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Three men and a drug: Peyote research in the 1890's

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The student of medicinal plants frequently finds it difficult to verify the often fantastic properties ascribed to a plant or a crude drug in folklore and native medicine. A brilliant exception, however, can be found in the Mexican hallucinogenic drugs 'peyotl', 'teonanacatl' and 'ololiuhqui'. In the case of these drugs, it is indeed possible to say that truth is stranger than fiction.

The first of these drugs to be chemically and pharmacologically investigated was 'peyotl' or 'peyote'. The drug 'peyote' (also called 'mescal buttons') consists of the dried tops of a cactus, *Lophophora williamsii* (syn. *Anhalonium lewinii, A. williamsii*), which grows in northern Mexico and in Texas. Though the Mexican Indians' ritual use of 'peyote' had been observed by the Spanish conquerors, their reports did not attract great attention and the drug remained obscure until the 19th century. The first botanical studies appeared in the 1840's, but the modern scientific interest in 'peyote' did not develop until forty years later, and can be traced directly to one person, Dr. John Raleigh Briggs, of Dallas, Texas.

John Raleigh Briggs (1851-1907)

Dr. Briggs graduated in St. Louis in 1880 and established himself in Dallas in 1882 as a specialist in diseases of the eye, ear, nose and throat. He was the editor for several years of various medical journals and a member of the city council of Dallas. As an editor, he wrote what he thought and had 'a gun on his desk and a lawyer on his staff to support his views'.

On 20 June 1886, this intrepid physician swallowed a piece of a 'curious fruit'. In the first article on 'peyote', which appeared a year later, he reported as follows:

'Learning first from my brother, who has spent several years among the different tribes of wild Indians, and subsequently from Mexicans, that both Indians and Mexicans eat this fruit for purposes of intoxication, I became interested in its physiological effects. The Indians use it that they may forget their troubles and see "beautiful visions"; such as *"buffalo and wild horses come up out of the earth"*. . . . At 10 a.m., June 20th, 1886, I ate one-third of one of these "buttons", or *prickly plants*, and, with pencil and paper and watch before me, awaited results.'

After 45 minutes Briggs's head began to ache and he felt dizzy. He noted that his pulse had reached 120. Soon after it rose to 160: 'It seemed to me my heart was simply *running away with itself*, and it was with considerable difficulty I could breathe air enough to keep me alive . . . Automatically I rushed to my able friend, Dr. E. J. Beall . . . He prescribed aro. spts. ammonia and whisky, in large doses, every few minutes.'

Half-an-hour later Dr. Briggs felt better, and in eight hours he felt normal again. In conclusion he wrote: 'I think it well worth the trouble to investigate the matter. One man's experience is worth but little, and it is to be hoped some enterprising experimenter will carry out the research. As to *myself*, I must admit I feel somewhat abstemious on the subject.'

Briggs's short article was the opening of an intensive era of peyote research. The Parke-Davis drug company in Detroit immediately made contact with Briggs to obtain more information. In a letter to Parke-Davis of 24 May 1887, Briggs wrote: 'There is so far as I can ascertain *absolutely* no literature in English on this plant . . . I should not think you would want large quantities of it—"by the bale". I am certain 2 buttons would kill a *white* man'.

Briggs also obtained a supply of the drug for Parke-Davis and samples were distributed to botanists, chem-

John Raleigh Briggs (1851-1907).

This article is based on 'Early Peyote Research: An Interdisciplinary Study' by Jan G. Bruhn and Bo Holmstedt (in Economic Botany 28: 353-390. 1974).

Peyote. Dried specimen (also called 'mescal button') sent by Briggs to Parke-Davis in 1887. *Scale in centimetres.*

ists, and pharmacologists. In a report from the analytical department of Parke-Davis, dated 5 July, we learn that the drug 'contains a large amount of alkaloid or rather alkaloids'. On 19 July a botanical report referred the drug to the cactus family and the genus *Anhalonium*. All this work was carried out behind locked doors. The 1880's were a time of tough competition between several young American drug companies.

Louis Lewin (1850–1929)

One of the scientists who had been contacted by Parke-Davis to evaluate the pharmacology and therapeutic value of the new drug, was the German toxicologist Louis Lewin. Lewin had received his M.D. in Berlin, where he also became 'Privatdozent' in 1881 and established his own laboratory and lecture hall. He published more than 200 scientific publications, among them a toxicology textbook, on the side effects of drugs, on arrow poisons, etc.

In 1887, Lewin visited the USA. From his handwritten diary* (a manuscript of 300 pages) it is evident that he was especially interested in visiting San Francisco's China Town, to see the smoking of opium, and Detroit, where he arrived on 16 September: 'My first errand was, of course, a visit to Parke-Davis . . . Mr. Wetzell showed us round the factory and the printing-shop—I had not expected such a magnitude and such a skilled exactitude of workmanship'. From Detroit Lewin brought with him a 'peyote' sample, which he promised to investigate.

After his return to Germany he extracted the drug in various ways and obtained a basic, syrupy substance which he called anhalonine. He studied this 'substance', which was in fact a crude mixture of alkaloids, in animal experiments and found to his surprise that it was intensely poisonous.

The exact botanical identity of the drug was still unknown, so Lewin turned over some of his material to the botanist Hennings, at the Royal Botanical Museum in Berlin. On 3 December, Hennings wrote to Lewin:

'Hochgeehrter Herr Doctor!

'I cannot wait to let you know that I have yesterday examined your cactus carefully and that I came upon very gratifying results . . . without any doubt, we have to do with a new species which I will take the liberty to name for you, as you are actually the discoverer of the plant, as well as of its toxic nature.'

On 10 February 1888, Hennings presented his paper 'Eine giftige Kaktee, *Anhalonium Lewinii* n.sp.' to the Botanical Society of Berlin. This was the first published

Louis Lewin (1850–1929). Picture taken about the time of his trip to the United States.

*The cited materials referring to Lewin have been kindly placed at the author's disposal by Professor Bo Holmstedt, Stockholm.

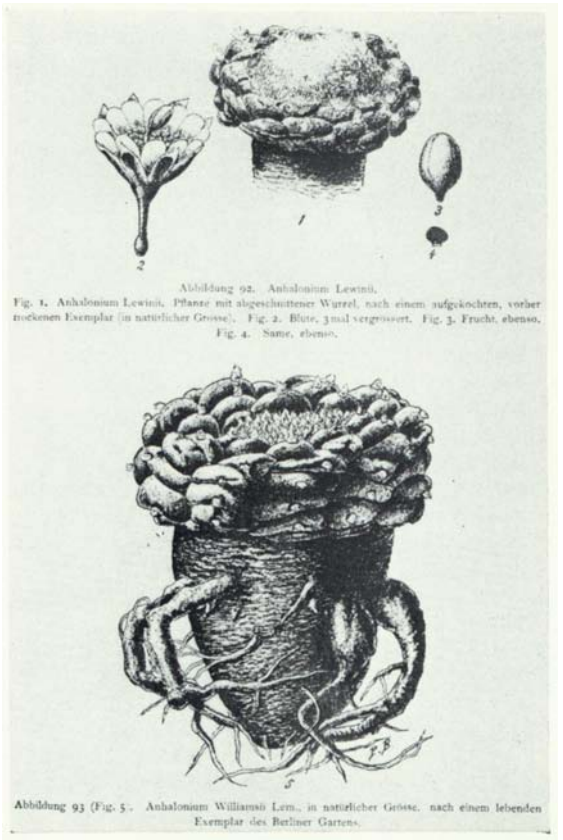


Abbildung 92. Anhalonium Lewinii.
Fig. 1. Anhalonium Lewinii. Pflanze mit abgeschnittener Wurzel, nach einem aufgekochten, vorher trockenen Exemplar (in natürlicher Grösse). Fig. 2. Blüte, 3mal vergrössert. Fig. 3. Frucht, ebenso. Fig. 4. Same, ebenso.

Abbildung 93 (Fig. 5). Anhalonium Williamsii Lem., in natürlicher Grösse, nach einem lebenden Exemplar des Berliner Gartens.

Anhalonium lewinii and A. williamsii. From Hennings's paper 'Eine giftige Kaktee, Anhalonium lewinii n.sp.' in Gartenflora 37: 410 (1888).

identification of 'peyote'. Unfortunately, Hennings's description, based on very limited and dried material, brought about an unparalleled nomenclatural confusion, which will not be further discussed here.

Shortly afterwards, Lewin published the first account of his chemical and pharmacological studies. He said in his summary: 'It has been proven for the first time that a cactus can possess an extraordinarily high toxicity.'

In the meantime, Parke-Davis had found a reliable source of the drug in Laredo, Texas. One year had then passed since Briggs's report, and one additional year later Parke-Davis marketed the tincture of *Anhalonium lewinii*. The company's catalogue of 25 February 1889, states that the product has 'marked physiological action similar to strychnine'. For the next few years the drug was experimented with as a cardiac stimulant and tonic.

Interest in 'peyote' now spread among botanists, chemists, and pharmacologists. It was not easy, however, to obtain the crude drug, and it was therefore of great importance when 42 kg of 'peyote' was dispatched from Mexico in 1891. This was received by Arthur Heffter, assistant in pharmacology at the University of Leipzig.

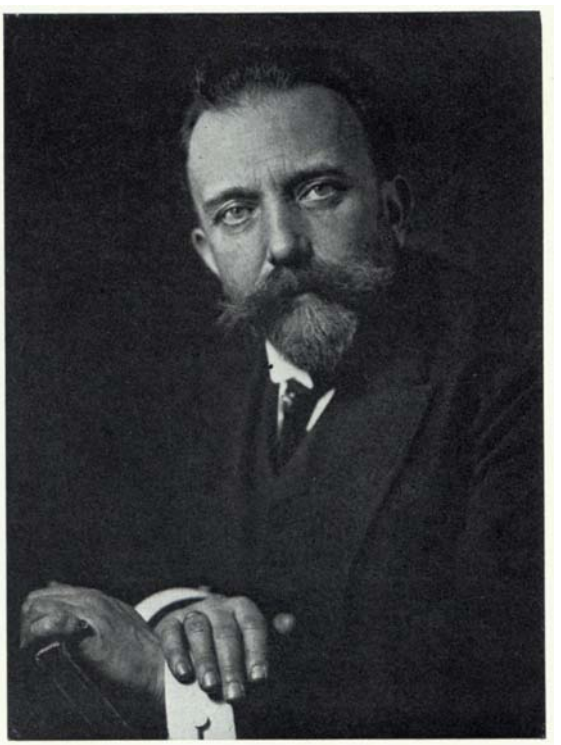
Arthur Heffter (1860–1925)

Heffter first studied chemistry and received his Ph.D. in Greifswald in 1883. After a few years as chemist he switched to study medicine in Leipzig and received his M.D. there in 1890. In 1908 he became professor of pharmacology at the University of Berlin. He is known for his studies of arsenic and strophanthine, but most of all 'peyote'.

Heffter crystallized two alkaloids from his plant material. He characterized them in animal experiments and also tested on himself whether the new compounds could explain the effects of the crude drug. In this way he found that one of the isolated alkaloids, pellotine, was an active sedative and hypnotic.

In the meantime Lewin had studied other problems, but when Heffter's first paper was published in 1894, he rushed to vindicate his position in this field. In two papers Lewin discussed his own and Heffter's results, as well as botanical aspects of 'peyote'. This brought him into conflict with the renowned cactus botanist Karl Schumann and Heffter's work was thereby overlooked.

In a letter to the editor, published on 6 April 1895, in the *Pharmaceutische Zeitung*, Heffter recognized Lewin's priority, but also showed that he, Heffter, had been first to isolate a *pure* alkaloid from 'peyote'. Lewin sent an angry reply to the editor and this animated exchange of letters developed into a life-long grudge between the two men. Lewin never worked with



Arthur Heffter (1860–1925).

peyote' again.

The drug had now been studied in human experiments in the USA and found to produce hallucinations. Attempts were also made to isolate the alkaloids, but Heffter's lead was too great. In 1896 he described four new, pure alkaloids, anhalonine, anhalonidine, lophophorine, and mescaline.

The following year he performed a series of self-experiments to find the active constituent of 'peyote'. On 5 June he tried the crude drug to learn about its effects, and confirmed the reported symptoms: colour visions, pupillary dilatation, loss of appreciation of time, nausea, and headache. He then extracted the alkaloids from the drug and ingested the extraction residue, a brown resin. This experiment was performed on 21 July and clearly established that the resin was ineffective.

Two days later it was time to investigate the activity of the total alkaloids. These produced the same effects as the whole drug. Heffter concluded: 'The peculiar actions of peyote on the visual apparatus must, therefore, be produced by one of its alkaloids'. All of the four new alkaloids were now tested by the thorough Heffter. Anhalonine and anhalonidine made him sleepy, lophophorine caused his face to flush and gave him an occipital headache.

On 23 November 1897, he took 150 mg of mescaline hydrochloride. In his laboratory notes we read '2.00 p.m. Violet and green spots appear on the paper during reading. When the eyes are kept shut the following visual images occur . . . carpet patterns, ribbed vaulting, etc. . . . Later on landscapes, halls, architectural scenes (e.g. pillars decorated with flowers) also appear. The images can be observed until about 5.30 p.m. Nausea and dizziness are at times very distressing . . . In the evening well-being and appetite are undisturbed and there is no sign of sleeplessness'.

He concluded: 'The results described above show that mescaline is exclusively responsible for the major symptoms of peyote poisoning'. Ten years had then passed since the publication of Briggs' report.

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What is a Species?

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Historical background

As long ago as 1832, John Lindley wrote 'A species is an assemblage of individuals agreeing with each other in all essential characters of vegetation and fructification, capable of reproduction by seed without change, breeding freely together and producing perfect seed from which progeny can be reared.' This is a remarkable definition when one realises that it emerged from an era in which the Doctrine of Special Creation was still widely held, and, specifically, before the publication of Darwin's and Wallace's theories on evolution.

The conventional taxonomy of the nineteenth century was the description and naming of all species of plants, and the construction of a hierarchical system of categories into which these could be fitted. The categories were defined largely on the basis of morphology, but the higher categories reflected some sort of affinity between the species. The justification for a static system of this type was the immutability of species.

It was early studies of the 'affinities' already referred to which prepared the way for the theory of evolution and, after the publication of the Origin of Species, the best classifications were those in which affinities could be interpreted as representing phylogeny, i.e. relationship by descent. However, the theory of evolution requires a dynamic interpretation of taxonomic categories, even though this had necessarily to be explained in the then current taxonomic language. The problems