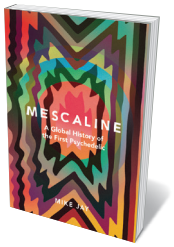
Peyote cacti at a plant nursery in Mexico.

ADAM WISEMAN

PHARMACOLOGY

The long, strange trip of mescaline

A chronicle tracing the drug's ancient roots and role in research grips **Alison Abbott**.



Mescaline: A Global History of the First Psychedelic
MIKE JAY
Yale University Press (2019)

Pharmacologists gave mescaline a fair trial. In the early and mid-twentieth century, it seemed more than plausible that the fashionable hallucinogen could be tamed into a therapeutic agent. After all, it had profound effects on the human body, and had been used for centuries in parts of the Americas as a gateway to ceremonial spiritual experience.

But this psychoactive alkaloid never found its clinical indication, as science writer Mike Jay explains in *Mescaline*, his anthropological and medical history. In the 1950s, the attention of biomedical researchers abruptly switched to a newly synthesized molecule with similar hallucinogenic properties but fewer physical side effects: lysergic acid diethylamide, or LSD. First synthesized by Swiss scientist Albert Hofmann in 1938, LSD went on to become a recreational drug of choice in the 1960s hippy era. And, like mescaline, it teased psychiatrists without delivering a cure.

ANCIENT HISTORY

Jay traces the chronology of mescaline use. The alkaloid is found in the fast-growing San Pedro cactus (*Echinopsis pachanoi*) that towers above the mountainous desert scrub of the Andes, and the slow-growing, ground-hugging peyote cactus (*Lophophora williamsii*) native to Mexico and the south-western United States. Archaeological evidence suggests that the use of these cacti in rites of long-vanished cultures goes back at least 5,000 years.

Europeans first came across peyote after Spain conquered Mexico in the early sixteenth century. (It is mentioned, for instance, in a mammoth study, *The General History of the Things of New Spain*, begun by scholar and friar Bernardino de Sahagún in 1529.) Attempts, largely by missionaries, to suppress its use were not successful. In fact, peyote rituals eventually spread to Native Americans of the US plains, such as the Osage Nation, after they were forced into reservations. Mescaline and peyote are now banned under US drug laws, but such ceremonial use is exempted.

Before the twentieth century, just a handful of people outside Indigenous American cultures had tried the extracts; but their reports sparked medical, spiritual and recreational interest for many decades. The powers of endurance needed to take the drug became more widely known: it induces hours of nausea and often vomiting before the hallucinations begin. (In contrast to alcohol, Jay ▶

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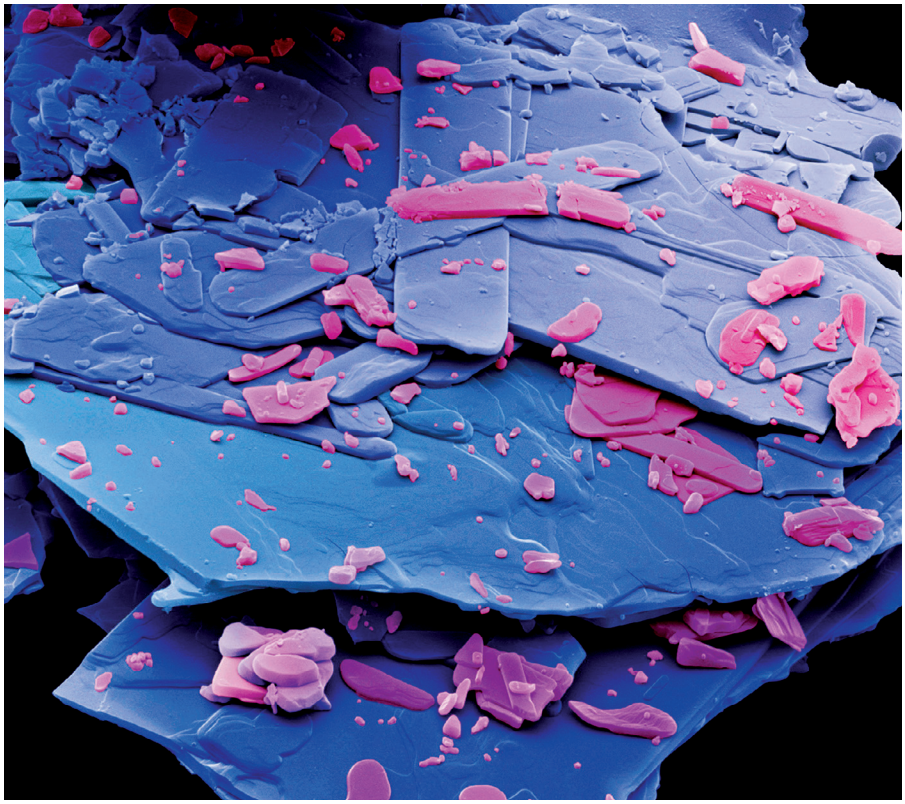
notes, mescaline gives you the hangover first.) The hallucinations are now thought to be caused mainly by mescaline binding to and activating serotonin receptors in the brain.

In traditional ceremonial use, the hallucination phase has been reported as consistently transporting. But outside these cultures, those eager to experiment have had disconcertingly unpredictable experiences. In 1887, Texan physician John Raleigh Briggs was the first to describe in a medical journal his own, rather violent, symptoms — including a racing heart and difficulties breathing — after eating a small part of a 'button', or dried crown, of a peyote cactus. The pharmaceutical company Parke–Davis in Detroit, Michigan, which had been investigating botanical sources of potential drugs from South America and elsewhere, took note. The company was seeking an alternative to cocaine, whose addictive properties had become apparent; it began offering peyote tincture as a respiratory stimulant and heart tonic in 1893.



DAVID MCCARTHY/SPL

Crystals of mescaline seen under a scanning electron microscope.

TRIAL AND ERROR

A flurry of scientific trials began. There was scant regard for ethics and safety — for the scientists, who frequently tested the mescaline themselves, or for test subjects. In 1895, two reports demonstrating the drug's unpredictability came out of what is now the George Washington University in Washington DC. In one, a young, unnamed chemist chewed peyote buttons and then noted down his symptoms: nausea followed by pleasant visions over which he had some control, then depression and insomnia for 18 hours. In the other, two scientists observed the drug's effects on a 24-year-old man, who became deluded and paranoid.

In New York City, pharmacologists Alwyn Knauer and William Maloney carried out a more extensive trial, including 23 people, in 1913. They hoped that mescaline, as a hallucinogen, might provide insight into the psychotic phenomena associated with schizophrenia. It didn't. The pair diligently recorded participants' running commentaries on their hallucinations, but found no common characteristics. (In later studies, people with schizophrenia could easily tell the difference between their own hallucinations and those induced by the drug.)

"Theories that mescaline might reveal the biological basis of schizophrenia were dashed."

The pace of trials picked up after synthetic mescaline became available. Chemist Ernst Späth at the University of Vienna was first to synthesize it, in 1919, and the German pharmaceutical company Merck marketed it the following year. Yet trial outcomes did not become more reliable or illuminating. Over the next couple of decades, theories that mescaline might reveal the biological basis of schizophrenia or help to cure other psychological disorders were serially dashed.

In parallel with these developments, artists and bohemians — mainly in Europe — were testing mescaline's creative potential. Psychiatrists and psychologists jumped onto that bandwagon. They administered it to writers, artists, philosophers; presented them with intellectual stimuli; and observed their responses. But as before, no pattern emerged. One British surrealist painter of the 1930s, Julian Trevelyan, found ingestion inspiring; another, Basil Beaumont, experienced "excruciating pain and fear". French philosopher Jean-Paul Sartre entered a grotesque hell, whereas British writer Aldous Huxley tripped into a magnificent world of expanded consciousness, described in his influential 1954 book *The Doors of Perception*.

Jay reports other, more surprising, enthusiasts. One was Frederick Smith, who in 1914 became head of the Reorganized Church of Jesus Christ of Latter-Day Saints, now the Community of Christ. Smith promoted the use of peyote during services, to induce the religious ecstasy he said he had experienced at ceremonies of various Native American nations.

During the Second World War, mescaline saw use in the infamous human experimentation programme of the Third Reich. Nazi physician Kurt Plötner forced concentration-camp prisoners to take mescaline to see whether it would serve as a 'truth serum' during interrogation. The US Office of Strategic Services, forerunner of the CIA, was testing mescaline as a 'truth drug' around the same time. However, the concept was quickly rejected: the nausea stopped participants trusting their interrogators. The CIA later recruited Plötner for a project that evolved into the mind-control programme MKUltra.

LSD took mescaline's research crown from the 1950s onwards (see M. Jay *Nature* **497**, 435–436; 2013). But its reign, too, petered out, under pressure from the drug-control lobby during the 1970s. In the past decade or so, as Michael Pollan's 2018 *How to Change Your Mind* chronicled, a smattering of research using hallucinogens has resumed. Mescaline is not among them.

This book is not always a simple read, with bit players jumping in and out and timelines sometimes hard to follow. The detailed descriptions of individuals' subjective experiences can overwhelm. But Jay deftly sets down the cultural and scientific history of mescaline in its heyday: a curious chronicle that deserves not to be forgotten. ■

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CORRECTION

The Books & Arts article 'A new lens on life's origins' (*Nature* **569**, 36–38; 2019) should have said that there are 20^{200} possible proteins 200 amino acids long.

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CORRECTION

The book review 'The long, strange trip of mescaline' (*Nature* **569**, 485–486; 2019) misstated Frederick Smith's role: he was head of the Reorganized Church of Jesus Christ of Latter-Day Saints, now known as the Community of Christ.

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