic plants for horses (Delaunois and Demoulin, 1998). In Bulgaria, multiple horses experienced signs of toxicity after eating chopped maize contaminated with *Datura stramonium* (Binev et al., 2006). The symptoms of acute toxicity were: mydriasis; complete refusal of food; lack of thirst, defecation, and urination; dry mucosae (oral, nasal, vaginal, and rectal); diffusely reddened conjunctivae; disturbances in locomotion; hyperesthesia; muscle cramps, and hyperreflexia. In South Africa, Naude et al. (2005) reported that an outbreak of intractable impaction colic affecting 18/83 horses was stopped by withdrawing hay contaminated with young *Datura* plants. In Spain, Soler-Rodríguez et al. (2006) described an outbreak of *Datura stramonium* poisoning in horses as a result of the ingestion of lucerne (alfalfa) hay contaminated with *Datura.*

In South Africa, eight mares were kept in a paddock for student training at the Department of Theriogenology at the Veterinary Faculty of Onderstepoort (Gerber et al., 2006). Two developed colic and of these one developed intestinal atony, underwent surgery, and was euthanased. Scopolamine was detected in the urine of the surviving horse for 3 days following the attack of colic. *Datura ferox* and possibly *Datura stramonium* plus several other weed species were identified in the hay that had been fed to these horses. Of five bales of hay examined, three contained *Datura.* Both the urine from the surviving horse and *Datura ferox* plant material selected from the hay were analyzed for atropine and scopolamine (Table 3).

'Day 1' in Table 3 is the day following the first indication of toxicity. The times of *Datura* ingestion are unknown, so the peak concentration at an earlier sample collection time could possibly have been much higher than those reported for one or both alkaloids. We also note that these alkaloid concentrations in plant material differ significantly from the data of Friedman and Levin (1989) who reported that the seeds of Jimson weed in the US contain atropine in a concentration of 1.69–2.71 mg/g and scopolamine in a concentration of 0.36–0.69 mg/g. However, the alkaloid content of *Datura* and its plant parts varies widely among species and with the season of growth as reported by Jalabova et al. (2012).

Respondek et al. (2006) investigated the urinary excretion of *Datura* alkaloids in horses. The authors reported that, at two tested doses, atropine was not detected in urine, while scopolamine at the lowest dose tested produced detectable concentrations in urine. We note that current routine equine drug testing technology is likely to be more sensitive than the analytical procedures used by Respondek et al. (2006).

Datura and scopolamine in racing

Considering the ubiquitous nature of *Datura* in the environment and the high sensitivity of modern analytical technology, it is not surprising that trace level identifications of scopolamine and

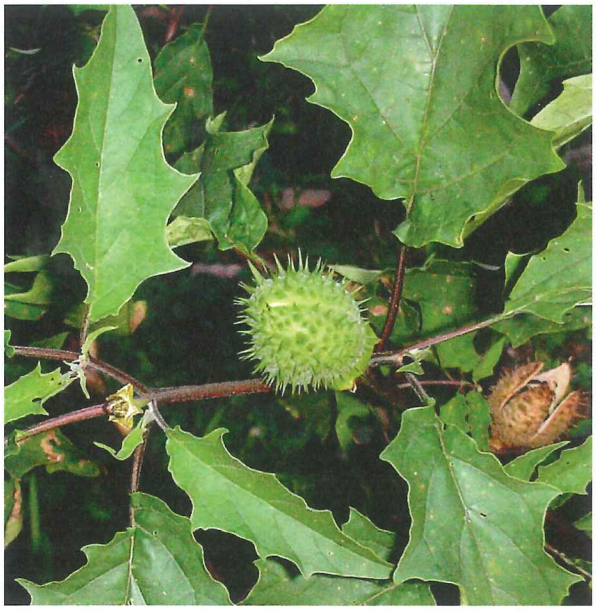

Fig. 3. Stages in the development of the Jimson weed seed pod (Thorn Apple). Left of center, the seed pod is beginning to develop after recently losing its trumpet shaped bloom, center is the fully developed pod, and on the right the mature pod has dried and opened to release its seeds.

atropine, as well as other environmental and dietary contaminants, are found in racehorse drug testing at trace concentrations that are pharmacologically ineffective (Tobin et al., 2012). Furthermore, these identifications often occur in small clusters, consistent with an episodic environmental source.

Since the first recorded scopolamine identification in racing in 1982, there have been about 30 identifications or episodes of identifications of scopolamine in equine urine (ARCI Records, 2013). In only two of these cases has atropine been detected in the urine. In many of these cases the presence of scopolamine has been attributed to dietary contamination by Jimson weed or other *Datura* species.

There have been several reported scopolamine identifications in the USA. In Illinois, one Standardbred horse was disqualified as winner of two races in 1982. The source of scopolamine was thought to be Jimson weed in hay and the trainer was suspended for 90 days with redistribution of purse. California had one scopolamine identification in 1990, and one in 1991. Santa Anita had an episode of scopolamine identifications involving seven horses and six trainers between February and April 1994. The scopolamine identifications were attributed to hay contamination by Jimson weed. Purses were forfeited and trainers placed on probation. Again, at Santa Anita in 1998, two scopolamine identifications resulted in purses being forfeited without trainers being fined. In 2005 at two California tracks there were two scopolamine identifications involving separate trainers. Purses were redistributed and the trainers fined $1500.[2] In 2007, at Golden Gate Fields in California, a scopolamine identification resulted in the purse being forfeited and the trainer being fined $1000. At Colonial Downs in Virginia in 2011 scopolamine and atropine plus other drugs were identified in a single horse, presumably the result of a therapeutic administration.

These and other cases with references are further elucidated in Table 4. No doubt, the sensitivity of analytical methodology has increased many fold during the 20 years or so since these identifications were recorded, and we are unable to determine if analysis of atropine was attempted in every case cited. Nevertheless, we believe the absence of findings of atropine in most of these cases is related to the low concentrations of atropine which are to be expected in most cases of ingestion of *Datura*, a trend addressed at length elsewhere in this document.

Accidental *Datura* contamination of animal food is not limited to herbivores. In England between December 2011 and February 2012, scopolamine and atropine were identified in five urine samples from Greyhound racing. According to a food company representative, *Datura* seed was identified in imported maize, which was a component of the dog food. The racing regulator's Disciplinary Committee determined that feed contamination with *Datura* was the most likely explanation for the positive samples.[3]

The forensic significance of urinary identifications of scopolamine and/or atropine

Due to the ever-increasing sensitivity of modern analytical testing technology, the identification of trace quantities of environmental substances in equine samples is becoming increasingly common. To deal with trace identifications of environmental substances, both human and equine drug testing organizations have adopted regulatory 'thresholds'.[4,5] A threshold (or cut-off or reporting level) is the concentration below which a substance is deemed to have no forensic or pharmacological relevance. Such identifications are not reported or 'called' positive, thereby avoiding unjustly penalizing horse owners or trainers.

Approaching the problem of low concentration scopolamine identifications, Louisiana has set a regulatory threshold for scopolamine of 75 ng/mL in urine, consistent with broadly similar regulatory thresholds for caffeine, morphine, and benzoylecgonine, three common environmental substances with thresholds in place in many states in the USA and elsewhere (RMTC, 2013). The only other scopolamine reporting threshold of which we are aware is in Europe where both scopolamine and atropine thresholds of 30 ng/mL in urine have been proposed (Bonnaire, 2013). The 75 ng/mL Louisiana scopolamine threshold is intended to be an 'environmental no-effect' threshold, which we note can be significantly different from the range of concentrations that may be encountered with innocent 'toxicological' exposures that can have potentially lethal consequences and generate concentrations of scopolamine which will greatly exceed the 75 ng/mL in urine.

The Louisiana 75 ng/mL regulatory threshold is consistent with what concentration data are available for naturally occurring scopolamine identifications and with the Respondek et al. (2006) administration data. This threshold is of the same order as the Asian Screening Limit of 25 ng/mL for the closely related therapeutic compound, n-butylscopolamine (Tobin et al., 2012). We note that the lack of quantitative data for naturally occurring scopolamine identifications is in large part due to the reluctance of racing chemists and regulators to make (or reveal) any good faith estimates of the concentrations of scopolamine and atropine in post-race urine samples.

A factor of interest with respect to scopolamine is that when identifications have occurred in a Thoroughbred racing environment there is a significant probability of more than one identification

[2] US$1 = approx. €0.74, £0.62 at 22 November 2013.

[3] See: Greyhound Board of Great Britain, Disciplinary Committee Inquiries Report, 15 May 2012; http://www.gbgb.org.uk/files/DC%20Findings_150512.pdf (accessed 6 October 2013).

[4] See: Controlled therapeutic medications. Racing Medication and Testing Consortium 2013; http://www.rmtcnet.com/resources/RMTC%20Therapeutic%20Substances%20List-July%202013.pdf (accessed 23 August 2013).

[5] See: Mandatory Guidelines for Federal Workplace Drug Testing Programs. Cutoff concentrations. Substance Abuse and Mental Health Services Administration. Department of Health and Human Services. The Federal Register 73 (228): Section 3.4.

Table 2
Datura: Cultural use as herbal medicine.

Region or language	Common name	Uses	Toxicity
Nepal	Dhaturo, Seto Dhaturo, Dahattur and Madak	Treatment of headaches, indigestion, sprains, and tapeworms	
Sanskrit speaking regions	Dhatturdhurtadhustura, Unmatta, Kanakahwaya, Dewatakitawasturi Mahamohi Shivapriya, Matulo Madanashchasya phale Matulaputraka	Pain relief, tonic, febrifuge	India 1950–1965. 2778 human deaths from ingestion
Brazil	Estramonio	Entheogen, analgesia	Toxicosis case from homemade toothpaste
China	Chan K'iue Tse *yáng jīn huā*	Traditional Chinese medicine for asthma, bronchitis, pain and flu	Mydriasis cases associated with herbal medicine use
English speaking regions	Thorn Apple, Jimson weed, Mad Apple	Recreational euphoric agent	'Moonflower' intoxication for euphoria
France	Chasse-taupe		
Spanish speaking regions	Trompetilla		
Nigeria		Treatment of insect bites and stings	Acute toxicosis from smoking flowers and drinking tea from seeds
Pakistan		Treatment of headaches and sagging breasts	
Mexico	Toloache	Herbal medicine – spasmolytic agent	

Table 3
Concentrations of alkaloids in a case of accidental equine exposure to *Datura* (Gerber et al., 2006).

Source	Concentration	
	Atropine	Scopolamine
Urine (day 1)	0.4 ng/mL	68 ng/mL
Urine (day 2)	<0.1 ng/mL	5 ng/mL
Urine (day 3)	None detected	0.4 ng/mL
Datura leaves	17 μg/g	1.9 mg/g
Datura stems	25 μg/g	1.2 mg/g
Datura seed	14 μg/g	1.5 mg/g

occurring (a cluster of events), which is entirely consistent with the identifications being due to a shared feedstuff or environmental source.

The question of whether or not identification of scopolamine without atropine detected in equine urine indicates that the substance did not originate from *Datura* plant ingestion or exposure, but from drug administration, was specifically addressed after a cluster of scopolamine identifications in California in 1994 (Lavin vs. CHRB, 1997).[6] In a *Datura* dosing experiment at the University of Iowa, the ratios of scopolamine to atropine in equine urine 'ranged from over 100:1 (higher levels soon after dosing) down to approximately 10:1 at lower levels (after some time had elapsed).' In one high-dose horse that suffered acute toxicity, the ratio of scopolamine to atropine was more than 1000:1 with concentrations of scopolamine reaching 10,000 ng/mL. Horses ingesting lower quantities of *Datura* showed no clinical signs of toxicity at scopolamine urine concentrations of 10–150 ng/mL (F.D. Galey and W. Hyde, personal communication).

Quantitatively equivalent oral doses of scopolamine and atropine were reported by Bonnaire et al. (2008) to result in urinary concentrations of scopolamine that were about 10 times the concentration of atropine. Gerber et al. (2006) reported, after accidental ingestion of *Datura ferox* by horses, urinary ratios of scopolamine to atropine of 170:1. Relatively straightforward calculations, based on the data presented by Respondek et al. (2006), suggest that quantitatively equivalent oral doses of atropine and scopolamine to horses will result in urine concentrations of scopolamine, which can be more than 60–300 times greater than the urinary concentration of atropine.

In light of these quantitative data, it is perhaps not surprising that equine exposure to, or ingestion of, *Datura* results in scopolamine with no atropine detected in urine, a finding consistent with available worldwide post-race testing data (Table 4) where only two of about 30 positive scopolamine findings from 1982 to date were also reported positive for atropine.

Scopolamine appears to be more orally bioavailable than atropine and, from the data of Galey et al. (1996), appears to have a longer terminal plasma half-life, which means that following repeated low concentration exposures to *Datura*, scopolamine will tend to have significantly higher urinary steady-state concentrations than atropine. In addition, atropine, with a p*K*a of 9.5, will be almost completely ionized at physiological pH values, which will restrict its ability to cross cell membranes, and presumably this helps to account for its relative lack of significant CNS pharmacological effects. On the other hand, scopolamine, with a p*K*a of 7.56, will have a significant non-ionized fraction at physiological pH values and as such will readily cross cell membranes.

With respect to interpretation of the forensic significance of urinary scopolamine findings, it appears that low concentrations of scopolamine, i.e., less than the 75 ng/mL Louisiana regulatory threshold, are forensically unremarkable and fully consistent with an environmental source (Galey et al., 1996), given the worldwide distribution of scopolamine-containing plants. If the individual's

[6] See: Lavin vs. CHRB (California Horse Racing Board). Leagle Eagle. http://www.leagle.com/decision/199732057CalApp4th263_1304 (accessed 9 August 2013).

Table 4
Worldwide detections of scopolamine in equine samples.

Substance	Location or jurisdiction	Date	Number of horses	Urine concentration, ng/mL	Source	Reference
Scopolamine	Illinois Racing Commission	October 1982	2		Jimson weed in hay	ARCI Records (2013)
Scopolamine	CHRB Los Alamitos	January 1990	1			ARCI Records (2013)
Scopolamine	Florida	1991	1			ARCI Records (2013)
Scopolamine	CHRB Santa Anita	February–April 1994	7	'Minute' 15–47	Jimson weed in straw bedding	ARCI Records (2013), Lavin vs. CHRB (1997)
Scopolamine	CHRB Santa Anita	January 1998	2			ARCI Records (2013), CHRB Press Release (1998)[a], CHRB Press Release (1998)[b], Thoroughbred Racing Communications (1998)[c]
Scopolamine	CHRB Los Angeles Turf Club	August–December 2005	2			ARCI Records (2013), State of California (2007)[d]
Scopolamine	South Africa	2006	2	>68	*Datura ferox* in hay	Gerber et al. (2006)
Scopolamine	CHRB Golden Gate	February 2007	1			ARCI Records (2013), Hollendorfer fined (2008)[e]
Scopolamine	Harness-racing New Zealand	2008	1			New Zealand JAR (2008)[f]
Scopolamine Atropine	Harness-racing New South Wales	2010	1		Hay containing *Datura*, live plant in stable area	Harness Racing New South Wales (2010)[g]
Scopolamine	Para-Equestrian New Zealand	2011	1			Equestrian Sports New Zealand: Para rider fined (2011)[h]
Scopolamine, atropine + other drugs	Virginia, Colonial Downs	July 2011	1		Presumed therapeutic drug administration	ARCI Records (2013)
Scopolamine	Singapore	2011	5		Feed contamination by *Datura* seed	Singapore Turf Club (2013)[i]
Scopolamine Atropine	Racing Victoria	2013	10 from 7 stables	'Low level traces'	Feed contamination by *Datura*	Racing Victoria (2013)[j,k]
Scopolamine	Research study	1996		~100 max	6.5 g *Datura* plant material, oral	Galey et al. (1996)
Atropine				~10 max		
Scopolamine Atropine	Research study	2008		25–140 10–25	Oral, 10 mg/day	Bonnaire et al. (2008)
Scopolamine	Research study	2006	2 of 5 3 of 5	30–50 30–220	Oral, 2 mg/day Oral, 5 mg/day	Respondek et al. (2006)
Atropine			0 of 5 0 of 5	Not detected Not detected	Oral, 5 mg/day Oral, 15 mg/day	

One author (TT) recalls reports of early scopolamine detections in English racing but has been unable to recover any records of same

[a] See: CHRB Press Release 1998. California Horse Racing Board; http://chrb.ca.gov/press_releases/PRMarch81998.htm (accessed 15 August 2013).
[b] See: CHRB Press Release 1998. California Horse Racing Board; http://chrb.ca.gov/press_releases/PRMarch251998.htm (accessed 21 August 2013).
[c] See: 'Two Lukas runners lose purse money'. Thoroughbred Racing Communications Thoroughbred Notebook 2013. http://www.isd1.com/trc/trc98/trc0324.html (accessed 20 August 2013).
[d] See: State of California 2007. California Horse Racing Board. CHRB Press Release Weekly Update. Sacramento: http://www.chrb.ca.gov/press_releases/2007_03_24_press_release.pdf (accessed 6 August 2013).
[e] See: 'Hollendorfer fined in scopolamine case'. *Bloodhorse*. 14 December 2008; http://www.bloodhorse.com/horse-racing/articles/48439/hollendorfer-fined-in-scopolamine-case (accessed 21 August, 2013).
[f] See: New Zealand Judicial Control Authority for Racing 2008. Non Race Day Inquiry – S.J. Boyd. Wellington. http://www.jca.org.nz/race-days/dummy-location_2001-01-01/hearing_dummy-location_2001-01-01_1476 (accessed 14 August 2013).
[g] See: Harness Racing New South Wales 2010. Stewards Update-Australian Harness Racing. Retrieved from Harness Racing New South Wales website: New Zealand. Judicial Control Authority for Racing. Non Race Day Inquiry – S.J. Boyd. Wellington. http://www.harness.org.au/news-article.cfm?news_id=13769 (accessed 4 September 2013).
[h] See: Para rider fined. 21 May 2011. Retrieved from http://www.horsetalk.co.nz/news/2011/05/173.shtml (accessed 13 August 2013).
[i] See: Singapore Turf Club, 1 January 2013. Retrieved from http://www.turfclub.com.sg/Racing/Pages/ViewRaceResult/2081/10 (accessed 15 August 2013).
[j] See: Racing Victoria 2013. Trainers tools kit notice – low trace levels of hyoscine and atropine. http://www.racingvictoria.net.au/TrainersToolkit/Notices/Veterinary/Low_level_traces_of_Hyoscine_and_Atropine.aspx (accessed 13 August 2013).
[k] See: Racing Victoria 2013. Stewards report – Hyoscine investigation, 14 August 2013. http://www.racingvictoria.net.au/TrainersToolkit/Notices/Veterinary/Low_level_traces_of_Hyoscine_and_Atropine.aspx (accessed 23 August 2013).

medication record is 'clean' and the concentration is low, and there are no other extenuating circumstances, then the overwhelming likelihood is that the positive finding is due to an innocent and forensically irrelevant environmental substance exposure.

If, as has occurred in many of the events listed in Table 4, there is more than one horse and/or trainer involved in scopolamine findings (as is often the case in Thoroughbred racing) then the probability that the event is an innocent inadvertent environmental contamination becomes overwhelming. This was the case in the 2013 Australian identifications, where the authorities soon concluded that the sources were of innocent environmental origin and took no action against the trainers. The Australian authorities' report drew specific attention to the relatively high sensitivity of testing/reporting levels in the laboratory making the initial scopolamine identifications in this matter, whereas at least two other laboratories had different and less stringent testing/reporting levels for scopolamine and would not have reported the samples positive had they done the initial screening.

Scopolamine and atropine are toxicologically active plant substances, and man has long been familiar with their pharmacological properties. As such, scopolamine and atropine are well identified, well understood and long and variously described and

used by virtually all human cultures. Considering the widespread distribution of scopolamine-containing plants, the random worldwide identification of ineffective trace levels of scopolamine in high sensitivity drug testing performed in racing horses should come as no surprise. In the first place, the horse, as a herbivore, is a target species, with the most likely source of scopolamine being fodder or bedding which includes scopolamine-containing plant materials, hay, or grain-based feed. Secondly, horses are kept, fed, and bedded in groups, so scopolamine exposure will usually involve more than one horse, giving rise to the classic cluster pattern of identifications so often seen in scopolamine identifications involving Thoroughbred racing horses.

Given these circumstances, the first response to scopolamine identification should be evaluation of the stated concentration. If the urinary concentration is of the order of the Louisiana 75 ng/mL threshold or less, this most likely indicates an inadvertent environmental source (even higher values do not exclude environmental exposures, as the 75 ng/mL is meant to be a 'no effect' threshold). The next step is to physically inspect the fodder, bedding and other environmental sources for scopolamine containing plant material. Failure to find contaminating plant material, however, does not mean that it does not, or did not, exist. *Datura*, for instance, is not uniformly distributed in a field or in hay. One bale of hay may contain significant quantities of *Datura*, but the next bale may contain none. Only one or two horses in a herd may be significantly affected. It is also advisable to promptly test the urine of other horses in the contact population for the presence of scopolamine and related substances. The samples, however, must be taken in the same manner as the sample in which the scopolamine was originality identified, i.e. usually a urine sample, and must be analyzed at the same level of sensitivity as the original samples. Looking for scopolamine in blood at the same level of sensitivity as a urinary positive is virtually certain to yield a negative and as such a forensically misleading result.

Additionally, if the concentration of scopolamine in the sample is low (<75 ng/mL), then the absence of atropine is unremarkable, and the only administrative action that should be required is (as taken by the Australian regulators) to notify affected or potentially affected horsemen to watch for scopolamine-containing plants and, if possible, to change their fodder/bedding source. Because of the very large between-plant differences in the actual concentrations of atropine and scopolamine, the apparently different oral bioavailabilities of these substances, and the longer plasma or urinary half-life of scopolamine compared to atropine, the failure to detect atropine as a urinary companion to scopolamine in no way allows one to conclude that a finding of scopolamine alone is evidence of administration of pharmacologically pure scopolamine.

One final matter needs to be explicitly set forth. With identification of a possible environmental substance such as scopolamine, racing chemists should be encouraged (perhaps required) to present their best good faith estimates of the concentrations of scopolamine, atropine, and other analytes present in the samples. Quantitative data are essential if the pharmacological and forensic significance of the findings, and comparisons with other reported identifications, are to be made. The reluctance of racing chemists or regulatory organizations to report (or reveal) their best good faith estimates of the concentrations of dietary and environmental analytes present in forensic samples is a major hindrance to our better understanding of the clinical and regulatory significance of these identifications. We believe that the preponderance of scopolamine identifications result from random inadvertent environmental or dietary exposure, and with respect to the great majority of racing cases presented in Table 4, are of no regulatory significance whatsoever.

Conclusions

Considering the widespread distribution of scopolamine-containing plants, the random worldwide identification of ineffective trace levels of scopolamine in high sensitivity drug testing performed in racing horses should come as no surprise. Because of the large between-plant differences in the actual concentrations of atropine and scopolamine, the apparently different oral bioavailabilities of these substances, and the longer plasma or urinary half-life of scopolamine compared to atropine, the failure to detect atropine as a urinary companion to scopolamine does not permit a conclusion that finding scopolamine alone is evidence of administration of pharmacologically pure scopolamine. We conclude that most equine scopolamine identifications result from random inadvertent environmental or dietary exposure, and with respect to the great majority of racing cases are of no regulatory significance. Quantitative data are essential if the pharmacological and forensic significance of the findings, and comparisons with other reported identifications, are to be made. We believe racing chemists and regulatory organizations should be encouraged, if not required, to release quantitative data as failure to do so is a disservice to the racing community and an impediment to the advancement of science.

Conflict of interest statement

None of the authors of this paper has a financial or personal relationship with other people or organizations that could inappropriately influence or bias the content of this paper.

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