

# Ketamine

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## Ketamine

**Primary Disciplinary Field(s):** Pharmacology, Anesthesiology, Psychiatry, Emergency Medicine

### 1. Core Definition

**Ketamine** is a unique pharmaceutical agent primarily classified as a **dissociative anesthetic**. It operates by disrupting the normal communication pathways between different parts of the brain, particularly between the limbic system and the cortex, leading to a state of profound analgesia (pain relief), amnesia, and a sensation of detachment from one's body and environment. This dissociative state is characterized by patients appearing awake but unresponsive to sensory input, hence the term "dissociative." Chemically, ketamine is an arylcyclohexylamine and functions primarily as an N-methyl-D-aspartate (NMDA) receptor antagonist. Its mechanism involves blocking the NMDA receptor, which plays a critical role in learning, memory, and synaptic plasticity, thereby modulating excitatory neurotransmission in the central nervous system.

Beyond its anesthetic properties, ketamine is also notable for its **psychedelic effects**, which contribute to its recreational misuse. These effects, which can include vivid hallucinations, euphoria, and a distorted perception of reality, emerge at sub-anesthetic doses. The drug's versatility allows for various routes of administration, and it can be formulated into different forms, including intravenous solutions, nasal sprays, and, in illicit contexts, tablets, pills, or powder. The complex interplay of its anesthetic, analgesic, and psychotomimetic properties makes ketamine a substance with significant medical utility and substantial potential for abuse, necessitating strict regulatory controls globally.

The unique pharmacological profile of ketamine has positioned it as an indispensable tool in specific medical scenarios, particularly where traditional anesthetics may be contraindicated or less effective. Its ability to maintain respiratory and circulatory stability, even at anesthetic doses, distinguishes it from many other general anesthetics that often cause significant cardiorespiratory depression. This characteristic has made it a preferred choice in emergency medicine, trauma care, and battlefield settings where maintaining vital functions is paramount. The dissociative state it induces, while sometimes unsettling, provides effective pain relief and sedation, allowing medical professionals to perform procedures without compromising the patient's physiological stability.

### 2. Etymology and Historical Development

The journey of **ketamine** from synthesis to widespread medical use and subsequent recognition of its therapeutic potential and risks is a compelling narrative in pharmacology. Ketamine was first synthesized in 1962 by chemist Calvin Stevens at Parke-Davis as a derivative of phencyclidine (PCP), a dissociative anesthetic that had proven effective but was associated with severe

psychomimetic side effects. The objective was to create a compound with similar anesthetic efficacy but a shorter duration of action and fewer adverse psychological effects. After initial preclinical trials, ketamine hydrochloride was introduced for human trials in 1964 by Dr. Edward F. Domino and Dr. Guenter Corssen, demonstrating its potential as a safer anesthetic alternative.

The medical utility of ketamine rapidly gained recognition, particularly during the **Vietnam War** in the 1960s. Its rapid onset of action, potent analgesic properties, and relatively stable cardiovascular profile made it an ideal agent for battlefield medicine. Soldiers suffering from severe **burns, traumatic injuries, and other sources of pain** greatly benefited from ketamine, as it allowed medical personnel to perform procedures even in austere environments without the need for complex monitoring equipment typically required for other general anesthetics. This historical context cemented ketamine's role as a vital tool in emergency and trauma settings, establishing its reputation for effectiveness in critical care.

Following its success in military applications, ketamine was approved for medical use in the United States in 1970. Throughout the subsequent decades, its clinical applications expanded beyond emergency and short-term procedures to include pediatric anesthesia, veterinary medicine, and situations where maintaining spontaneous respiration was crucial. However, concurrently with its medical proliferation, reports of recreational misuse began to surface, largely due to its potent psychedelic effects. This duality--its profound medical benefit alongside its potential for abuse--has defined ketamine's complex trajectory in pharmacology and public health, prompting ongoing research into its mechanisms, therapeutic windows, and responsible regulation.

### 3. Medical Applications

From its inception, **ketamine** has been celebrated for its versatility and efficacy across numerous medical disciplines. As a primary **anesthetic drug**, it is frequently employed for induction and maintenance of anesthesia, particularly in situations where airway reflexes need to be preserved or where cardiovascular stability is a concern. Its unique pharmacological action allows patients to maintain spontaneous breathing and protective airway reflexes, which is a significant advantage in emergency settings, field operations, and in patients with compromised respiratory function. This characteristic makes it a valuable agent for short surgical procedures, diagnostic interventions, and for managing critically ill or injured patients.

Beyond its role as a general anesthetic, ketamine is also a potent **analgesic**. It provides effective pain relief, especially for severe acute pain, and can be used in sub-anesthetic doses for this purpose. Its analgesic properties are particularly beneficial in managing pain associated with trauma, burns, and chronic pain syndromes, where traditional opioids may be less effective or carry a higher risk of respiratory depression. The combination of analgesia, sedation, and amnesia induced by ketamine makes it an excellent choice for painful procedures, allowing patients to

undergo necessary medical interventions with minimal distress and discomfort.

Furthermore, ketamine's broad utility extends to its application as a sedative in critical care environments, particularly for agitated or combative patients requiring intubation or other invasive procedures. Its rapid onset and relatively short duration of action make it manageable for titrating sedation levels. In pediatric anesthesia, ketamine is often favored due to its bronchodilatory effects and its ability to maintain hemodynamics, which is crucial in young patients. Its use in these diverse settings underscores its importance in modern medicine, providing a reliable and often life-saving option for clinicians facing complex patient presentations.

#### 4. Misuse and Adverse Effects

Despite its significant medical benefits, **ketamine** is also widely recognized for its potential for misuse, largely due to its profound **psychedelic effects**. It has gained notoriety as a recreational drug, often known by the street name "**special K.**" Individuals who misuse ketamine may experience a wide range of psychological and physiological effects, even at moderate doses. These can include intense **hallucinations**, vivid and often bizarre visual and auditory distortions, and a powerful sense of **euphoria**. These effects contribute to its appeal in recreational settings but also underscore the significant risks associated with its unsupervised use.

The adverse effects of ketamine misuse extend beyond psychological alterations to significant physiological impacts. Users may experience **confusion**, disorientation, and impaired cognitive function, which can lead to dangerous situations. Cardiovascular effects such as an **increased heart rate and blood pressure** are common, posing risks, particularly to individuals with pre-existing heart conditions. Other observed effects include **anxiety**, agitation, and in some cases, aggressive or **violent behavior**. Physical manifestations can include **slurred speech**, impaired motor coordination, and **blurred vision**, all of which compromise an individual's ability to function safely and rationally.

At higher doses, the risks associated with ketamine escalate dramatically, leading to more profound and potentially life-threatening experiences. These severe effects can include an intense "**out of body experience**" or a sensation often described as a "**near death experience,**" which, while sought after by some users, can be terrifying and disorienting. The most severe consequence of high-dose ketamine ingestion is **coma**, where the individual becomes completely unresponsive, risking respiratory depression and other critical complications. Furthermore, a deeply concerning aspect of ketamine's misuse is its application as a **date-rape drug**. Its rapid onset of **immobilizing effects**, coupled with its ability to induce amnesia and confusion, makes victims vulnerable and unable to resist or recall events, presenting a serious public health and safety threat.

## 5. Therapeutic Potential and Research

Beyond its established role as an anesthetic, **ketamine** has emerged as a groundbreaking subject of research in psychiatry, particularly for its rapid-acting antidepressant effects. Traditional antidepressant medications often take weeks to months to show efficacy, leaving patients in prolonged distress. In stark contrast, studies have demonstrated that ketamine can induce significant antidepressant effects within hours of administration, offering a lifeline for individuals suffering from severe and treatment-resistant depression, including those with suicidal ideation. This rapid response is a paradigm shift in the treatment of mood disorders, opening new avenues for immediate intervention in mental health crises.

The mechanism by which ketamine exerts its antidepressant effects is distinct from conventional antidepressants. Instead of primarily targeting monoamine neurotransmitters (like serotonin or norepinephrine), ketamine's antidepressant action is believed to stem from its antagonism of the NMDA receptor. This blockade is thought to trigger a cascade of neurobiological events, including the activation of the mTOR (mammalian target of rapamycin) pathway and the subsequent synthesis of brain-derived neurotrophic factor (BDNF). These processes lead to the rapid formation of new synaptic connections (synaptogenesis) and restoration of synaptic function in key brain regions associated with mood regulation, such as the prefrontal cortex. This neuroplasticity, which essentially allows the brain to "rewire" itself, is hypothesized to be crucial for its mood-lifting properties.

Research indicates that **ketamine, with the right dosage** and under controlled medical supervision, may actively help **repair brain lesions due to stress**. Chronic stress and depression are often associated with neuronal atrophy and reduced synaptic density in critical brain areas. By promoting neuroplasticity, ketamine may counteract these damaging effects, effectively "rejuvenating" neural circuits. This ability to rapidly alleviate depressive symptoms and potentially restore brain health offers immense hope for patients who have not responded to other treatments, lifting their mood and improving their overall quality of life. Ongoing clinical trials are exploring different routes of administration, optimal dosing regimens, and the long-term efficacy and safety of ketamine and its enantiomers (e.g., esketamine) for various psychiatric conditions, including bipolar depression, post-traumatic stress disorder (PTSD), and obsessive-compulsive disorder (OCD).

## 6. Regulatory Status

Given its powerful effects and potential for misuse, **ketamine** is subject to strict regulatory controls globally. In the United States, it is categorized as a **controlled substance** under the federal Controlled Substances Act, specifically designated as a Schedule III non-narcotic substance. This classification signifies that ketamine has accepted medical use but also possesses a moderate to

low potential for physical and psychological dependence, as well as a moderate potential for abuse. The Schedule III designation imposes stringent regulations on its manufacturing, distribution, prescribing, and dispensing, aiming to strike a balance between allowing legitimate medical access and preventing diversion for illicit use.

The controlled substance status requires medical practitioners to adhere to specific guidelines when prescribing ketamine, including detailed record-keeping, secure storage, and monitoring for signs of abuse or diversion. Pharmacists are also subject to strict regulations regarding its dispensing. These measures are critical to mitigate the risks associated with ketamine's recreational popularity, particularly its identification as "special K" on the street and its potential role as a date-rape drug due to its immobilizing and amnesic properties. The regulatory framework is continually reviewed and updated to adapt to evolving patterns of use and emerging scientific understanding of the drug.

Internationally, ketamine's status also reflects its dual nature. It is listed on the World Health Organization's List of Essential Medicines, underscoring its crucial role in global healthcare, especially in low-resource settings. However, its potential for abuse has led many countries to implement national controls similar to or even stricter than those in the U.S. These international and national regulations are vital for managing the complex ethical, medical, and social challenges posed by a drug that is both a life-saving medicine and a substance with significant abuse potential. The ongoing development of new ketamine-based therapies, such as intranasal esketamine for depression, further necessitates careful regulatory oversight to ensure patient safety and prevent misuse while maximizing therapeutic benefit.

## 7. Further Reading

[Ketamine - Wikipedia](#)

[Drug Scheduling - U.S. Drug Enforcement Administration \(DEA\)](#)

[WHO Model List of Essential Medicines - World Health Organization \(WHO\)](#)

[Ketamine and its use in mental health - PMC \(PubMed Central\)](#)

[SAMHSA - Ketamine for Depression](#)