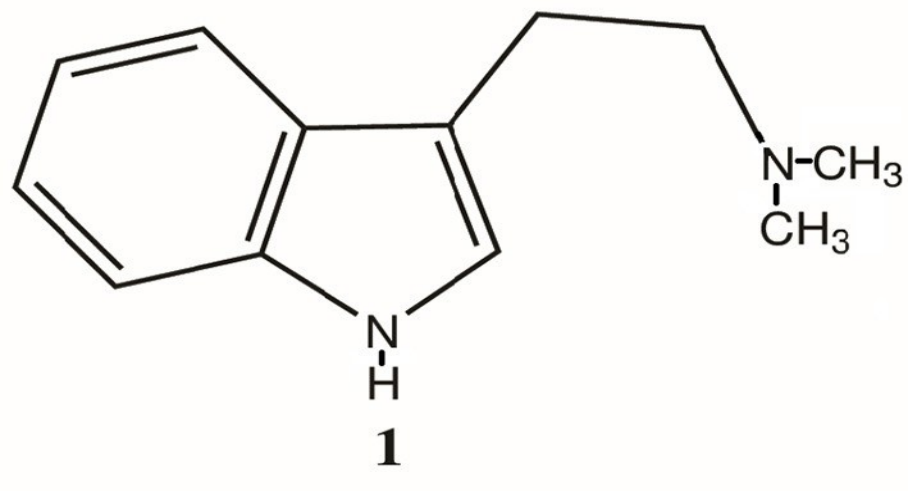
N,N-Dimethyltryptamine (DMT)



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Brief History

"In terms of Western culture, DMT was first synthesized by a German-Canadian chemist, Richard Manske, in 1931 (Manske, 1931) but was, at the time, not assessed for human pharmacological effects. In 1946 the microbiologist Oswaldo Gonçalves de Lima discovered DMT's natural occurrence in plants (Goncalves de Lima, 1946). DMT's hallucinogenic properties were not discovered until 1956 when Stephen Szara, a pioneering Hungarian chemist and psychiatrist, extracted DMT from the Mimosa hostilis plant and administered the extract to himself intramuscularly (Szára, 1956). This sequence of events formed the link between modern science and the historical use of many DMT-containing plants as a cultural and religious ritual sacrament (McKenna et al., 1998), their effect on the psyche and the chemical structure of N, N-dimethyltryptamine." (1)
Since 1955, the substance has been found in a host of organisms: in at least fifty plant species belonging to ten families, and in at least four animal species (2)
DMT is one of the major psychoactive compounds found in various shamanistic compounds (e.g., ayahuasca, hoasca, yagé) used in South America for centuries

Pharmacology

NN-DMT is a classical psychedelic substance of the tryptamine class.The combined data demonstrate that DMT is formed from tryptophan , a common dietary amino acid, via the enzyme aromatic L-amino acid decarboxylase (AADC). formation of TA and its subsequent N, N-dimethylation. The enzyme indolethylamine-N- methyltransferase (INMT) uses S-adenosyl-l-methionine as the methyl source to produce N-methyltryptamine and then DMT .

Considering that tryptamine formation, itself a trace biogenic amine, is essential for the formation of DMT and given its own rapid metabolism by monoamine oxidase (MAO) as well, demonstrating its availability for the biosynthesis of DMT is also relevant to a complete elucidation of the overall pathway. "We should not rule out the possibility that the biosynthesis and transport of DMT can and does occur from the periphery, however. Peripheral DMT, especially if synthesized in tissues that

bypass liver metabolism on first pass, may also serve as a signaling compound from the periphery to the brain." (1)
DMT's psychedelic effects are believed to come from its efficacy at the 5-HT2A receptor as a partial agonist. However, the role of these interactions and how they result in the psychedelic experience continues to remain elusive. DMT does not have direct effects on DA receptors, but indirectly alters the levels of dopamine, with resulting neurochemical and behavioral effects. Similarly, DMT also alters levels of acetylcholine. (5)
DMT is endogenous, produced internally in mammals, and it is often associated with peak experiences such as birth and death. (Strassman is the main proponent here) Although there is data associating it with the pineal gland in the brain, this is not set in stone scientifically as of yet. It may be associated with other parts of the brain too. This pineal view was contested by David E. Nichols in 2018, who argued that the pineal gland secretes insufficient amounts of DMT to produce psychoactive effects.
In 2019, a study by Jimo Borjigin demonstrated in rat brains that brain neurons with the two enzymes required to make DMT were not just in the pineal gland but also in the neocortex and hippocampus.

Potential Benefits

In September 2020, an in vitro and in vivo study showed that DMT present in the ayahuasca infusion promotes neurogenesis. (3)

In 2018, a study demonstrated neuroplasticity induced by DMT and other psychedelics through TrkB, mTOR, and 5-HT2A signaling. (4)
Because of its role in nervous system signaling, DMT may be a useful experimental tool in exploring how the brain works, and may also be a useful clinical tool for treatment of anxiety and psychosis. (5)
There has been a report that DMT is neuroprotective. (6)

Ayahuasca has been reported to decrease the percentage of CD3 and CD4 lymphocytes, but to increase the number of natural killer cells (Dos Santos et al., 2011). It has been hypothesized that DMT might increase activity of the immune system and could prove useful as a treatment for cancer.

N,N DMT may be useful in the future for treating substance abuse but because there is so little data and the experience so intense, it is far too early to ascribe this benefit as of yet. Certainly the ayahuasca brew has shown to be helpful in this regard (Gabor Mate & others, including shamans have explored this) but results are inconsistent- sometimes very promisng but sometimes underwhelming.

Positive effects on mood& anxiety have been found in a 2019 study on rats with microdoses of N,N DMT (7)

General Effects

Among psychedelics, DMT is known for its unique ability to produce short-lived but intense visionary states and complete hallucinations. It is thought to produce its effects by binding to serotonin receptors in the brain, although the precise mechanism is not fully understood. Depending on the dosage and method of administration, the effects of DMT can range from mild psychedelic states to powerfully immersive life-altering experiences which are often described as the ultimate displacement from ordinary consciousness in which users report experiencing ineffable spiritual realms or alternate dimensions. It's also commonly reported to encounter 'beings' of unknown origin after consuming a high dose of DMT. Terrence Mckenna and Dr. Rick Strassman have both studied and popularized this phenomenon.
Wakefulness - The administration of DMT with an MAOI (as with ayahuasca) can extend the effects for long enough to suppress the user's urge to sleep

A longer listing of possible effects is found at the psychonautwiki page.

CAUTION : Anxiety seems to manifest more consistently with (smoked) DMT in comparison to other psychedelics and it's oftenly present during the come up phase, fading off while the user enters the peak. This effect may be related to the drug's capacity to produce high levels of memory suppression given that the feeling itself is oftenly described as if one's consciousness is losing touch with reality or that the mind is being ripped apart. In very high doses the user may suffer the perception that they are being driven to insanity against their will, getting disintegrated or even fall into the not uncommon delusion that they are dying. The practice of grounding exercises & spiritual preparation can help the user to deal with this effect.

Dosage

WARNING: Always start with lower doses due to differences between individual body weight, tolerance, metabolism, and personal sensitivity.

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- Smoked Dosage

Threshold	2 mg
Light	10 - 20 mg
Common	20 - 40 mg
Strong	40 - 60 mg
Heavy	60+ mg

Duration
Total
5 - 20 minutes
Onset
20 - 40 seconds
Come up
1 - 3 minutes
Peak
2 - 8 minutes
Offset
1 - 6 minutes
After effects
10 - 60 minutes

- Intramuscular injection of DMT (up to 80 mg; 0.2- 1 mg/kg; 30-60 minutes duration)
- Intranasal administration of DMT (unknown dosage ranges, presumed similar to those of smoked/vaporized DMT, unknown duration)

-Oral ingestion with an MAOI will extend the duration to multiple hours as with ayahuasca brews and create a much different experience (Note -this paper deals primarily with the smoked form)

A trip sitter is recommended with this substance that often is smoked in heavy doses.

Short-acting intense trips may cause mental and physical side effects days after the hit has been taken.
The overwhelming effects often require post-processing. It may take 2 days before physical side effects become noticeable, like shift in hearing. Using additional substances without a break (2 days + a few days to recover if you notice any side effects) increases the risk to get a bad post-trip

Interactions/Contraindications

N,N-DMT is contraindicated in children, and in pregnant and lactating women. Avoid taking if you're feeling highly nervous, stressed or depressed. It is not recommended for those with serious hypertension, anxiety, or mental health concerns.
Avoid mixing with any other substances in general, due to it's overwhelming effects.
Driving or operating machinery while under the influence should be strictly avoided. (Although it's virtually impossible that you would even be capable)
Unlike most highly prohibited substances, DMT has not been proven to be addictive or physiologically toxic. Adverse reactions such as severe anxiety, delusions and psychosis are always possible, even for experienced users, and particularly for those predisposed to mental disorders.
DMT appears to have limited neurotoxicity and other adverse effects except for intense cardiovascular effects when administered intravenously in large doses. (5)
Even though DMT may not produce physical toxicity, severe psychological adverse effects can occur.

References

1) https://www.frontiersin.org/articles/10.3389/fnins.2018.00536/full
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3) Morales-Garcia, JA; Calleja-Conde, J; Lopez-Moreno, JA; Alonso-Gil, S; Sanz-SanCristobal, M; Riba, J; Perez-Castillo, A (28 September 2020). "N,N-dimethyltryptamine compound found in the hallucinogenic tea ayahuasca, regulates adult neurogenesis in vitro and in vivo". Translational psychiatry.

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6) (Frecska, 2008)
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