

THE HISTORY OF HYOSCINE

Hyoscine (and its levo-rotatory isomer, scopolamine) is one of the tropine alkaloids found in a variety of Solanaceous plants. Together with atropine, hyoscyamine, and tropine, it is found in a wide variety of plant genera, in many parts of the world.

As a group these alkaloids exert two quite separate effects on mammals exposed to them — an anticholinergic effect, and a central nervous system depressant effect. This combination of properties, their potent effects with very small dosage, and their widespread distribution has made them famous in the history of all recorded cultures. We review here the history of hyoscine (or scopolamine) under the headings of

- (a) its role as an intoxicant,
- (b) its role as a poison, and
- (c) its pharmacological role in medicine.

The Solanaceae, the family of plants producing these alkaloids, include the Deadly Nightshade (*Atropa belladonna*), henbane (*Hyoscyamus niger*), thorn-apple (*Datura stramonium*), and the Angels Trumpet (*Datura candida*).

Until the early nineteenth century, hyoscine was not separated as a separate substance, but occurred in extracts and tinctures containing a cocktail of the plant-derived cholinergic blocking drugs.

Hyoscine as an intoxicant

Studies of the recent and contemporary use of hyoscine (with its related tropine alkaloids found in the Australian native corkwood (1) suggest that its use as an intoxicant, was well recognised in pre-bronze age cultures. Although no written records exist from a number of such cultures, a review of anthropological writings, relating to use of hyoscine-containing plants as intoxicants, indicates that such use was certainly known in neolithic cultures (such as those of the Aztecs, and the Chamico in India (2)). The extensive anthropological writings concerning its use as an intoxicant, by contemporary Australian aborigines (3-6), indicate that its use would have also been widespread in hunter-gathering palaeolithic communities in those parts of the world where hyoscine-containing plants grew readily.

The Brisbane physician, Joseph Bancroft (who discovered the nematode which causes filariasis — subsequently called *Wuchereria bancrofti* after him) wrote extensively about the use of hyoscine containing extracts, by the Australian Aborigines (3,4). The group of plants that were used as the primary source of

this intoxicant material were (and remain) the Australian native Corkwood, *Duboisia* of which three species — *hopwoodii*, *leichhardtii*, and *myoporoides* occur extensively in those parts of Australia where climatic and soil conditions are appropriate (1).

Australian aborigines prepared, until some 80 years, an extract widely called « pituri », which was traded along the pre-contact trade routes and which was graded carefully by the aborigines as « high quality » or « low quality » material. It was used primarily as a narcotic in initiation and other ceremonies, but its potent pharmacological effects were well recognised, and it was also used as an emu and fish poison. The aborigines selected, from their wide ethno-botanical pharmacopoeia, genera which were low in atropine alkaloids, and relatively high in the hyoscine group. (hyoscine differs from atropine primarily in the fact that it produces much more sedation.)

King, survivor of the ill-fated Burke and Wills expedition (the first attempt to cross Australia from south to north) wrote that when his food became so scarce as barely sufficient to support life, he « sometimes obtained a chew of pitchiri, which soon caused (him) to forget his hunger and the miseries of his position » (7).

In contemporary palaeolithic groups, and probably in prehistoric tribes as well, the secret of the preparation of atropine and hyoscine extracts was jealously guarded by the old men of the tribe (5). It is known from contemporary anthropological writings, that in such palaeolithic groups, the younger men only were allowed to accompany the party to the water which were nearest to sources of the intoxicant plants. In the case of pitcheri, in Australia, the younger men and women stayed and prepared the bags to hold the prepared leaves, and gathered food for the old men who did the harvesting. These were placed in a hole formed by raking out the ashes from a campfire, and completely covered with hot sand, and were left to cook for several hours. When the steamed pitcheri (containing the hyoscine and other alkaloids) was considered to be sufficiently cooked the sand was raked off. When thoroughly dry, the leaf material was beaten with the edge of a boomerang to break it up. All big twigs were picked from this material, and the clean cooked tips were then placed in specially prepared bags (5).

The great secret lay in the length of time that was needed for the steaming, and this was not taught (and even then to men only) until their beards were grey.

In the Australian palaeolithic situation, fresh extracts of the hyoscine-containing leaves was not liked so well. These were made up into a wad, and were chewed until a compact firm chewable mass had been obtained. This was passed from man to man in the tribe, and « when not being chewed was usually stowed behind the ear ». Skin on this part of the head of the old people in the tribe was bleached a queer blue-grey colour from the saturated juices from such wads which had been placed behind the ear (5).

This form of hyoscine intoxication was known to have had very little apparent effect on older people who had been in the habit of using it for years, and true habituation seems to have been achieved. In the case of young people however, it was known to produce a peculiar and sometimes « swollen bestial look ». The effects were known to be relatively short-lasting, and most were worn off on the following day.

Datura species are known over for their hallucinogenic qualities, and are reported from many other parts of the world as playing an important part in intoxicant ceremonies, particularly those involved in sorcery and witchcraft. The Jivaros of Brazil used it to produce vivid hallucinations and sometimes transient madness « during which the elders often had to restrain the novice by force » (8).

It is believed that *Datura* was not introduced into Europe until the early part of the fifteenth century, when gipsies were first said to have brought stramonium from the East. At that time, village witches were known to prepare intoxications of stramonium, and old women sometimes brewed a drink from henbane which is known to bring forgetfulness from hunger and grief.

Jimson weed, or thornapples are natives to the West Indies, and were first brought to the Europeanised new world from the West Indies in the seventeenth century. Medieval witches are known to have employed the use of hyoscine and related tropine alkaloids quite extensively. Although in most cases infusions were prepared by boiling the appropriate plants, occasionally inhalation of potent hyoscine containing fumes is also recorded (8).

In recent times, henbane chewing by young members of counter-culture movements has again achieved some notoriety, not only in Europe but also in Australia as well (9).

Hyoscine as a poison

Hyoscine and its related alkaloids kill by a combination of their peripheral anticholinergic effects, and by their central depressant effects. Gross tachycardia results from vagal inhibition; this goes on to heart failure. Hyperthermia may also occur, and permanent brain damage from survivors of atropine-induced hyperthermia are well recognised. After a period of mania (in the case particularly of atropine and related alkaloids), or of profound depression (in the case of hyoscine and hyoscyamine), profound depression leading to apnoea ensues.

In Roman times, extracts from the deadly nightshade were used to produce obscure and often prolonged poisoning. As the plant is extremely potent, tiny amounts cannot be detected, and this combined with its relative stability when heated, allowed ancient court poisoners to include the hyoscine-related group of drugs surreptitiously in a variety of foods. Henbane (especially the Egyptian variety *Hyoscyamus muticus*) has long been used throughout Europe in this role (10). It is important not to confuse « henbane » with « hemlock » (*Conium maculatum* — now naturalized in many parts of the New World including Australia (11)); this latter was another poison used as a major ingredient of the « poison cup » used to execute political prisoners in ancient Greece.

It is believed that extracts from belladonna (from « Mekilwoort ») were used by King Duncan of Scotland in 1045 to drug invading Danish pirates. It is believed that he mixed extracts from these alkaloids, in their beer. « The Scots heereupon took the juice of the Mekilwoorth berries and mixed the same in their ale and bread, sending it thus spiced and confectioned, and in great abundance unto their enemies. They... fell to eating and drinking... till the operation of the berries spread in such sort through all the parts of their bodies, that they were in the last brought into a fast dead sleep, that in manner it was impossible to awaken them » (8).

In the fifth century Hindu medical compendium, the *Susrata*, there are listed over 700 medicinal plants, among which the depressant effects of *Hyoscyamus* are described (12).

Atropine and hyoscine alkaloids were also used as poisons in the court intrigues in India (in the current (1982) best seller, M.M. Kaye's « The Far Pavilions » extracts from *Datura* are used with deadly effect, to this purpose).

The potency of this group of alkaloids was well recognized by the eighteenth century, and the name of the parent plant *Atropa belladonna* was so named by

Linneus after Atropos, the senior of the Three Fates, who finally cuts the thread of life.

Medicinal uses of hyoscine

The first record of hyoscine is that of the use of its parent plant, *Hyoscyamus*, which is referred to in the Ebers Papyrus in Egypt, in 1550 B.C. In that document it was recommended for what was probably colic and abdominal discomfort — « magic in the belly ». Cullumbine, writing in Drill's Pharmacology, believes this use in colic was related to nematode and cestode infestation by roundworms and tapeworms (13).

Subsequent to its knowledge and use by Egyptian physicians, hyoscine containing remedies were also listed in Greek herbals (e.g. that of Dioscorides).

In herbals of the twelfth to eighteenth centuries, plants (which we now know to have contained hyoscine) are extensively mentioned. The « virtues » claimed for hyoscine in the seventeenth century are truly remarkable. In Gerarde's « Heballe or Generall Historie of Plantes » in 1633 (15) one reads

- (a) it stayeth bleeding and the disease in women ;
- (b) asswageth the paine, and tumors of womens breasts, and
- (c) easeth the paine of the tooth socketts by montebanke Toothdrawers which runne about the countrie ».

It is interesting to note that hyoscine and its related drugs have little or no intrinsic analgesic effects, but its cerebral effects (in pharmacological doses) include drowsiness, euphoria, dreamless sleep and amnesia, often with a retrograde period (1). *Hyoscyamus* was an essential ingredient of the famed « spongia somnifera », the widely used anaesthetic of medieval Europe. This was a sponge steeped in a water or wine mixture of opium, lettuce, hemlock, *hyoscyamus*, mulberry juice, mandragora and ivy. This was dried for storage and moistened when ready to be inhaled or its juice swallowed by the patient before operation (12).

Some of the earliest scientific experimentation with *hyoscyamus* was made by Anton Storck (1731-1903), and the first of the tropine alkaloids were isolated in relatively pure form by Pierre Robiquet in France in the early 1800's.

Hyoscine has a special place in the history of obstetrics, with the production (with morphine) of « twilight sleep ».

With the increasing clinical knowledge of the amnestic effects of hyoscine, the combination of narcotic analgesia with hyoscine amnesia was tried in Germany first in 1902 by von Steinbuchel (14). Its use was first popularised in Freiburg, and it came to be called Freiburg Dammerschlaf (Twilight Sleep). In 1903, von Steinbuchel reported 20 cases of labour in which scopolamine (0.3 mg) and morphine (10.0 mg) had been used in combination, to produce analgesia in labour (16). He used the preparations in solution, « freshly boiling each one separately », and « of the 20 cases, only one remained entirely unrelieved of her pain ». The use of the new combination spread rapidly in Germany, Poland and France. In 1904, Wartapetian described the results following its use in another 20 cases (17), and in the following year (1905) Gauss (18) described its use in 500 cases. He used both powdered scopolamine and the drug in tablet form. He preserved the drug carefully away from light and from moisture, separately sterilizing the scopolamine and the morphine before their final addition. « The woman in labour fell into a quiet sleep between pains, from which she was aroused at each new contraction ; objectively, the contractions remained painless but subsequently, the more intelligent patients admitted that they were suffering little » (19). Later, the patients became thirsty, but « amnesia could be produced in every case ».

After a deep sleep following the scopolamine labour, they awoke « strong, refreshed and frequently ready to eat and act as if nothing unusual had happened » (14).

Hyoscine is used extensively today as a pre-medication prior to anaesthesia, and further derivatives of it, and new routes of administration (by topical absorption through the skin over the mastoid process) are currently being developed to exploit its anti-emetic properties to prevent travel sickness. It is certain that when its history is reviewed in future years, new and full chapters (of which we know nothing today) will have to be written.

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