The Veterinary Journal 199 (2014) 324–331

Contents lists available at ScienceDirect

The Veterinary Journal

journal homepage: www.elsevier.com/locate/tvjl

Review

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

Kimberly Brewer [a], Levent Dirikolu [b], Charlie G. Hughes [c], Thomas Tobin [c,*]

[a] 1711 Lakefield North Court, Wellington, FL 33414, USA
[b] College of Veterinary Medicine, University of Illinois at Urbana–Champaign, Urbana, IL 61802, USA
[c] The Maxwell H. Gluck Equine Research Center, University of Kentucky, Lexington, KY 40546, USA

ARTICLE INFO

Article history:
Accepted 6 December 2013

Keywords:
Scopolamine
Penalties
Atropine
Horses
Racing

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

* Corresponding author. Tel.: +1 859 218 1092.
E-mail address: ttobin@uky.edu (T. Tobin).

1090-0233/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tvjl.2013.12.013

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.

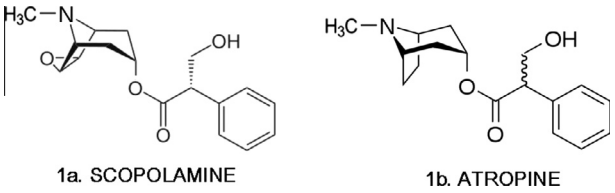

Fig. 1. The primary tropane or belladonna alkaloids found in *Datura*: scopolamine, p*Ka* 7.75, and atropine, p*Ka* 9.50.

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.