

Dextromethorphan (DXM)

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Dextromethorphan has been used around the world as a cough medicine since the 1950s. It suppresses the central nervous system (CNS) to alleviate coughing. Dextromethorphan preparations available in Finland include Resilar®, Redol Comp® and Sir Ephedrin®. They can only be bought at pharmacies and some are prescription-only. There are a number of English street names for preparations containing dextromethorphan, including CCC, robos and skittles. In Finland, they are known as "Ressut".

Historically, dextromethorphan abuse has been relatively rare; however, since 2000 it has grown steadily. People who use DMX recreationally tend to be children and young adults aged 12 to 20. In large doses dextromethorphan can have a similar effect to ketamine, phencyclidine (PCP) or LSD. The latest research suggests that it causes both mental and physical addiction. Currently, there is little data available on prevalence and incidence. However, evidence suggests that it is not highly addictive. Users develop a tolerance, requiring larger doses to produce the same effect. This also increases the risk of side effects.

It is possible that recreational users consider dextromethorphan a safe "high" as it has been on the market for decades and is easily available through pharmacies, particularly in the United States. It is also affordable and can be bought legally. Sufficient data are not available to assess its effect in large doses and in long-term use, which may reinforce the public perception of dextromethorphan as a safe substance. The rise in dextromethorphan abuse has recently led to calls from scientists for all dextromethorphan preparations to be available by prescription only.

Mechanism of action

Dextromethorphan ((+)-3-Methoxy-N-Methylmorphinan) has previously been classed as a synthetic opiate, similar to codeine. Based on current knowledge, it would be inappropriate to class DMX as an opiate as it does not bind to opiate receptors. When DMX is used recreationally, one of the key mechanisms of action is its ability to act as an NMDA receptor antagonist. This, in turn, suppresses glutamate, a central nervous system agonist. This can also cause central nervous system depression. Importantly, dextromethorphan is also a sigma-1 receptor agonist. Administered in large or extremely large doses, dextromethorphan may also bind to opiate receptors, inhibit serotonin reuptake, increase dopamine levels and cause adrenergic symptoms, including elevated blood pressure and heart rate.

Dextromethorphan is well absorbed orally within 30 minutes. Used as a cough medicine, the desired effect is usually achieved within 15–30 minutes. When it is abused, the effects are slower to commence. DMX is subject to significant first-pass metabolism, thereby reducing its bioavailability. Its half-life is 2 to 4 hours. The duration of the effect is approximately 3 to 8 hours, depending on the dose. The rate of metabolism varies between individuals and some may be more susceptible to the intoxicating effect at lower doses. The duration of the effect may also vary and the side effects, including nausea, may affect users differently.

Effects and side effects

The medically recommended dose for adults when used as an antitussive or cough suppressant is 90–120mg per day, split into 30mg one-off doses. At this dosage, users will not experience intoxication, euphoria or addiction. Minor overdoses do not usually lead to side effects.

Dextromethorphan and its metabolite dextrorphan are so-called dissociative agents, responsible for producing out-of-body experiences. Hallucinations similar to those produced by phencyclidine (PCP) and ecstasy (MDMA) are also common. Some users report hallucinations that are distinctive from those produced by LSD, including closed-eye visual hallucinations. The exact effects are dependent on the individual, dose, tolerance and any other alcohol and medicines consumed concurrently. Table 1 lists the different stages of intoxication. The effects of the earlier stages may not be felt during the latter stages, a particular feature of dextromethorphan.

Table 1. Possible effects of dextromethorphan at different levels of intoxication.

Stage 1

Alertness
Agitation
Visual and aural symptoms
Euphoria
Stage 2
Strong visual and aural symptoms
Impaired balance
Hallucinations
Increased energy
Stage 3
Reduced visual acuity and hearing
Intermittently lowered level of consciousness
Increased reaction time
Impaired cognition
Mania or panic
Partial dissociation
Stage 4
Complete dissociation

Hallucinations and delusions
Loss of coordination

In addition to the information listed in Table 1, the following potential effects have been recorded in the scientific literature:

- Brain damage
- Altered temporal awareness
- Energetic or warm sensations
- Flashbacks
- Impaired respiration
- Dizziness
- Difficulty concentrating
- Hypertension
- Coma
- Rigors
- Dry mouth
- Pruritus (itching)
- Clumsiness
- Sense of floating
- Liver impairment
- Altered sense of identity
- Kidney impairment
- Increased heart rate
- Vomiting
- Nausea
- Psychosis
- Aphasia
- Changes to pupillary reflex
- Nystagmus (involuntary eye movement)
- Sensory changes
- Sleepiness
- Tremors
- Tiredness

The most serious adverse effects are more likely to occur with large doses. Continuous or frequent use also increases the risk of serious adverse effects. When your judgement is impaired you are also more vulnerable to hazards, which, at worst, may lead to permanent disability or death. There are a few reports of deaths attributed to dextromethorphan but they are not common, even with large doses. It should be noted that the current literature on dextromethorphan as a cause of respiratory arrest is contradictory.

Additives and combination medications

Additives, including ethanol and sweeteners, and other active ingredients, such as salbutamol and efedrin, contained in dextromethorphan preparations, pose an added risk to recreational users. The more dextromethorphan a recreational user needs to produce a high, the more unwanted substances they will be consuming. These unwanted substances can lead to significant adverse effects and, in some cases, be more dangerous than dextromethorphan itself. This is why some users first treat dextromethorphan preparations with petroleum derivatives. The treatment may remove some of the unwanted substances but amateurs also run the risk of exposing themselves to further compounds, including petroleum, and additional dangers, such as variable concentrations.

In Finland, dextromethorphan is often sold as a bromide salt. Current literature on bromide suggests that long-term use may lead to poisoning but no case reports are available.

Addiction

Studies have suggested that dextromethorphan can cause physical addiction. Long-term, high-dosage use is required for withdrawal symptoms to occur. One study reported symptoms on the third day after last usage. Symptoms may be similar to those produced by withdrawal from opiates, including:

- Feeling cold
- Restlessness
- Myalgia (muscle pain)
- Depression
- Vomiting
- Diarrhoea
- Sleep disturbances
- Night sweats

Drug interactions

Some medications are known to interact with dextromethorphan. The most important of these are the so-called MAO inhibitors (including moclobemide) and SSRIs (including fluoxetine). These increase the risk of serotonin syndrome. Symptoms include pyrexia, tremors, confusion and anxiety. Symptom onset occurs after a couple of hours. Severe cases may be fatal. The use of alcohol, lithium, tricyclic antidepressants, clonazepam, pethidine, ecstasy (MDMA), tryptophan and St John's wort are all contraindicated. Medicines metabolised by the CYP2D6 enzyme, including bupropion, and medicines that bind to the NMDA receptor, including memantine, increase the risk of serious side effects. Data on interactions with illicit drugs and alcohol are not available or are very limited. It is therefore important that all concomitant use be considered potentially dangerous and avoided at all times.

Overdoses

The signs of overdose include agitation but also slowness and drowsiness. Treatment is usually symptomatic and there is no antidote currently available. Activated charcoal and stomach pumping may help if administered and performed promptly. It is not recommended to induce vomiting as this could result in aspiration. There is no conclusive evidence for the effectiveness of naloxone in the treatment of dextromethorphan overdose.

American guidelines (Chyka et al.) from 2007 recommend that emergency treatment be sought if more than 7.5–10mg/kg has been ingested. For a male weighing 80kg this equates to some 600–800mg of dextromethorphan. It should be noted that Pharmaca Fennica defines a lethal dose as approx. 500mg. In reality, a lethal dose is likely to be considerably higher than this. The Erowid database sets an "average" dose at 200–400mg and a high dose at 300–600mg. Anyone who has taken a smaller dose but goes on to develop stronger symptoms, including pyrexia (fever) or clearly impaired consciousness, should seek emergency medical treatment or at the very least contact the Poison Information Centre (Myrkytystietokeskus). If they have combined dextromethorphan with other drugs or alcohol, the threshold for seeking treatment should be even lower.

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