

Datura Stramonium L. - Narcotic, Anodyne or Poison?

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Abstract

The plant species Daturastramonium L., which is a member of the Solanaceae family was well known to the Greeks and Romans as a soporific, narcotic and anodyne. Modern pharmacology and phytochemistry ascribe these properties to the plant's possession of with tropane alkaloids. We can now understand how the ancient herbalists determined a particular dosage to achieve a desired effect.

Keywords: *Daturastramonium L.*, alkaloids, soporific, anodyne, phytochemistry

Introduction

Daturastramonium L. was the source of a very popular drug used in ancient times, due to the pain-relieving properties it possessed and the sleep that it induced. However, it was also known to be a troublesome, highly poisonous plant. Indications were ascribed by several secondary medicinal resources and, since *Datura* seemed to have many synonyms (see Nomenclature), it is evident that herbalists knew this plant together with its properties. The ancient Romans and Greeks knew (or claimed to know) the physiological effects of medicine on the human body and we found several texts written by Dioscorides¹ (40–90 A.D.), Theophrastus² (ca 370–285 B.C.), Celsus³ (fl. 37 A.D.) and Pliny the Elder⁴ (23–79 A.D.) about these.

During training as a pharmacist, one of the questions commonly asked is: “What is the effect of a certain drug?” Out of a classicist’s view one would ask: “Why did the ancient doctors specifically prescribe *Datura* for pain or to induce sleep?” When you look at the above questions as a pharmaceutical classicist, they could be combined as: “Which active ingredients in *Datura* exert the property of inducing sleep or relieving pain?” or “Did *Datura* really induce sleep (or was it a case of mind over matter)?” Did the drug really work?

The phytochemical properties of crude drugs have predictable physiological effects in the living human. Therefore, presuming that humans have not changed except incrementally in their physiological chemistry over the short span of two millennia, one can likewise document the effects of narcotics and analgesics in Graeco-Roman pharmacology, provided that the botanical sources and their manufactured forms are carefully identified. A secondary assumption is that both ancient and modern plants carry identical phytochemical properties, so that the descriptive nomenclatures of modern botany and phytochemistry reveal multiple pharmacological principles and their actions in ancient drugs, as well as their potentially undesirable side effects.

The questions also arise as to how ancient herbalists determined the correct dosage and whether valid indications were ascribed to this specific plant. Comparing the alkaloids found in this plant to their known effects gives one the opportunity to prove the validity of the early accounts of the use of this plant.

¹See Figure 1.

²See Figure 2.

³See Figure 3.

⁴See Figure 4.

Ancient use of *Datura*

Datura as soporific, narcotic and local anodyne

Dioscorides, as well as Theophrastus, (Theop. *H.P.* 9.11.5) concluded that *Datura* was used as *hypnotikon* (sleep-inducer) (Diosc. 4.74). Theophrastus likewise indicates that when a draught was prepared of bruised bark soaked in wine, it induced sleep.

The *De Medicina* of Cornelius Celsus records that *Datura* was not only used to induce sleep, but also as a topical anodyne for local pain relief. It also has an astringent effect due to the presence of tannin (5.20.3).

Pliny the Elder, however, wrote the following on *Datura*:

"*Quin et alterum genus quod halicacabonvocantsoporiferumestatqueetiamopiovelocius ad mortem, ab aliismorion, ab aliis moly appellatum*" (*H.N.* 21.180).

"There is besides another kind, with the name of *halicacabos*, which is soporific, and kills quicker even than opium, by some called *morion* and by others *moly*."

The mental effect of *Datura* in the process of inducing sleep

When Dioscorides describes the property (*dynamis*) of the *strychnosmanikos* root, he remarks that a *drachma*⁵ of the substance taken with wine engenders not unpleasant mental images, but if two *drachmai*⁶ are quaffed, you could lose your wits for as long as three days (4.75). He warns that too large a quantity will have a fatal effect.

Theophrastus writes that the plant called *strychnos* induced sleep, caused madness^{7,8} and upset the mental powers. Celsus also refers to the use of *Datura* to soothe the insane. He writes that *solarium*, which the Greeks call *strychnos*, is one of the plants which simultaneously "repress" (*reprimunt*) and "cool" (*refrigerant*) (2.33.2). He writes:

"*Utile etiam in quibuscumque viribus duae herbae sunt, solanum et muralis, sisimul ex utraque suo expresso caput impletur. Cum febris remisit, frictione utem dum est, parcius tamen in iis, quoniam in his, qui nimis tristessunt*" (3.18.9).

"Whatever the patient's strength, the two herbs, bitter-sweet (i.e. *Datura*) and pellitory, are beneficial, if the head is wetted with the juice expressed from both simultaneously. When the fever has remitted, recourse should be had to rubbing, more sparingly however, in those who are overly sad".

The following quote from Pliny's *Historiae Naturalis* proves that he obtained the same information about *Datura*'s effects from his sources:

"*Drachmae enim pondere... imaginesque conspicuas obversari demonstrantes, duplicatum hunc modum legitima mensuram facere, quidquid vero adiciatur ponderis praesentari mortem*" (*H.N.* 21.178).

"... a dose of one *drachma*⁹... [the users are] speaking of hallucinations and realistic visions; that a double dose causes downright insanity; any repeated ingestion moreover to the dose bringing instant death".

Nomenclature

The ancients referred to *Datura* with different names. Reasons for that could include the era (B.C. or A.D.), the culture (Latin or Greek) or even traditional folklore.

The ancient Greek physician, Pedanius Dioscorides, lists a number of names for what they called thorn apple (*Datura stramonium* L.), suggesting that he and his sources were very familiar with the plant. He writes: "*The thorn apple which some called perseion, others perisson, others anydron, others pentodryon, others enory, others thryon, and others orthogyion...*" (4.73.1). The more common name was *doryknion*,¹⁰ a term preferred by

⁵3.411g.

⁶6.822g.

⁷Theop. *H.P.* 9.11.6.

⁸Theop. *H.P.* 9.19.1.

⁹3.411 g.

¹⁰Δόρυ = spear.

Dioscorides to Crateuas¹¹ two alternatives, namely *Haliccacibon* or *calleas* (Diosc. 4.74). Ancient warriors used the juice of the plant which they called *doryknion* to dip their spear points in before battle.

The poison was freely available since the plant grows everywhere and the ancients believed that the soldiers instantly killed whomever they injured with these spears. Those who censured the drug less severely gave it the name *manikon*, i.e. "maddening"; those who, from evil motives, tried to keep its nature secret called it *erythron*, i.e. "red"; it was also called *neuras*, i.e. "exciting the nerves", or *perisson*, which can mean either (a) "superfluous" or (b) "extraordinary" (Jones 1951:287).

Today *Daturastramonium* L. is also known as Jimsonweed, Devil's apple, Devil's trumpet, Thorn apple, Belladonna, Metelnut, Deadly nightshade and Solanum, and in Afrikaans as Stinkblaar, Olieblaar, Olieboom, Olieneut and Steekblaar. The seeds are also often referred to as malpitte (i.e. crazy seeds) in Afrikaans.

Dosage

The following translation from Theophrastus' text gives us an indication of the amount of *Datura* used to obtain the desired effect:

"The kind¹² which produces madness (which some call *thryoron* and some *peritton*) has a white hollow root about a cubit¹³ long. Of this three twentieths of an ounce¹⁴ in weight is given, if the patient is to become merely sportive and to think himself a fine fellow; twice this dose¹⁵ if he is to go mad outright and have delusions; thrice the dose,¹⁶ if he is to be permanently insane; (and then they say that the juice of centaury is mixed with it); four times the dose¹⁷ is given, if the man is to be killed (*H.P.* 9.11.6).

Dioscorides gives a warning, saying that if too much of the *doryknion* is ingested, it kills (4.74). With his warning about *strychnosmanikos*, he is more specific: four *drachmai*¹⁸ of the substance will prove fatal (Diosc. 4.75). Theophrastus agrees with Dioscorides about the quantity which would prove fatal (*H.P.* 7.15.4).

Antidote

Dioscorides prescribes an antidote (*antipharmakon*) for *strychnosmanikos*. He writes that large quantities of hydromel¹⁹ should be taken to induce vomiting (4.75).

Must was regarded as particularly efficacious against *doryknion* when it had been used on the spear points of warriors.²⁰ According to Aristotle, a draught of woman's milk is a very effective antidote to *doryknion*,²¹ and Pliny similarly mentions raw milk²² and ass's milk.²³ Pliny also adds sea-urchins, a decoction of sea-crab,²⁴ oysters²⁵ or myax^{26,27} to the list of cures.

Modern science of Datura

Daturastramonium L. and *Daturatatula* L. are two different species found in South Africa but, according to Watt *et al.* (1962:946), there is much evidence that these annual weeds are variations of the same species, as it is often impossible to distinguish the one from the other.²⁸

¹¹Chief physician of Mithridates VI of Pontus (120-63 B.C.).

¹² See Plin. *H.N.* 21.177 -179, Diosc. 4.73.

¹³30 cm.

¹⁴4.3 g.

¹⁵8.6 g.

¹⁶12.9 g.

¹⁷17.2 g.

¹⁸13.664 g.

¹⁹ Hydromel is a mixture of honey and water.

²⁰Plin.*H.N.* 23.30.

²¹Plin.*H.N.* 28.74.

²²Plin.*H.N.* 28.129.

²³Plin.*H.N.* 28.158.

²⁴Plin.*H.N.* 32.58.

²⁵Plin.*H.N.* 32.59.

²⁶*Myrtusaxillaris* Sw.

²⁷Plin.*H.N.* 32.95.

²⁸For the physical appearance of the *DaturaStramonium* L. plant, see Figure 5.

The main difference is the flowers. Hutchings (1996:280) refers to *D. tatula*L. as a synonym for *D. stramonium* L. *Datura* is a naturalised plant and is not indigenous to South Africa (Germishuizen *et al.* 2003:914) but is found in gardens, along roadsides and other waste or cultivated land. According to Arnold *et al.* (2002:129), *Datura* is administered only to humans.

Phytochemistry

Modern phytochemistry reveals that, except for the stimulant cocaine, all the significant tropane alkaloids are found in the potato family, the *Solanaceae*. Liquid chromatography, photodiode array and mass spectrometry (Steenkamp *et al.* 2004:31-39) were also used to conclude that the alkaloids present in *Datura* include scopolamine²⁹ and atropine³⁰ (not less than 0.3% of total alkaloid content) present in varying concentrations in all the different parts of the plant, which are classified as anticholinergics (Sweetman 2002:463). These constituents are present in all parts of the plant, in variable concentrations (dry leaves contain 0.2-0.65% of tropane alkaloids, of which atropine makes up not more than 70% and scopolamine 20%) (Van Wyke *et al.* 2004:123). This implies that all parts of the plant can induce delirium and hallucinations (Hoffmann 2003:122).

Evans writes that at the time of collection, atropine and scopolamine are usually present in the proportion of about two parts atropine to one part scopolamine, but in young plants scopolamine is the predominant alkaloid. The larger stems contain little alkaloid (not more than 3%), and the seeds contain about 0.2% of mydriatic alkaloids. The roots have a higher proportion of alkaloids than the aerial parts (Evans 2002:343), but the leaves contain about 0.5% of alkaloids.

Pharmacokinetics

Hyoscyamine (atropine) lacks CNS (central nervous system) activity because of poor penetration through the blood-brain barrier into the brain (Brown *et al.* 1996:150), caused by the water solubility of the plant. Tropane alkaloids are usually fat soluble and are readily absorbed through the skin (Lewis *et al.* 1977:419).

Pharmacology

The complete ester of tropine and tropic acid is essential for the antimuscarinic action of atropine, since neither the free acid nor the base exhibits significant antimuscarinic activity (Brown *et al.* 1996:149). Atropine and scopolamine paralyse the parasympathetic nervous system (antispasmodic effects) by blocking the action of effector cells of the acetylcholine released at nerve endings. It also stimulates the central nervous system (Dreisbach *et al.* 1987:346).

Atropine competitively inhibits the action of acetylcholine (ACh) at the acetylcholine receptor in the nerve synapse, thereby preventing the parasympathetic nervous system from sending out electrical nerve impulses. The parasympathetic nervous system regulates non-volitional/subconscious activities (such as sweating, breathing, and heart rate) and when it is prevented from sending out signals, the heartbeat and breathing become extremely irregular. It is known that atropine has anticholinergic activity-for example it blocks constriction of the iris with resistant, mydriasis results (Brown *et al.* 1996:150).

Scopolamine lacks the central stimulant action of atropine; its sedative properties make it effective in the control of motion sickness. Scopolamine hydrobromide is employed in preoperative medication, usually with papaveretum, some 30-60 minutes before the induction of anesthesia (Evans 2002:344).

a. Other uses

Atropine and scopolamine differs quantitatively in antimuscarinic actions because of the difference in permeability. Scopolamine has prominent central effects at low specific doses because of its ability to cross the blood-brain-barrier, while atropine lacks this ability (Brown *et al.* 1996:150).

²⁹ The molecular structure of scopolamine can be seen in Figure 6.

³⁰ The molecular structure of atropine can be seen in Figure 7.

This drug is also successfully used in conditions that include neuralgia,³¹ chronic rheumatism, lumbago,³² myalgia,³³ pleurisy,³⁴ pulmonary tuberculosis and mastitis³⁵ (Lee 2007:79). The daturine alkaloids also cause cycloplegia,³⁶ and it is used in combination with morphine in obstetrics to induce "twilight sleep". It is also used in criminology as the so-called "truth-drug" (Avery *et al.* 1959:51), because it induces disturbed consciousness and at the same time causes loss of short term memory (twilight sleep) (Martin 2002:712). In Europe the seeds and plant extracts were used in the treatment of mania, epilepsy, melancholy, rheumatism, convulsions and madness (Lewis *et al.* 1977:167).

Datura causes dryness of the mouth; this property can be used to control excessive salivation, for example in Parkinson's disease (Williamson 2003:418).

Atropine is used today in a sulphate form, in eye drops or intravenously, to stimulate the central nervous system and inhibit the nerve endings of the secretory glands secretory glands' nerve endings (Rossiter 2012:569). Scopolamine (synonymhyoscine), in butylbromide form, is used mainly for its antispasmodic action of the gastrointestinal, biliary and genitourinary tracts. Oral absorption is poor and duration of action brief. CNS effects include drowsiness and fatigue. A preparation containing the crude form of the purified active ingredient in South African pharmacopoeia is Buscopan[®] (Rossiter2012:46).

Administration of the drug

Because of their anticholinergic action the leaves are burnt and the smoke inhaled to alleviate bronchospasms (Robbers *et al.* 1999:112). Duke adds (1985:161) that the leaves may be smoked in a pipe, alone, or with other herbs like belladonna and tobacco. Mexican Indians take the decoction, made from the leaves, to relieve parturition pains (Duke 1985:161). Pulverised seeds in fermented drinks or infusion of leaves and twigs lead to intoxication and hallucinations (Lewis *et al.* 1977:402). Macerated seeds in alcohol are used as an ointment for rheumatism, neuralgia, haemorrhoids and abscesses as a homeopathic cure (Duke 1985:161).

Dosage

It is calculated chemically that the maximum daily dose of atropine may not exceed 2 mg. The prepared Stramonium BP consists of a finely powdered drug, adjusted to an alkaloid content of 0.23-0.27% (Evans 2002:343). In eye drops, the concentration may not exceed 3%, while 0.5% is the minimum effective concentration. When patches are used which are pasted behind the ear (against motionsickness), the active ingredient is approximately 1.5% scopolamine (Van Wyket *et al.* 2004:123).

Toxicity

Van Wyk writes that 100mg of *Datura* constitutes a lethal dose for humans (Van Wyket *et al.* 2002:86). Human poisoning by *Datura* is due mostly to the seed (commonly known as "malpitte" in Afrikaans) (Van Wyket *et al.* 2002:86; Steenkamp *et al.* 2004:31–39). The chief constituents of the leaves, unripe capsules and especially the seeds are scopolamine and largely L-atropine. Even small amounts of leaves or seeds can be fatal (Lewis *et al.* 1977:54), although leave-poisoning is much less common (Watt *et al.* 1963:942). Accidental inclusion of the seed in foodstuffs has caused poisoning (Watt *et al.* 1963:949) and it has happened that children sucked the nectar from the flowers. The seed, which has been broken or powdered, produces more rapid effects. The seed contains less active principals than the leaf, stem and root (Watt *et al.* 1963:950). The leaves also cause poisoning when they are accidentally collected as wild spinach (in the Tswana tradition known as "marogo"). The marogo (Tswana) dry leaf in South Africa has yielded up to 0.36% of alkaloids, of which the chief component is atropine (Watt *et al.* 1963:952). Hutchings (1996:280) reports that there was a tragic episode of poisoning among the Zulu people after they had cooked the leaves of *Datura* to eat as vegetables.

³¹ A severe burning or stabbing pain often following the course of a nerve (Martin 2002:464).

³² Pain in the lumbar or loin region, of any cause or description (Martin 2002:400).

³³ Pain in the muscles (Martin 2002:448).

³⁴ Inflammation of the lung-pleura, often due to pneumonia (Martin 2002:542).

³⁵ Inflammation of the breast, usually caused by bacterial infection via damaged nipples (Martin 2002:414).

³⁶ Paralysis of the ciliary muscles of accommodation in the eyes (Martin 2002:172).

a. Effects of *Datura* poisoning

High doses of atropine lead to restlessness, irritability, disorientation, hallucinations and delirium. Scopolamine in therapeutic doses causes central nervous system depression, manifested as drowsiness, amnesia, fatigue, and a dreamless sleep (Brown *et al.* 1996:150). Symptoms of belladonna poisoning are the same as those for atropine, and include dilated pupils, tachycardia, hallucinations, blurred vision, loss of balance, a feeling of flight, staggering, a sense of suffocation, paleness followed by a red rash, flushing, husky voice, extremely dry throat, constipation, urinary retention, and confusion. The skin can completely dry out and slough off. Fatal cases present with a rapid pulse that turns feeble (Lee 2007:80).

Due to the extremely high risk of overdosing, many deaths and hospitalizations are reported from recreational use. The effects of *Datura* have been described as a living dream: the patient loses and regains consciousness and converses with imaginary or absent people. The effects can last for days. Very few other substances produce the same effects as tropane alkaloids, i.e. very vivid hallucinations and an inability to distinguish between real and unreal stimuli (Hoffmann 2003:122).

Current antidote

Tincture of belladonna contains 30 mg of atropine alkaloids per 100mL. The fatal dose of atropine (or scopolamine) in children may be as low as 10mg (Dreisbach *et al.* 1987:345). In case of poisoning it is necessary to delay absorption by the administration of activated charcoal. Physostigmine or pilocarpine is used intravenously as antidote (Dreisbach *et al.* 1987:37).

Conclusion

Although the ancients used *Datura* as a soporific and local anodyne, they could not make a definite statement why the plant would exert the specific effects discussed in this article. This became possible with the development of the modern technology and scientific understanding. Although our only sources on ancient medicine are the available texts of ancient medicine and treatment, it has become possible to compare the records of the ancient effects (merely what the people experienced) with the modern analytical results. We are able to explain in terms of the characteristics of the alkaloids why atropine would not produce anesthesia but why both atropine and scopolamine have a paralyzing effect on the nervous system. We can conclude that atropine is the culprit why *Datura* cannot be classified as a narcotic drug. Due to the scopolamine content (and the combination of scopolamine with atropine), the employment of *Datura* as a soporific and local anodyne in antiquity is valid and thus why the treatment would be successful.

Although the ancient Romans and Greeks lived close to nature, they probably observed the physiological effects that this plant had specifically on the patients they treated. Thus, to answer the question of how the ancient medical practitioners determined specific dosages, and after comparing the lethal dosages prescribed by them, the most obvious answer is trial and error. Calculations indicate clearly that the ancients prescribed certain dosages that were almost 4 times greater than that which modern pharmacology considers being safe. We can thus conclude that the constitution of people was either much stronger in ancient times than in the 21st century, or that the translators were not accurate when converting the amounts mentioned in the ancient texts.

Even though *Datura* was (more regularly) used for generations (and remains in use) as anodyne and even soporific, it is of great importance to remember that it is a poison and the distinct possibility of accidental poisoning is real. It not only relieved pain during ancient surgery, but also killed people. Tolerances develop easily with regular use of this plant product, an indication that this is not such a harmless hallucinogenic plant as one may think. The side effects which have been mentioned for *Datura*, explain its sombre reputation and its association with the devil (it is also called Devil's apple). It is not an innocent herb at all, even when taken in moderate doses.

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Figure 1: Theophrastus of Eresus



<http://classicpersuasion.org/pw/diogenes/dltheophrastus.htm>

Figure 2: Pedanius Dioscorides of Anazarbus



http://www.greekmedicine.net/whos_who/Dioscorides.html

Figure 3: Aulus Cornelius Celsus



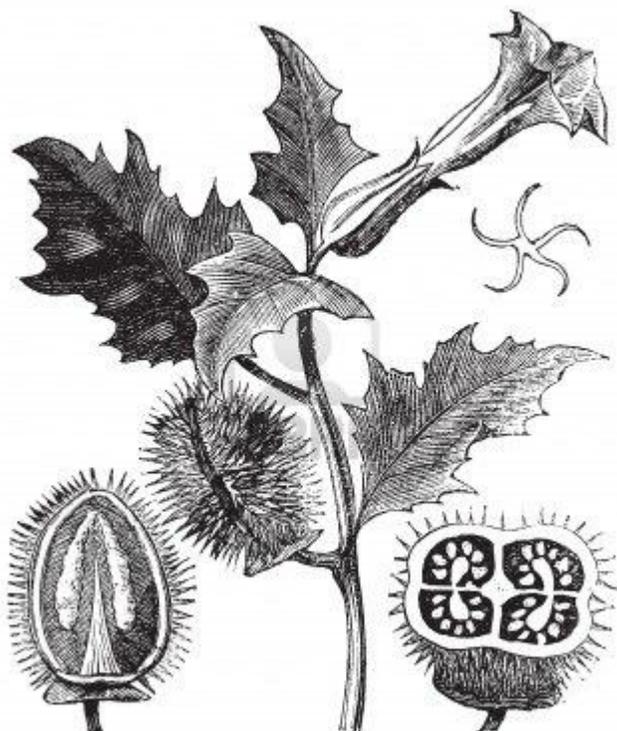
<http://www.philosopedia.org/>

Figure 4: Pliny the Elder



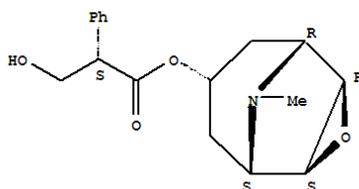
http://en.wikipedia.org/wiki/Pliny_the_Elder

Figure 5: The *Datura Stramonium* L. plant as it is known today



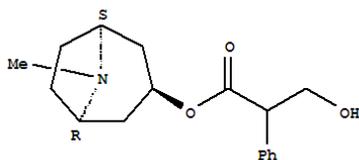
http://www.123rf.com/photo_13770844_thorn-apple-or-jimson-weed-or-datura-stramonium-vintage-engraving-old-engraved-illustration-of-thorn.html

Figure 6: The molecular structure of scopolamine



<http://www.lookchem.com/NewSell/memberproductdetail.aspx?spid=2050775>

Figure 7: The molecular structure of atropine



<http://www.lookchem.com/NewSell/memberproductdetail.aspx?spid=1749028>