PAPER

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Solanaceae IV: *Atropa belladonna*, Deadly Nightshade

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ABSTRACT The Deadly Nightshade, *Atropa belladonna*, is a plant surrounded by myth, fear and awe. In antiquity, the Greeks and the Romans knew that it contained a deadly poison. In medieval times, it was widely used by witches, sorcerors and professional poisoners. Linnaeus later codified its remarkable properties as the genus *Atropa*, the Fate that slits the thin spun life and the species belladonna because of its power to dilate the pupils. In the 1830s, the pure alkaloid l-atropine was isolated from the plant. This proved to be a significant tool in the study of the autonomic nervous system leading to the identification of acetylcholine as an important neurotransmitter in mammals. When pure atropine became available, it caused a large number of deaths, whether by accident, suicide or homicide.

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In this, the final article of a short series on the Solanaceae, I describe the deadly nightshade (*Atropa belladonna*), a plant hallowed by long tradition as one of the classic poisons of antiquity. Extracted from the plant is the alkaloid atropine (dl-hyoscyamine) which was to prove a cornerstone in the study of autonomic pharmacology. The use of atropine as a homicidal poison seemed to have gradually faded away but then in the 1990s, Dr Agutter in Edinburgh attempted, in a spectacular fashion, to poison his wife with the pure alkaloid. This has become a landmark example, in so far as Agutter wove a tangled web of deceit in order to divert attention from his nefarious activities. Indeed the case ranks with that of Crippen (with hyoscine) or Armstrong (with arsenic) as benchmarks in the history of forensic medicine. Fortunately, no deaths occurred in the Agutter poisoning case, but this was more due to good luck than other factors.

THE PLANT

The *Atropa* genus comprises a group of four species of erect perennial herbs (see Figure 1). They have simple typical alternate leaves and bell shaped five-lobed flowers. The genus is widely distributed from Western Europe to the Himalayas. The best known species is *Atropa belladonna* which has erect stems up to two metres in height. The fruit is a purple-black berry. All parts of the plant are poisonous (particularly the berries.)[1]

NIGHTSHADE IN MYTHOLOGY

The plant was well known to the Ancient Greeks and indeed it is a strong candidate for the drug (or potion) that the sorceress Circe administered to the sailors on Odysseus' ship. This subsequently drove them mad and 'turned them into swine'! Odysseus resisted the poison by taking the antidote 'moli' which was probably either the snowdrop (*Galanthus nivalis*) or the snowflake (*Leucojum vernum*).[2]

FIGURE 1 Deadly Nightshade. *Atropa belladonna.* Courtesy of the Library of the Royal College of Physicians of Edinburgh.

The Greeks realised the plant was extremely poisonous and they therefore identified it with one of the three Fates. Clotho spins the thread of human life; Lachesis measures it off and Atropa (the Inflexible) severs it.

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Hence the quotation 'Comes the Blind Fury that slits the thin spun life.'[3] Interestingly, Lachesis, the Disposer (or Measurer) also gave her name later to the anticholinergic drug lachesine (now rarely used).

The plant Atropa later became associated with the Greek cult of Dionysius (Bacchus to the Romans). Worshippers of these gods took wine and then dissolved in this liquid ivy, Atropa and other drugs to make a magic potion. On taking this decoction the devotees passed into a trance in which they danced with abandon and committed lewd and libidinous acts. Those initiated into the rite were promised eternal life and continued sexual potency! These Bacchanalian orgies presage those which would be carried out by the medieval witches (see below).

One problem that the Greeks faced was that initially Atropa was confused with the mandrake (Mandragora).[4] Indeed they are closely related members of the Solanaceae family. Subsequently, Dioscorides recognised that Atropa was, in fact, a distinct plant and should not be used in preference to the mandrake because it was much more poisonous than the latter.

WITCHES AND ATROPA

The deadly nightshade was an important plant in the witches' pharmacopoeia. The hags also used mandrake; henbane and hemlock. (The reader is referred to earlier articles in this series.[3a]) Atropa was pre-eminent because it was regarded as one of the Devil's favourite plants. The story goes that he sprinkled the plant with his own blood every night of the year and regularly took cuttings for his malign purposes. On only one night did he neglect his duties. That was Walpurgis night (the 30th of April) when he had other far more important things to do in taking part in the Black Mass celebrations.[5]

Witches (and wizards), recognising that the plant had found favour in the eyes of the devil, would use it as a constituent of their flying ointments. These were also known as the 'sorcerors pomade'. The usual combination employed in a flying ointment was nightshade, hemlock, mandrake and henbane pounded into an ointment with bear's grease.[6] This was then rubbed into the skin, genitals and vagina. The witch would then experience delusions; hallucinations and sometimes sensations of levitation or flying. Sexual arousal could also ensue together with orgasm! Witches also took, on a regular basis, small amounts of nightshade by mouth in order to practise divination (fortune telling). This was generally recognised as being potentially dangerous. Conversely the peasants had a popular superstition that if a sprig of deadly (or woody) nightshade was kept in the house, then this would ward off evil spirits, preventing fiends from attacking their families, homes or livestock.

BELLADONNA

The species name for the deadly nightshade derives from the dramatic effect that the plant has on the eye and its functions. The eye occupied a central place in traditional healing, being regarded as the window to the soul.

Matthiolus (Pietro Andrea Mattioli 1501–1577) was a distinguished physician practising in Sienna in Italy. Amongst other things he wrote a great commentary on the botanical works of the Greek physician Dioscorides. He also described the custom of the ladies of Venice who put Atropa into their eyes in order to dilate their pupils. As a result tincture of Atropa became known as 'bella-donna' (or beautiful lady). When Linnaeus undertook his outstanding formal classification of the plant kingdom in the 1700s, he incorporated both ideas: the generic name Atropa (the cutting or deadly Fate) and the species name belladonna (an interesting conjunction).

THE ADVENT OF THE HERBALISTS

Throughout the medieval period the deadly nightshade was largely confined to the hidden world of witches, wizards and folkhealers. Then in the sixteenth and seventeenth centuries herbalists and apothecaries arrived on the scene and they embarked upon a systematic study of useful and dangerous plants. The major figures in Britain were Gerard, Culpepper and Parkinson.

Gerard called the plant the lethal Solanum or Sleepy Nightshade.[7] He recounts three cases of poisoning with the berries and instructs the readers of his Herball to banish these pernicious plants from their gardens. Otherwise, he said, women and children will lust after the shining black berries which are so beautiful. He concludes however that they are 'vile and filthie'.

Eventually the plant came to be included in pharmacopoieas and dispensatories. One of the classic descriptions is that by Andrew Duncan in the Edinburgh Dispensatory of 1803.[8] He says that Atropa can be used with benefit in the following disorders:

1 Several febrile illnesses, particularly the plague.
2 In nervous diseases such as palsy, apoplexy, epilepsy, chincough (whooping cough), hydrophobia, melancholy and mania.

Duncan advises that the powdered leaves (or root) should be used first and if these fail then an infusion in warm water can be tried. The dose of all these preparations should be gradually increased on a day by day basis until 'tension in the throat' developes. It would then be imprudent to increase the dose further! In other words the toxic threshold had been passed. Duncan also mentions that Professor Reimarus, a Continental eye specialist, had used the infusion of Atropa to dilate the

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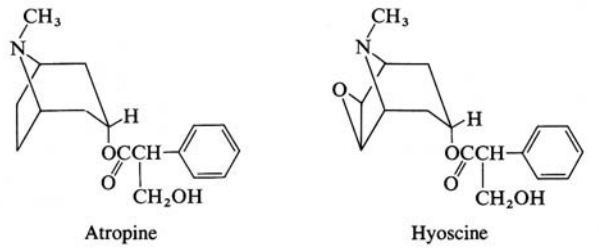

FIGURE 2 The chemical structures of the closely related anticholinergic alkaloids atropine and hyoscine. The only difference between the molecules is the extra oxygen atom in the tropane ring of hyoscine.

FIGURE 3 Belladonna porous plaster British Pharmaceutical Codex. About 1950, from a specimen in the author's collection.

pupil in order to facilitate the removal of cataracts. This episode marks the beginning of the use of mydriatic drugs in intraocular surgery.

SOLVING THE CHEMICAL CONUNDRUM

At around the time that Duncan was compiling his dispensatory in Edinburgh, in the early 1800s, chemistry began its great leap forward with the work of Sir Humphrey Davy in London, and the activities of the French and German chemists. In particular, in Paris an assault was made on the plant kingdom and a number of important alkaloids were isolated and characterised, including quinine, morphine and strychnine. Atropine was isolated from the roots of belladonna in 1831 by Mein a German apothecary.[9] In the plant, it occurs as the laevorotatory isomer of the compound, i.e. l-hyoscyamine, but during extraction it partially isomerises to the dextro compound. Accordingly, atropine is a racemic mixture of the two alkaloids and is properly called dl-hyoscyamine. In structure it is closely related to the alkaloid hyoscine and in many ways their actions are similar (see Figure 2).

MEDICAL USE OF BALLADONNA PLASTERS AND LINIMENT

From the middle of the nineteenth century to the late 1950s, belladonna was incorporated into plasters (and liniments). These could be purchased over the counter at pharmaceutical chemists; apothecaries and druggists (see Figure 3). The public had a high regard for such medications as they often saved an expensive visit to the doctor.[10]

These preparations were used in a wide variety of conditions including neuralgia, chronic rheumatism, lumbago, myalgia, pleurisy, pulmonary tuberculosis and acute mastitis. They seemed to have some analgesic and counterirritant effect and were less vicious than those plasters which incorporated the mustard plant. (*Brassica juncea* or *nigra*). Combinations with other plants were sometimes used. A famous (or infamous) example was the plaster that also included an extract of the monkshood (*Aconitum napellus*). This plant produces the deadly alkaloid, aconitine, which can cause cardiac and respiratory failure. Murderers were known to purchase this deadly plaster. They would then steep off the two alkaloids, aconitine and atropine in order to use the resulting poisonous liquid for their deadly activities.

ATROPINE POISONING

After the pure alkaloid was isolated, poisoning inevitably occurred, either deliberate or accidental. The largest collection of clinical cases ever brought together was that by Witthaus in 1911.[11] He described a series of 682 patients (or individuals). Three hundred and seventy-nine were caused by preparations of belladonna (eye drops; plasters or liniments) and 303 by the pure alkaloid atropine. More than 500 of these poisonings were deemed to be accidental; there were also 37 suicides and 14 murders. The number of deaths reported was 60 (approximately 12%). This was of course before the days of intensive care and artificial ventilation. Since 1911, and Witthaus' classic series, atropine poisoning has become rare. Plasters, liniments and eye drops have either become obsolete or have been banned.

At the present time, it is much more difficult to obtain supplies of atropine. The drug is largely, if not entirely, confined to hospitals, pharmacies, research laboratories and drug companies. As a result, it is doctors, anaesthetists, pharmacists and research scientists who can obtain the pure alkaloid with relative ease in the course of their daily work. As we shall see in the case of Dr Agutter, described below, access to, and availability of the alkaloid, helped to determine the direction of the successful enquiry that was pursued by the police. Of course the most common type of poisoning still remains that of children, who swallow the attractive black berries of the plant, but they usually survive.

FIGURE 4 *Datura stramonium* also known as the Angel's trumpet or Jimson Weed. Courtesy of the Library of the Royal College of Physicians of Edinburgh.

CLINICAL MANIFESTATIONS OF ATROPINE POISONING[10]

When atropine (or Atropa) is administered in overdose (by accident or design) a peculiar conjunction of symptoms and signs results which can be summarised as follows:

> 'Hot as a hare, blind as a bat, dry as a bone, red as beet and mad as a hen.'

When this peculiar constellation is observed, then the diagnosis becomes relatively straightforward and the only confusion tends to be with poisoning by other Solanaceae such as the henbane (Hyoscyamus) or the thorn apple (*Datura*, the Jimson weed) (See Figure 4).

Hot as a hare

Pyrexia is common, particularly in young children. Some patients seem to be more sensitive than others to this effect on the temperature regulation systems. The temperature of the body usually starts to rise about one hour after ingestion and peaks at 6–8 hours.

Blind as a bat

One of the classical features of atropine is dilation of the pupils due to the effect on the sphincter muscle of the iris. Accommodation is also affected and the vision becomes blurred. In severe cases, the iris becomes invisible and the effect can last for several days (indeed for as long as a fortnight) when the other signs of poisoning have long abated.

Dry as a bone

An early sign (or symptom) of atropine overdose is suppression of salivation by the anticholinergic action on the salivary glands (which have a parasympathetic innervation). As a result, there is a profound dryness of the mouth and throat and this results in severe thirst together with difficulty in swallowing.

Red as a beet

Flushing of the face accompanied by a general vasodilatation of the skin are common early signs of intoxication. When this is accompanied by pyrexia (as described above) then the overall impression is that of a febrile exanthem. In former days a common misdiagnosis was that of scarlet fever (scarlatina) but at the present time it would be more likely to be measles or roseola infantum.

Mad as a hen

The central anticholinergic effects of atropine can result in a bizarre mental state resembling mania. Speech may become incoherent and unintelligible. This, together with an accompanying ataxic gait, can make the patient appear to be under the influence of alcohol. Mental changes also include restlessness and agitation; the patient may pluck at the bedclothes. Later as the patient becomes somewhat clearer in mind, they may complain of hallucinations particularly those of a visual kind. Commonly reported examples include butterflies flitting about, or silk curtains wafting in the wind. This type of disturbance is relatively pleasant but patients may also see persons (or animals) who are threatening to attack them. The syndrome resembles that of delirium tremens seen during alcohol withdrawal and may be confused with it.

Finally, in the clinical presentation, it should be noted that atropine often produces a sinus tachycardia of 120 to 160 beats per minute and a polymorph leucocytosis of 12–17,000 per cubic mm. Both these features can suggest a viral or bacterial infection rather than a drug intoxication (see above). It should be noted also that atropine often

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paralyses the detrusor muscle of the bladder resulting in urinary retention and making catheterisation inevitable.

BIZARRE CAUSES OF POISONING

When the history of ingestion of berries is clear, and the plant is rapidly identified there are usually few problems with the diagnosis. However, where the poison has passed through an intermediate animal (or vehicle), then the diagnosis can be difficult and confusing. For example the meat from cattle and rabbits which have grazed on *Atropa belladonna* can be toxic.[10]

In another peculiar outbreak, three individuals were poisoned by eating honey (one severely).[10] On analysis the honey contained significant amounts of atropine. Presumably, in all these three instances, the cattle, rabbits and bees were relatively immune to the toxic effects of the alkaloid. The sweet taste of honey obviously masked the bitter taste of the alkaloid to a degree (compare the case of Dr Agutter described below). In all such cases, it is essential that any residue of the suspected foodstuff be preserved for analysis.

OTHER PLANT POISONS THAT RESEMBLE ATROPINE

Real difficulty in diagnosis may arise when the individual has been exposed to a plant that resembles belladonna in its toxic properties. Such plants include henbane, Solanum species,[12] and *Datura stramonium* (Devil's trumpet, Jamestown or Jimson weed).[13]

Solanum species

These include *S. dulcamara* (woody nightshade or bittersweet) and *S. nigrum* (the black nightshade).[12] The former has fruits that resemble redcurrants and in the latter they look like blackcurrants. Both these plants contain the toxic alkaloid solanine. The syndrome produced therefore resembles that caused by 'greening' potatoes as described in an earlier article in this series. In contrast to *Atropa belladonna*, diarrhoea predominates with these plants, rather than constipation (a useful diagnostic point).

Datura stramonium (the thornapple or Jimson weed)[13]

Datura (and Brugmannsia, its near relative) grow naturally in tropical and subtropical climates and survive outdoors in Devon and Cornwall (see Figure 4). They are also common conservatory and greenhouse plants. Different species contain differing amounts of l-hyoscyamine and l-hyoscine. When taken in overdose, atropinic effects tend to predominate. Drug abusers use the plant for its hypnotic and hallucinogenic effects. The seeds, leaves and roots are all poisonous. Groups of 'hippies' have arisen from time to time who have used Datura as a psychadelic drug. In the Far and Middle East, it has been used from time immemorial both as a means of committing suicide and as a method of drugging strangers in order to rob them.

With the increasing popularity of conservatories in the UK, the author has noted a number of specimens of very healthy Daturas flourishing in this environment, where the owners did not realise that they are harbouring a potential hazard. In this respect, a report in the *British Medical Journal* in 2000 makes fascinating reading. A general practitioner developed a unilateral dilatation of the pupil after working in his conservatory.[14] He had presumably brushed against one of his Angels' trumpets (Datura species). As can be imagined, this phenomenon caused considerable diagnostic difficulty but the condition eventually resolved without complication. The plant should therefore be treated with circumspection as the seeds have been known to kill children. For more information on Datura the reader is referred to Polson; Green and Lee.[10]

THE LETHAL DOSE OF ATROPINE[15]

Susceptibility to the toxic effects of atropine varies widely from individual to individual. Death has occurred after as little as 100 mgm and yet instances have been described where the patient has survived even after taking as much as 500 mgm. Children are more sensitive to the alkaloid and death has occurred after as little as 10 mgm by mouth. Definite symptoms of intoxication have been produced by one milligram when administered as eyedrops. The average lethal dose quoted by Polson, Green and Lee[10] is somewhere between 90 and 130 mgm. In the Agutter case (described below) it became clear that the dose administered to Mrs Agutter was not sufficient to kill.

When Witthaus described his large series of cases in 1911 the mortality was approximately 10%.[11] In the modern era, death is rare with the advent of stomach wash-out, artificial ventilation, together with diazepam, to control convulsions. Specific antidotes, such as physostigmine and pilocarpine, to correct the relative deficiency of acetylcholine – both peripherally and centrally – are rarely used. Generally speaking, the poisonous alkaloid is eliminated from the body in 72 to 96 hours and the patient then makes an uninterrupted recovery. Blurred vision and difficulties with micturition may persist for up to ten days. Fortunately, those poisoned usually have no recollection either of their bizarre behaviour or the frightening hallucinations that accompanied the delirium.

R. V AGUTTER: SAFEWAY'S DEADLY TONIC

Although atropine poisoning is now rare, physicians, nurses and paramedical staff should be on their guard for unusual symptoms that develop following eating or drinking. This is very well illustrated by the attempt of Dr Agutter to poison his wife in East Lothian in 1994.[16]

The story starts on a late summer's evening in a lodge house near Edinburgh. Dr Paul Agutter, a research scientist and lecturer in biology, poured his wife Alexandria a large gin and tonic. Apart from alcohol (and quinine) the refreshing drink also contained atropine! The presence of the bitter substance quinine helped to disguise that of the equally bitter alkaloid atropine. His wife was not aware of anything untoward. Five minutes later, she was in agony complaining of pain in the throat, thirst, nausea, dizziness and visual hallucinations. She was later to describe these as being like 'a gossamer silk effect' and these are characteristic of poisoning by an anticholinergic drug.

Doctor Agutter then behaved in a somewhat peculiar manner. Confronted by his wife who appeared to be seriously ill, he did not ring the Emergency Services but simply left a message on his general practitioner's answer-phone! Fortunately the call was relayed to a locum practitioner who decided to go immediately to the house. He also alerted the Paramedical and Ambulance Services.

When these people reached the house, Dr Agutter told them that he suspected that the tonic water had been contaminated with a poison. He handed the bottle over to the ambulance men. He had also had ample time to dispose of the glass of drink but had failed to do so. This would prove to be one of the errors that would serve to convict him. An ambulance technician insisted on seeing the glass and poured its contents into a jam jar, in order that this could be taken away for further analysis.

It then transpired that other similar cases had occurred in Edinburgh and the surrounding districts. The family of the Sharwood Smiths was affected, in particular Mrs Smith and her son Andrew (aged 18). They had also fallen ill after drinking tonic water. By a strange coincidence, Mrs Smith's husband, Geoffrey, was a consultant anaesthetist. He was able to tell the police that he suspected that the poison was atropine as a result of his knowledge and use of the drug in his clinical practice. The police forensic analyst was called out and he identified the poison which indeed proved to be atropine.

On the following day, Safeway stores throughout the UK removed all bottles of Indian tonic water from their shelves. At a press conference, the company asked the citizens of Edinburgh (and its vicinity) to return immediately all bottles of tonic water purchased at their Hunter's Tryst branch over the previous few weeks. It was later confirmed by the Forensic Science laboratory that six bottles of tonic water had been 'spiked' with atropine.

A mild degree of hysteria then gripped the local community. Several hundred telephone calls were received at the dedicated police line. Matters were not helped, when, as so often happens in such circumstances, a young man wrote to a local newspaper claiming that he was the poisoner. Later, the same 25-year-old was detained under the Mental Health Act and charged with wasting police time.

When the contaminated bottles of tonic came to light, Dr Agutter claimed that somebody else had adulterated the bottles in Safeway and that he, and his wife, were the innocent victims of a psychopathic poisoner. Two facts would emerge that would be extremely damaging to his version of events.

First came the evidence of a student at Napier College (where Agutter was on the Faculty). This student, by complete coincidence, worked part-time as a shelf stacker at the Hunter's Tryst store. He had observed a man putting bottles back on the shelf where soft drinks (including Indian tonic) were held. His description of the man involved fitted perfectly with that of Dr Agutter. Security tapes from Safeways were reviewed and these confirmed that Dr Agutter had been in the store on the day in question. Unfortunately, although the specific camera that observed the bottled drinks area was working, the tape recorder linked to it was not.

The second damaging line of evidence was produced by Dr Howard Okely, a forensic scientist who carried out quantitative tests on the specimen of gin and tonic which had been removed from Mrs Agutter's glass. He determined that the concentration of atropine in this specimen was 292 mgm per litre, whereas a bottle of Safeway tonic found at the Agutter's house contained only 103 mgm per litre. Allowing for dilution of the tonic by the gin, led to the inescapable conclusion that a person (or persons) unknown had added additional atropine to the drink in the form of atropine powder or a more concentrated atropine solution. Agutter would later claim that the 'poisoner' might have left powder in the neck of the bottles that he had taken home to East Lothian. This could have raised the concentration of atropine in his wife's drink.

Dr Okely also carried out analyses on the other contaminated bottles of tonic and found concentrations of atropine ranging from eleven to seventy-four mgm per litre. In summary, all the contaminated bottles of tonic water had much lower concentrations of atropine than that in the glass from which Mrs Agutter had drunk at her home.

As a result of all this evidence, Dr Agutter was arrested some two weeks after the original incident. Subsequently he was charged with the attempted murder of his wife. On questioning, he admitted freely that he had bought two bottles of Indian tonic water from Safeway at Hunter's Tryst. He had also noticed that on one of the bottles the seal was broken. He had decided not to throw this bottle away and told the police that he realised, in the light of the events which had followed, that this had

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been extremely stupid. The police also asked him about traces of atropine that had been found on the cassette case in his car. He had no convincing explanation for this finding but suggested that the outside of one of the bottles had been damp and the atropine had gone from bottle to cassette (via his hand).

In his summation, Lord Morison, the trial judge, described the weight of evidence against Dr Agutter as largely circumstantial but nevertheless compelling. The jury agreed with these conclusions and found Dr Agutter guilty of the attempted murder of his wife. Lord Morison therefore sentenced Dr Agutter to twelve years imprisonment for what he (the judge) described as a 'cold blooded calculated crime'. He had also put at potential risk other innocent members of the public.

Doctor Agutter appealed against the verdict on two grounds: firstly that the evidence was largely circumstantial and secondly that crucial forensic samples had been mishandled by the police. Lord Ross, on behalf of the three Judges of Appeal, rejected these arguments. He concluded that Lord Morison had not misdirected the jury and that the verdict was sound and secure. Dr Agutter served out his sentence and was next heard of in Birmingham where he was teaching at the University as a Lecturer in Medical Ethics!

QUESTIONS ARISING FROM THE AGUTTER CASE

A number of interesting points arise:

1 Why was atropine the poison of choice?
2 How did Dr Agutter gain access to supplies of the poison?
3 Was a mistake made in relation to the dose?
4 What were his motives in attempting to murder his wife?

1. The way atropine was used

Dr Agutter knew about the bitter taste of atropine as he had discussed this property of the alkaloid with the Sharwood Smiths. He had the brilliant idea of putting the poison into Indian tonic water. Quinine is one of the bitterest substances known. He was probably also seduced by the fact that, until the last thirty years, atropine has been very difficult to detect and measure in body fluids and tissues. However modern techniques of chromatography and mass spectrometry have made it possible to detect, identify and measure minute amounts of atropine, such as those on the cassette in Dr Agutter's car.

2. Where did the atropine come from?

Dr Agutter claimed that he had last handled atropine in a biological experiment at Napier College three years before the poisoning incident occurred but never since. It is possible that he had covertly ordered the alkaloid once again and secreted it somewhere for possible use. This would not have aroused undue suspicion as he could have been planning a legitimate experiment at the University. By coincidence, as an anaesthetist, Dr Sharwood Smith would have had routine access to ampoules of atropine. He wondered whether he would come under suspicion by the police and voiced his fears to Dr Agutter when the latter went to lunch at the Smiths. Paul Agutter simply laughed and told him that such anxiety was ridiculous!

3. The administered dose of the alkaloid

An average fatal dose of atropine is approximately 100 mgm. Mrs Agutter would therefore have needed to swallow approximately 330 ml of the mixture to receive this dose, i.e. one third of a litre. When the symptoms hit, she stopped drinking and probably took in no more than 50 mgm, sufficient to intoxicate but not to kill. Agutter had not fortified the tonic with sufficient extra atropine, which was a serious miscalculation. He waited for his wife to die but she did not. Events then got out of his control as the general practitioner, paramedics and ambulance arrived.

4. What were the motives for Dr Agutter's behaviour?

A few weeks before he attempted murder, Dr Ross Langlands, a general practitioner in East Lothian, received a message from Dr Agutter who appeared to be deeply distressed. He said that he might consider taking his own life. Dr Langlands went to Agutter's house and was told by him that his relationship with his wife was over. She was 'contemptuous towards him'. He admitted that he was having an affair with a young woman who was putting pressure on him to leave his wife. He described a number of financial problems. Dr Agutter later signed a mandate to release Dr Langland's evidence to the police (which may have been unwise!).

All in all, this was a sophisticated and calculated attempt by Dr Agutter to commit a perfect murder and also to throw suspicion on an imaginary psychopath. It was backed up by his considerable scientific knowledge and experience. But for the miscalculation as to the dose of atropine and his subsequent panic at the scene of the attempted murder, he might well have succeeded. For further details of the case, the reader is referred to the *Scotsman*'s day-by-day coverage of the trial (starting on 24 January 1995).[16]

After the trial, Chief Superintendent John McGowan of the Lothian and Borders Police, who had been in charge of the investigation, concluded:

> 'Dr Agutter was an educated clever man who had everything going for him. He went to extraordinary lengths to plan what could have

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been the perfect crime. We are not talking about a split personality here but a calm, collected and very dangerous person.'

CONCLUSIONS AND REFLECTIONS ON THE FAMILY SOLANACEAE

No No, Go not to Lethe, neither twist
Wolfsbane, tightrooted for its poisonous wine.
Nor suffer thy pale forehead to be kissed
By nightshade ruby grape of Proserpine.

Thus does John Keats (1795–1821) in his *Ode to Melancholy* summarise the deadly effects of atropa and aconitum as he contemplates his own death or suicide.

The present article on the deadly nightshade brings to an end this short series on the Solanaceae in which I have examined in some detail the history and properties of the potato, the mandrake, the henbane and belladonna. There are many others in this fascinating plant amily which pressed to be considered but constraints of time and space eliminated them.

Those plants that have been considered have told a compelling story that has travelled from the mists of antiquity in Peru and the Middle East, to Greece and Rome, and then onwards to medieval Europe, witchcraft and necromancy. Finally, hyoscine and atropine, in modern times, have helped to unravel the secrets of the parasympathetic division of the autonomic nervous system. In particular, these alkaloids, with the assistance of physostigmine (from the Calabar bean of West Africa), would make it possible to identify the cholinergic neurotransmitter acetylcholine. Had pure atropine and hyoscine not been available at the end of the nineteenth century this process would have taken a great deal longer. I believe that the family Solanaceae, resembles the Roman god Janus, looking two ways, forward to the good and medical progress and yet also backward towards evil; witchcraft and murder most foul.

Two quotations illustrate this ambivalence admirably. In John Milton's *Comus*, reflecting on a Bacchanalian orgy, he refers to the God having 'First from out the purple grape crushed the sweet poison of misused wine'; an allusion to the practice of disguising poison with wine (reminiscent of Agutter, atropine and quinine). Finally we can also remember the Ancient Latin epigram attributed to Roman law 'Abusus non tollit usum', which being translated, would be given as 'The abuse of a substance (or thing) should not weigh against its good or proper use'. These two thoughts summarise succinctly man's long and chequered relationship with the Solanaceae.

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