

N,N-dimethyltryptamine (DMT) and Ayahuasca

*By Drug Science and
Small Pharma*



Part I - History and Law



Drug Science

Drug Science was formed by a committee of scientists with a passionate belief that the pursuit of knowledge should remain free of all political and commercial interest

Founded in 2010 by Professor David Nutt, following his removal from his post as Chair of the Advisory Council on the Misuse of Drugs, Drug Science is the only completely independent, science-led drugs charity, uniquely bringing together leading drugs experts from a wide range of specialisms to carry out ground-breaking research into drug harms and effects

The Drug Science mission is to provide an evidence base free from political or commercial influence, creating the foundation for sensible and effective drug laws. Equipping the public, media and policy makers with the knowledge and resources to enact positive change

Drug Science want to see a world where drug control is rational and evidence-based; where drug use is better informed and drug users are understood; where drugs are used to heal not harm



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Small Pharma

Led by an experienced team committed to making a difference for people suffering from mental health conditions, Small Pharma believes that together, as a community, we can help unlock cutting edge science and bring new therapies to treat mental health disorders

Small Pharma is a virtual biopharmaceutical company on a mission to improve mental health by progressing psychedelic therapies to the clinic. At Small Pharma, they have identified the field of psychedelic medicine as an exciting and unexplored area of drug discovery, with the ability to completely transform our understanding and approach to mental health. As compounds neglected by risk averse traditional pharma, the Small Pharma team are passionate about becoming the R&D leaders of psychedelic drug discovery and development

Small Pharma funds clinical trials of DMT and related psychedelic compounds as a tool to augment psychotherapy for the treatment of depression and other mental health conditions. Their current focus is to unlock the exciting potential of DMT therapy as a treatment for Major Depressive Disorder



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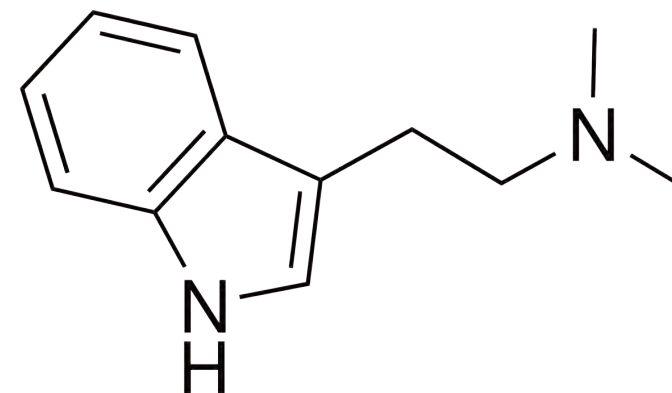


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What is DMT?

Dimethyltryptamine (DMT) is an indole alkaloid and tryptamine derivative, chemically similar to the neurotransmitter **serotonin (5-HT)** and other classical psychedelic drugs, such as psilocybin

DMT has been shown to bind to a range of receptors including many of the serotonergic receptors, alpha receptors and the Imidazoline 1 receptor, although it's believed that it's primary hallucinogenic and interoceptive effects occur through its action on the serotonergic **5-HT_{2A} receptor**



DMT is a naturally occurring substance found in a wide variety of plant and animal species including:

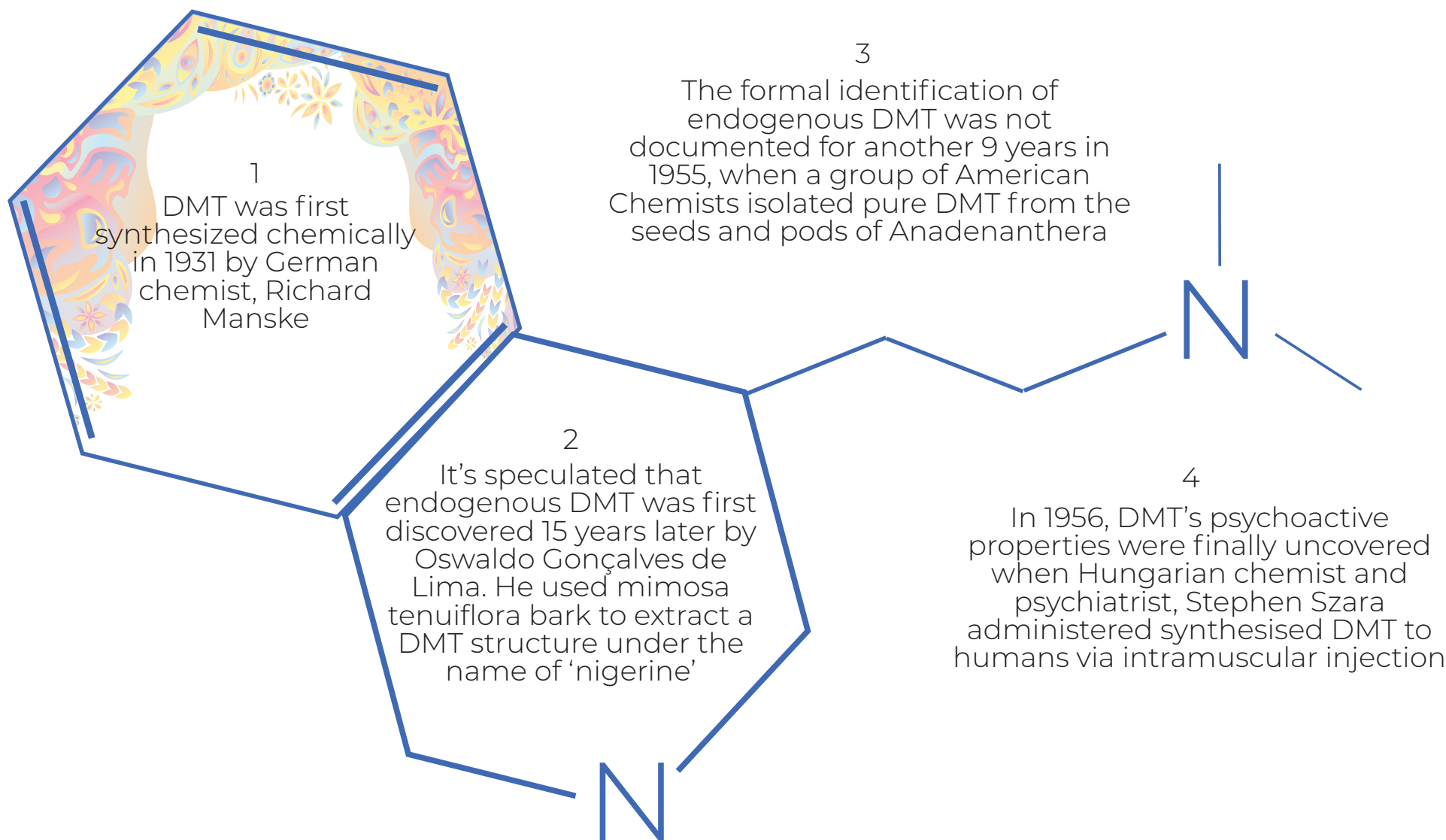
- over 50 plant species (belonging to 10 different families)
- 3 mammalian species (including humans)
- 1 alcyonacea species (i.e. soft coral)

DMT can be synthesized chemically, or via chemical extraction from these DMT-containing plants

DMT is rapidly broken down in the body and converted into the metabolites indole-3-acetic acid (IAA) and DMT-N-Oxidase (DMT-NO), which can be detected in the blood and urine

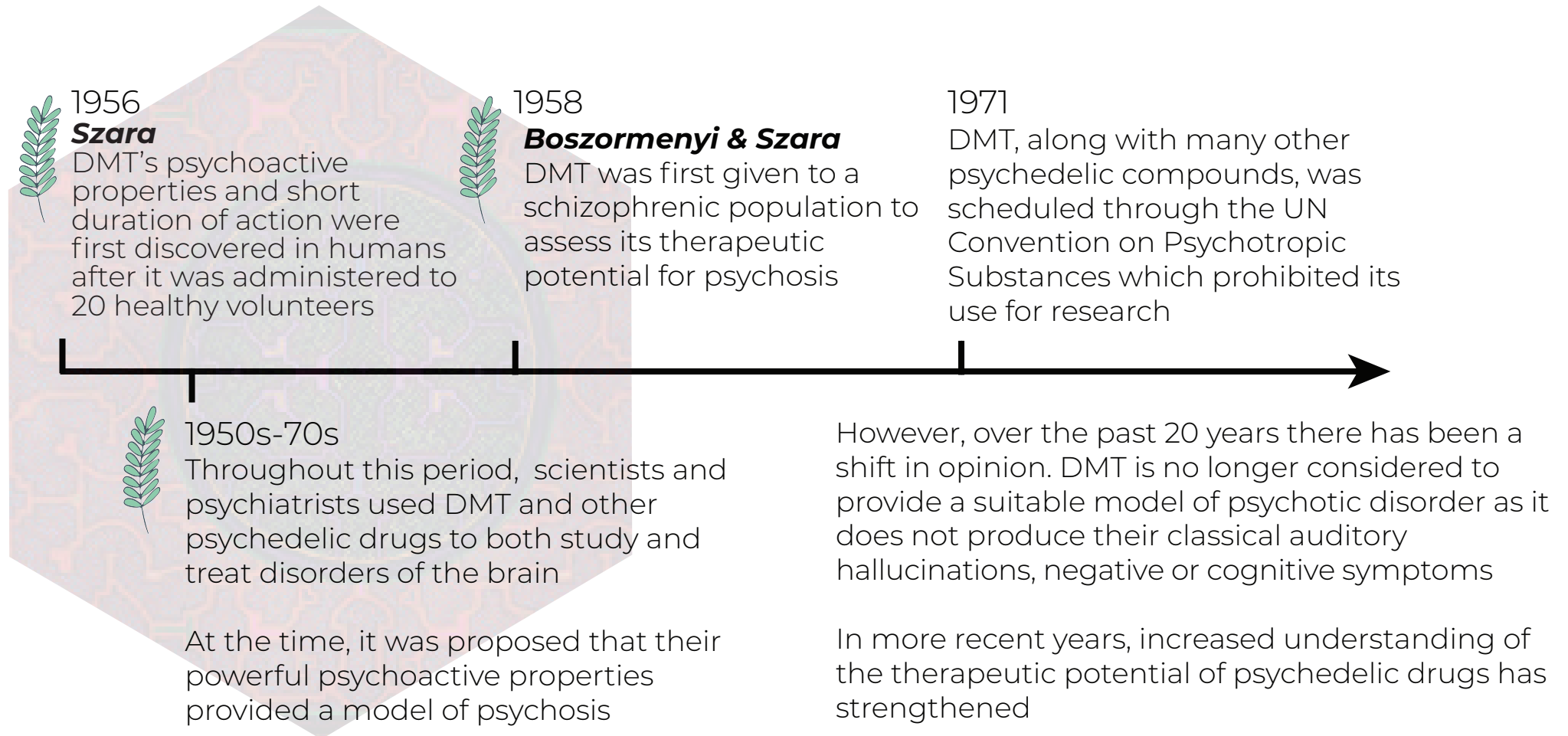


The discovery of DMT



First wave of human DMT research

A small number of human studies using DMT in the 1950s - 1970s helped to characterise its powerful psychoactive properties, fast metabolism and safe physiological profile



What is Ayahuasca?

“Ayahuasca” is a word of the indigenous Quecha people of the Peruvian and Ecuadorian Amazon

Translated to “Vine of the soul”, Ayahuasca is a brew which is traditionally made by boiling the stems of the vine *Banisteriosopsis caapi* and leaves of the shrub *Psychotria viridis*



Banisteriosopsis caapi – a South American hallucinogenic vine in the Malapighiaceae plant family and is rich in β -carbolines such as harmine, tetrahydroharmine and harmaline

These compounds are reported to inhibit the rapid metabolism of DMT in the body, as well as exhibit psychoactive properties

Different source plants and preparation methods can be used. Chemical variations between different plants and techniques can cause wide variations in the levels of constituent components



Psychotria viridis – a shrubby flowering plant in the Rubiaceae coffee plant family and contains DMT

DMT is the main psychoactive component of Ayahuasca and is largely responsible for the hallucinations and enhanced emotions associated with ayahuasca ceremonies

History of Ayahuasca use

Although, the exact discovery and origin are unknown, ayahuasca has a millennia-old history of ceremonial use in religious and spiritual settings for healing and therapeutic purposes in Mesoamerican cultures

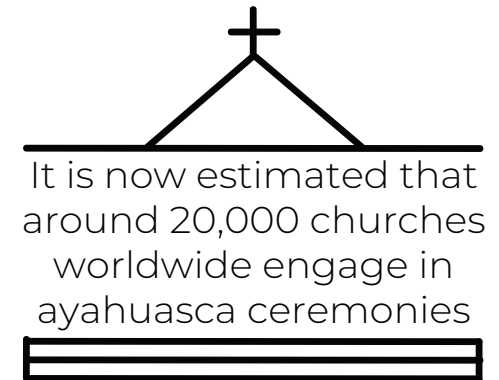


Despite increased global popularity, ayahuasca has largely maintained its traditional roots as an important element of shamanic traditions and alternative medicine

The powerful action of ayahuasca was adopted in certain South American religious practices such as those used by the União do Vegetal (UDV) and Santo Daime sects

The UDV was crucial for the Brazilian government's permission for ayahuasca use in certain religious settings in 1987

This was the **first government approval of religious psychedelic use for non-indigenous people in over 1600 years**



It is now estimated that around 20,000 churches worldwide engage in ayahuasca ceremonies

Throughout the 1990s, ayahuasca gained popularity from North American tourists. Year on year, its popularity has grown amongst people from all over the world in search for a unique **entheogenic experience**

Convention on Psychotropic Substances

The Convention of Psychotropic Substances is a United Nations treaty signed on 21st February 1971, designed to control the use of all psychoactive drugs

Under this treaty, DMT was given a schedule 1 status which prohibited any medical and recreational use, as well as severely restricting its use in research

Certain exemptions are made to states where, when at the time of signature, naturally occurring DMT-containing plants are grown in the wild and are used for traditional spiritual or religious purposes

At present no plants or any endogenous DMT containing material are controlled under the UN treaty and under international control. However, these materials cannot be traded internationally

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TALK ABOUT WHY
PSYCHEDELICS
WERE BANNED**

National schedules

US schedule 1

UK schedule 1

Australia schedule 9

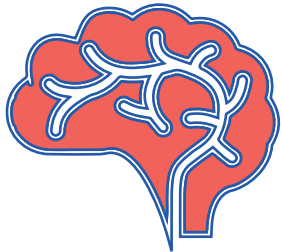
Research is permitted with requisite ethics approvals, with both state and national permits

All of these Schedules explicitly specify no medical use, high abuse potential and high risk when used in a clinical setting

The start of the Psychedelic Renaissance

In **1994, Dr. Rick Strassman** revived psychedelic research with the **first federally approved psychedelic study** since their ban in the 1970s. This pioneering study investigated the biological and psychological effects **using various doses of DMT**

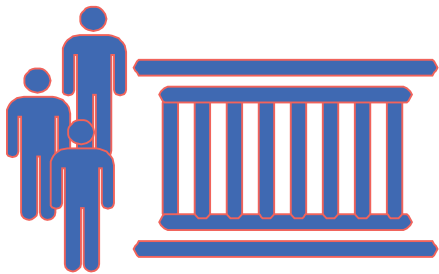
The decision to use DMT was made for several reasons:



Scientific

One theory on the origin of psychosis, which speculated DMT as a potential endogenous toxin, enabled Strassman to argue that DMT could be used to better understand schizophrenic disorder

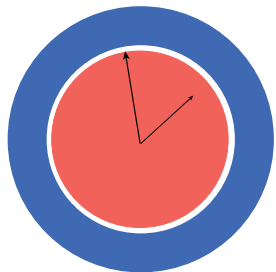
Since then, this theory has been largely rejected



Political

DMT was relatively unknown and did not have the reputation that the more 'conventional' psychedelic drugs (e.g. LSD, psilocybin) carried. This made the authorities more accepting of DMT's use

Strassman's proposed study was also less prone to bias as DMT's unfamiliar nature meant its effects were less anticipated by study participants



Practicality

DMT's short duration of action when administered intravenously, made the study's protocol less practically demanding and minimised the length of any potential acute adverse reaction, compared to longer acting psychedelic drugs

The battle for approval

It took Strassman **two years to resolve the regulatory hurdles** necessary to gain the necessary approvals to conduct human research with psychedelic drugs

1. Federal approval



Strassman had to go through a number of regulatory bodies, including:

- Institutional review board (IRB)
- Food and Drug Administration (FDA)
- Drug Enforcement Agency (DEA)

These agencies **required evidence for the safe, ethical and potential value for human use of DMT**, which according to its Schedule 1 drug definition had *“no medical value”* and *“could not be used safely, even under medical supervision”*

2. Research grade DMT

Another significant problem was finding a **research grade DMT**, with **high enough purity for human consumption**. The supplies of the drug available from chemical companies were all lab-grade i.e. *“not intended for human use”*

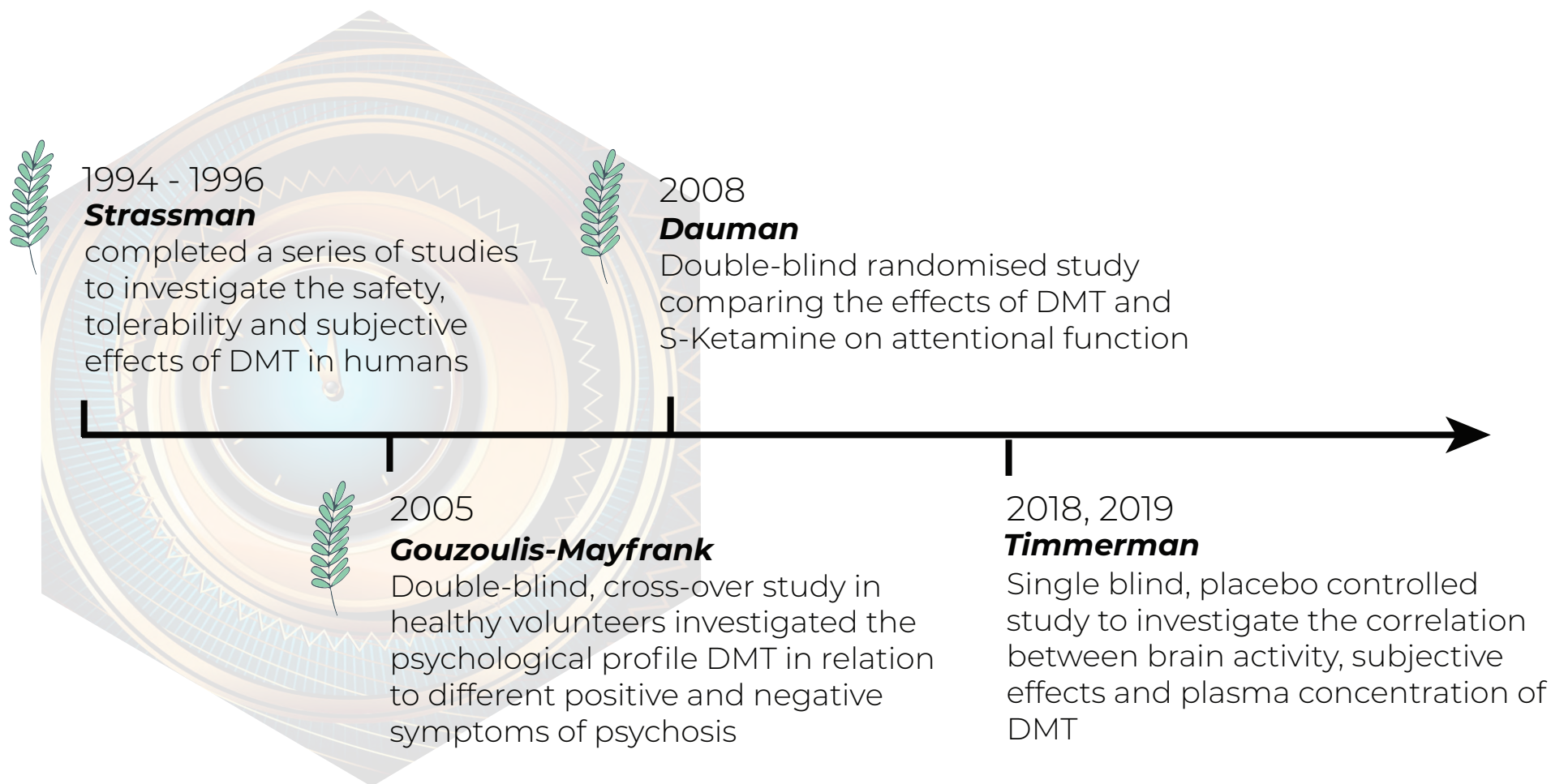
Eventually, Pharmacologist and Chemist, Dr David Nichols agreed to make DMT to the specifications imposed by the FDA



Although regulatory bodies are more accepting of psychedelic research today, the financial costs and regulatory hurdles are still a significant issue

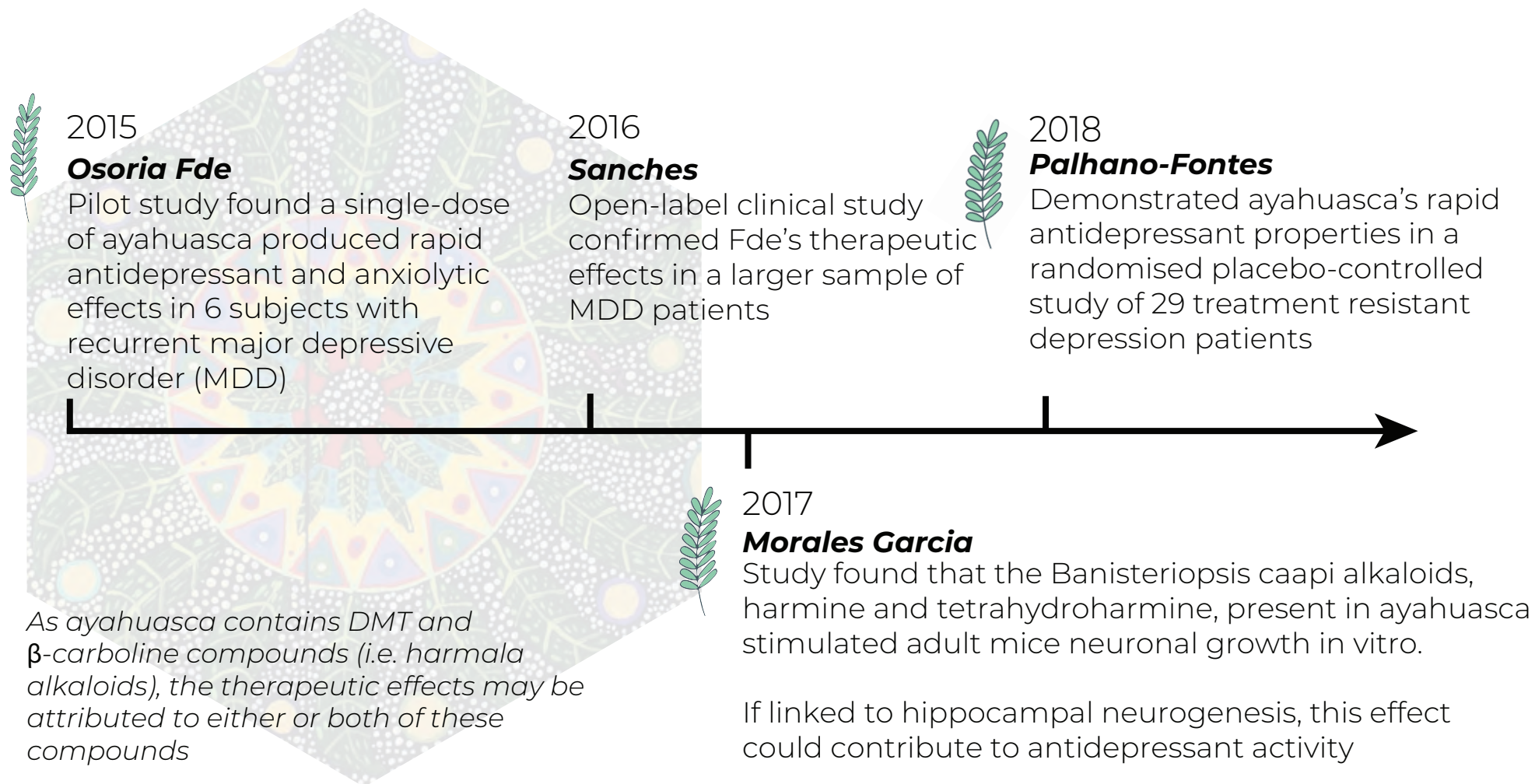
Unlike most other fields of medical research, few government funding agencies or pharmaceutical companies are willing to fund and explore the use of psychedelics due to the negative stigma and costs associated with strict approvals and the required **Home Office licences (UK)**

Renaissance of DMT research



* years denote years of associated published work

Clinical research of Ayahuasca



* years denote years of associated published work

Use in society and counterculture

A recent global drug survey (2019) and increased anecdotal evidence suggests that the popularity of DMT and ayahuasca are on the rise

However, the use of DMT and ayahuasca, 4.2% and 1.1% respectively, remains significantly less than more commonly known psychedelics drugs (LSD: 17.5%, magic mushrooms: 14.8%)

Survey respondents reported **DMT as having the most desirable effect profile** of the four psychedelics queried, **owing to its rapid onset of action** and **fewer reports of negative effects**



- During the 1960s, DMT was sometimes referred to as the “Businessman’s lunch” or “Businessman’s trip” as one could experience a full psychedelic trip during the timeframe of a typical corporate professional’s lunch break
- DMT’s powerful and sometimes life-changing effects have been reported to create new perspectives on life which holds therapeutic potential for the treatment of mental health disorders



- A so called ‘Ayahuasca industry’ has boomed in the past 20 years due to increased global media coverage of the healing and spiritual power of ayahuasca
- Hundreds of locals and tourists in search of a spiritual, therapeutic or life-changing experience are drawn to ayahuasca healing centres in the Amazon each year. These experiences have largely upheld their shamanic routes
- Ayahuasca’s popularity has led to the emergence of many one-day ceremonies and month-long retreats in other areas of the world, such as Costa Rica, Netherlands, Spain and Portugal

International Law




Comparison DMT and Ayahuasca

DMT

- DMT is **not orally active** due to its quick metabolism in the human body
- In its pure form, DMT is a **white crystalline powder or solid**. It has a potent and unusual smell and taste which has been compared to burnt plastic and new shoes
- It is **fast acting** (0 - 2 mins) and has a **short duration** (30 - 60 mins) of action
- Recreationally, DMT is usually **inhaled or injected. Intravenous (iv)** administration is most commonly used in research
- Doses vary depending on route of administration, **iv dose range from 0.02 - 0.25 mg/kg** DMT (freebase) in research literature
- The acute effects of the DMT experience include **intense visions** and **changes in experiences of reality** and **feelings of near death and euphoria**

Ayahuasca

- The harmala alkaloid compounds in ayahuasca inhibit the breakdown of DMT in the body, making it **orally active**
- Ayahuasca tea (also known as daime, yajé, yagé, natema) is a **bitter beverage** that sometimes manifests as a black sludge
- Its duration of action can last between **2 - 6 hours**, which varies between different people and concoctions
- The brew is traditionally **drunk** in healing ceremonies, overseen by a shaman
- Concentration of DMT in ayahuasca brews can **vary widely** due to chemical variation of the source plants and preparation methods, the average dose of **DMT is around 27 mg**
- The acute effects of the ayahuasca experience include **introspection, changes in perception and reality**

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- There is **no evidence to suggest that DMT and ayahuasca are addictive**
 - The greatest risk associated with DMT and ayahuasca use are due to the **unpredictable and varied** nature of reactions between different users
 - It is believed that DMT and ayahuasca have **high therapeutic power for many mental health disorders**, however, their transient psychological effects make their use **unsuitable for people with potential for psychotic episodes**
 - The intense psychedelic effects of DMT and ayahuasca, characterised by extreme distortions of colours, sounds, time and so called out of body experiences **can cause feelings of anxiety, distress and confusion**. Some users report experiencing near-death-like experiences
 - Ayahuasca can be associated with **'purging'** which usually involves vomiting or diarrhoea. Some people believe is integral to the ayahuasca experience. DMT can also cause these symptoms however, it is less common. Other physiological effects include increased **heart rate and blood pressure**



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