Journal of Community Pharmacy Practice
Vol: 04, No. 02, July-Dec 2024
ISSN: 2799-1199, DOI: 10.55529/jcpp.44.1.9

Research Paper

Psychoactive drug MDMA

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Article Info

Article History:
Received: 03 Mar 2024
Revised: 11 May 2024
Accepted: 19 May 2024
Published: 03 July 2024

Keywords:
MDMA
Ecstasy
PTSD
Dopamine
Serotonin

ABSTRACT

Background: 3,4-Methylenedioxymethamphetamine (MDMA; ecstasy, molly) is a synthetic psychoactive drug that produces increased empathy, emotional connection, and heightened sensory percepstion. After early use as an adjunct to psychotherapy and widespread recreational use, it was placed under strict legal control in many countries. Recent research has renewed interest in its therapeutic potential, particularly for post-traumatic stress disorder (PTSD).
Objective: To review the pharmacological effects of MDMA, its historical and cultural significance, the current evidence for MDMA-assisted therapy, and the debate over its legal status.
Methods: Narrative review of the pharmacological, historical, clinical, and policy literature on MDMA, with emphasis on clinical trials of MDMA-assisted psychotherapy for PTSD and on regulatory and legal frameworks across jurisdictions.
Results: MDMA acts mainly by releasing serotonin and inhibiting its reuptake, with lesser effects on noradrenaline and dopamine and increased oxytocin signalling. Acute risks include hyperthermia, hyponatraemia, and cardiovascular strain, and heavy or repeated use raises concern about serotonergic neurotoxicity. Clinical trials report reductions in PTSD symptom severity when MDMA is combined with structured psychotherapy. Limitations include functional unblinding, expectancy effects, variable therapist conduct, and limited long-term safety data. Legal and regulatory approaches differ considerably between countries.
Conclusions: MDMA-assisted therapy shows therapeutic promise, but larger and more rigorous trials, standardised treatment protocols, and long-term safety monitoring are needed. Drug policy should be guided by evidence while still addressing the harms of unsupervised recreational use.

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Journal of Community Pharmacy Practice (JCPP)

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1. INTRODUCTION

From a diverse spectrum of backgrounds and demographics, underscoring its appeal to a broad audience. Nevertheless, despite the importance and size of the dance drug scene, there hasn't been much scientific study into its drug usage behaviours. Ecstasy use among "ravers" is widely believed, although little is known about the precise drugs used in the scene or the connections between the drug use and going to dance events. By shedding light on drug use patterns among "ravers" and the significance of dance events in influencing these patterns, this thesis seeks to fill up these knowledge gaps. The study will utilize a quantitative methodology to assess the level of drug use among "ravers," and it will statistically examine any associations between drugs and dance music genres that may be discovered. By carrying out this investigation, the study hopes to offer an in-depth knowledge of the drugs used in the party drug scene and how common their use is. Additionally, it will look into the connections involving drug usage and attending dance activities as well as 'ravers' who take drugs in environments irrelevant to the dance the scene. It's essential to comprehend the drug usage trends in the dance drug scene in order to create successful harm reduction plans and preventative programs. This thesis intends to add to the present knowledge of the entertainment drug phenomena in the 1990s by addressing these knowledge gaps and informing future actions as well as policies in this sector

Emphasising its appeal to a broad audience. Nevertheless, despite the importance and size of the dance drug scene, there hasn't been much scientific study into its drug usage behaviours. Ecstasy use among "ravers" is widely believed, although little is known about the precise drugs used in the scene or the connections between drug use and going to dance events and the significance of dance events in influencing these patterns, the study will utilize a quantitative methodology to assess the level of drug use and it will statistically examine any associations between drugs and dance music genres that may be discovered. By carrying out this investigation, the study thorough understanding of the drugs used in the dance drug scene and how common their use is. Additionally, it will look into the connections between drug usage and attending dance events who take drugs in environments unrelated to the dance scene. Understanding the patterns of drug use within the dance drug scene is crucial for developing effective harm reduction strategies and prevention initiatives. By filling these knowledge gaps, this thesis will contribute to the existing understanding of the dance drug phenomenon in the 1990s and inform future interventions and policies in this area. The pharmacology of chemicals used as dance drugs, including MDMA, has been extensively studied. This study incorporates knowledge from medical resources that concentrate on psychiatric, psychological, biochemical, and neurological issues. Particularly, amphetamine drug research has received a lot of concern. This new concept drug's primary considerations include not merely its chemical structure or physical characteristics, as implied by its "ecstasy" moniker, but also its desired effects and the particular setting in which it is intended to be ingested. In contrast to conventional medications, which are categorized primarily based on aspects like price or purity, this drug is made with the intended effects in mind and is intended to be used in a certain situation or context. The techno and house varieties of music that is electronic were major influences on the emergence of the rave scene in the latter part of the 1980s and early 1990s.

Ravers cherished a spirit of optimism, community, and spiritual discovery as they enjoyed all-night party events that were frequently fuelled by substances like Methamphetamine. The blending of subcultures and inspirations was not exclusively a natural process. The emergence of a wide variety of alternative subcultures was a long process that occurred over several decades as various counterculture activities borrowed from and were inspired by one another. A distinctive style of dancing associated with the gabba music genre. It involves fast, energetic movements, often characterized by quick kicks and jumps.

The hardcore warriors in Italy have embraced this dance style, but with their own unique twist. The hardcore warriors in Italy have added their own stylistic variations to the gabber dance. They are distinguished by their crazy colored Mohawk, instead of the traditional shaven heads often associated with the gabba scene. Their attire includes cyber apparel such as studded collars, fluorescent leggings, and flashy tight tank-tops. They also engage in face painting, further enhancing their unique look. One notable ritual among the hardcore warriors is the construction of a human pyramid. This ritual originated in a room called Sala, which was originally dedicated to metal music, at Number One, a club in Cortefranca, Brescia. Even after the locals transitioned to techno music, the heavy-metal moshpit continued. By 2000, the ritual had evolved into a human tangle, with hardcore warriors climbing on top of each other to construct a monolith. The first person to reach the top of the pyramid and touch the ceiling was crowned the emperor of the gabba kingdom. The hardcore warriors in Italy have created their own distinct subculture within the gabba scene. They have collided, both figuratively and physically, with the traditional gabba mother-culture, bringing their unique style, rituals, and dance moves. The presence of the hardcore warriors adds diversity and creativity to the overall gabba culture in Italy [1], [2], [3].



Figure 1. MDMA Crystal Powder

1.1 Pharmacological Effects

MDMA primarily affects the serotonergic, dopaminergic, and noradrenergic systems in the brain. It increases the release of serotonin, leading to feelings of euphoria, emotional connection, and increased empathy. Dopamine and norepinephrine release contribute to heightened energy and focus. However, MDMA can also cause adverse effects like hyperthermia, dehydration, and bruxism (teeth grinding). Additionally, potential neurotoxicity, particularly with repeated use, remains a subject of ongoing research. MDMA's psychoactive effects stem from its influence on several key neurotransmitter systems in the brain, primarily serotonin (5-HT), dopamine (DA), and norepinephrine (NE) [4].

Serotonin: MDMA increases the release and inhibits the reuptake of serotonin, leading to elevated levels in the synaptic cleft [4]. This surge in serotonin is primarily responsible for the characteristic effects of MDMA, including feelings of euphoria, emotional warmth, empathy, and increased sociability [5].

Dopamine: MDMA also increases dopamine release, contributing to the feelings of pleasure, motivation, and increased energy levels associated with the drug [6].

Norepinephrine: MDMA's effect on norepinephrine is less pronounced but contributes to the stimulant properties of the drug, such as increased alertness and heart rate [7].

Physiological Effects: In addition to its effects on neurotransmitters, MDMA also produces various physiological effects:

Hyperthermia: MDMA disrupts the body's ability to regulate temperature, leading to a potential rise in core body temperature (hyperthermia) [8]. This can be dangerous in hot environments or with strenuous physical activity.
Dehydration: MDMA increases heart rate and sweating, which can lead to dehydration if fluids aren't adequately replaced [9].
Bruxism: MDMA can cause involuntary clenching of the jaw (bruxism), leading to teeth grinding and jaw pain [10].
Cardiovascular Effects: MDMA can increase heart rate and blood pressure, potentially putting strain on the cardiovascular system, especially in individuals with pre-existing heart conditions [11].
Potential Neurotoxicity: There is ongoing debate regarding the potential neurotoxic effects of MDMA. Some studies suggest that repeated use might damage serotonin-producing neurons in the brain, although the long-term consequences of this remain unclear. Further research is needed to definitively determine the extent of MDMA's neurotoxic potential [12], [13].

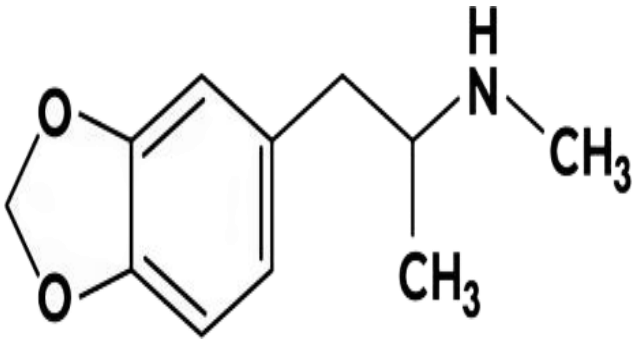


Figure 2. Chemical Structure of MDMA Drug

1.2 History and Culture

MDMA's origins can be traced back to the early 20th century, but it gained notoriety in the 1980s as a recreational drug within the underground rave scene. Its association with dance music and feelings of connection fostered a subculture that continues to influence popular culture today. However, concerns about safety and abuse led to its classification as a Schedule I drug in the United States by the DEA in 1985, signifying a high potential for abuse and no currently accepted medical use. MDMA's story is a fascinating tapestry woven with scientific exploration, therapeutic experimentation, and a vibrant underground scene.
Early Synthesis (1912): MDMA was first synthesized in 1912 by German chemist Anton Köllisch working for Merck [14]. However, its psychoactive properties remained undiscovered for decades.
Therapeutic Exploration (1970s): In the 1970s, American psycho pharmacologist Alexander Shulgin rediscovered MDMA and began exploring its therapeutic potential [15]. He documented its effects in his book "PIHKAL: A Chemical Love Story" (although the book itself is not a scientific source, it can be referenced as a historical document of early exploration). Therapists started using MDMA in sessions to facilitate emotional processing and communication between patients and therapists [16].
Underground Rise (1980s): By the late 1970s, MDMA use trickled into the counterculture scene. In the 1980s, it exploded in popularity within the burgeoning underground rave scene in the United States and Europe [4]. The association with electronic dance music, all-night parties, and a sense of communal connection cemented MDMA's cultural image as "ecstasy" or "molly."
Legal Restrictions (1985): Concerns about safety and potential for abuse led to MDMA's classification as a Schedule I drug in the United States by the DEA in 1985 [17]. This classification signifies a high potential for abuse and no currently accepted medical use, hindering further research.
Enduring Legacy: Despite its legal restrictions, MDMA's cultural influence continues. References to "ecstasy" appear in music and popular culture, and the drug retains a presence in some nightlife circles. However, the focus has shifted towards potential therapeutic applications, with renewed research exploring its benefits for treating mental health conditions.

2. RELATED WORK

MDMA-Assisted Psychotherapy for PTSD: This area has seen significant research. A 2017 study by Mithoefer et al. titled "3, 4-Methylenedioxymethamphetamine (MDMA)-Assisted Psychotherapy for Treatment-Resistant Post-Traumatic Stress Disorder: Study Design and Preliminary Results" explored the use of MDMA-assisted therapy for chronic PTSD. The study showed positive results in reducing PTSD symptoms [18].

Neurochemistry of MDMA: Understanding how MDMA works in the brain is crucial. A 2018 review by Liechti et al. titled "The Pharmacology of MDMA: A Review" delves into the neurochemical effects of MDMA, including its influence on serotonin and dopamine [19].

3. METHODOLOGY

Despite its Schedule I status, research on MDMA-assisted psychotherapy has shown promising results. Studies suggest it can be effective in treating PTSD by facilitating emotional processing and reducing fear responses in a controlled therapeutic setting. Initial research also indicates potential benefits for anxiety disorders and social anxiety. MDMA-assisted psychotherapy has shown promise in treating several mental health conditions characterized by social and emotional dysfunction. While PTSD and social anxiety disorder are at the forefront of current research, the therapeutic potential of MDMA may extend to other areas.

Treatment-Resistant Depression: Major depressive disorder (MDD) is a debilitating condition affecting millions worldwide. Early-stage studies suggest that MDMA-assisted therapy could help individuals with treatment-resistant MDD by facilitating emotional processing, reducing negative self-beliefs, and enhancing feelings of connection [20].

Anxiety Disorders: Social anxiety disorder is just one facet of the broader category of anxiety disorders. MDMA's ability to promote emotional openness and decrease social inhibitions could be beneficial for individuals struggling with generalized anxiety disorder or specific phobias [21].

Addiction Disorders: Substance abuse and addiction are often rooted in underlying emotional trauma or distress. MDMA-assisted therapy could potentially help individuals confront these underlying issues, fostering healthier coping mechanisms and reducing the desire to use addictive substances [22].

End-of-Life Distress: For terminally ill patients, MDMA-assisted therapy may alleviate anxiety and depression associated with death, allowing for a more peaceful acceptance of their situation and improved quality of life in their remaining time.

Autism Spectrum Disorder (ASD): Social interaction difficulties are a core feature of ASD. While research is limited, some studies suggest that MDMA's ability to enhance empathy and social connection might improve social interaction skills in individuals with ASD. However, more research is required to confirm these findings. It is important to note that these applications are still in the early stages of exploration. Rigorous clinical trials are needed to establish the safety and efficacy of MDMA-assisted therapy for these conditions. Additionally, the integration of psychotherapy into the treatment plan appears to be crucial for maximizing the therapeutic benefits of MDMA [23].

3.1 Legal and Ethical Considerations

The therapeutic potential of MDMA is counterbalanced by legal and ethical considerations. Its classification as a Schedule I drug hinders further research and clinical trials. Additionally, ethical concerns regarding patient safety and potential risks associated with the drug necessitate careful consideration and stringent protocols for therapeutic use [24]**.** The potential therapeutic applications of MDMA-assisted psychotherapy present a unique set of legal and ethical considerations. While research suggests promising results, several challenges must be addressed before widespread adoption becomes a reality.

3.2 Legal Status

Schedule 1 Classification: MDMA is currently classified as a Schedule I drug in many countries, including the United States according to the Controlled Substances Act (CSA) (Drug Enforcement Administration [DEA], 2023). This classification signifies a high potential for abuse and no accepted medical use. The growing body of research on its therapeutic potential contradicts this classification and may lead to reclassification efforts.

Regulation and Access: If reclassified, establishing regulations for MDMA-assisted therapy would be crucial. This includes defining qualifications for therapists, protocols for administration, and monitoring procedures to ensure patient safety and ethical conduct. The Multidisciplinary Association for Psychedelic Studies (MAPS) has developed a comprehensive framework for MDMA-assisted psychotherapy that could serve as a model for regulatory bodies.

International Disparity: Legal frameworks surrounding MDMA vary significantly across countries. The International Narcotics Control Board (INCB) classifies MDMA in Schedule I of the 1971 Convention on Psychotropic Substances (INCB, 2023). However, some countries have granted exemptions for research purposes. This disparity creates challenges for international research collaboration and potential issues for individuals seeking treatment abroad.

3.3 Ethical Considerations

Informed Consent: Due to the powerful psychoactive effects of MDMA, obtaining informed consent from participants in clinical trials requires meticulous attention. Participants must fully understand the potential risks and benefits, including the potential for emotional distress during therapy sessions, as outlined by the ethical principles outlined in the Belmont Report (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1978).

Vulnerability and Exploitation: MDMA-assisted therapy may be particularly appealing to individuals with severe mental health challenges. Strict ethical guidelines are necessary to ensure these vulnerable populations are not exploited or pressured into participating in research. The International Society for Ethical Considerations in Research & Healthcare (ISECRH) has developed principles specifically regarding research with vulnerable populations (ISECRH, 2023).

Therapist Bias: Therapists involved in MDMA-assisted therapy should be free from personal biases regarding the drug. Additionally, the potential for therapists to have prior recreational experience with MDMA raises concerns about professional boundaries and potential conflicts of interest. The American Psychological Association (APA) has established ethical guidelines for psychologists, which can be applied to therapists involved in MDMA-assisted therapy. Addressing these legal and ethical considerations is critical for ensuring the responsible and safe development of MDMA-assisted therapy. Open dialogue between researchers, clinicians, legal experts, and policymakers is required to establish a regulatory framework that fosters therapeutic innovation while protecting patient safety and upholding ethical principles.

3.4 Here are Some Additional Points to Consider

Cost and Accessibility: MDMA-assisted therapy is likely to be expensive due to the intensive therapeutic approach required. Strategies to ensure equitable access to this treatment for different socioeconomic groups will be necessary

Cultural Considerations: The cultural context surrounding mental health and substance use can influence perceptions of MDMA-assisted therapy. Culturally sensitive approaches to treatment development and implementation are crucial.

Long-Term Effects: Research on the long-term safety and efficacy of MDMA-assisted therapy is still ongoing. Continued monitoring of patients is essential for understanding the potential for delayed adverse effects. By acknowledging and proactively addressing these legal and ethical considerations, the path forward for MDMA-assisted therapy can be navigated responsibly, paving the way for a potential new tool in the fight against mental health challenges.

4. RESULTS AND DISCUSSION

MDMA, commonly known as ecstasy or molly, is a psychoactive substance primarily known for its empathogenic and euphoric effects. Research on MDMA often focuses on its therapeutic potential for treating mental health conditions such as PTSD and depression. Studies suggest that MDMA-assisted therapy can facilitate emotional openness and trust, making it easier for patients to address trauma or difficult emotions during therapy sessions. However, there are also concerns about its potential for misuse and long-term neurotoxic effects on the brain, particularly with repeated use. It's a complex topic with ongoing research and debate in both scientific and public health communities.

5. CONCLUSION

MDMA presents a unique case study. It is a powerful substance with both potential benefits and inherent risks. Further research is crucial to establish its therapeutic efficacy while mitigating potential risks. Open discussion surrounding its legal status is also necessary to advance research and explore its potential role in mental healthcare.

5.1 Future Directions

As research on MDMA-assisted psychotherapy progresses, future directions include large-scale clinical trials to solidify its efficacy for various mental health conditions. Additionally, the development of safer analogs of MDMA with reduced neurotoxic potential could be explored. Open communication and collaboration between scientists, policymakers, and mental health professionals are essential in navigating the path forward for MDMA.

Acknowledgments

The authors have no specific acknowledgments to make for this research.

Funding Information

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Author Contributions Statement

Name of Author	C	M	So	Va	Fo	I	R	D	O	E	Vi	Su	P	Fu
Amit Prasad Rath	✓	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓

C : **C**onceptualization
M : **M**ethodology
So : **So**ftware
Va : **Va**lidation
Fo : **Fo**rmal analysis
I : **I**nvestigation
R : **R**esources
D : **D**ata Curation
O : Writing - **O**riginal Draft
E : Writing - Review & **E**diting
Vi : **Vi**sualization
Su : **Su**pervision
P : **P**roject administration
Fu : **Fu**nding acquisition

Conflict of Interest Statement

The authors declare that there are no conflicts of interest regarding the publication of this paper.

Informed Consent

All participants were informed about the purpose of the study, and their voluntary consent was obtained prior to data collection.

Ethical Approval

Not Applicable.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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How to Cite: Amit Prasad Rath. (2024). Psychoactive drug MDMA. Journal of Community Pharmacy Practice (JCPP), 4(2), 1-9. https://doi.org/10.55529/jcpp.44.1.9

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