

NATIONAL HIGHWAY TRAFFIC SAFETY ADMINISTRATIC

Drugs and Human Performance Fact Sheets

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Diphenhydramine

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Ketamine

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Phencyclidine (PCP)

<u>Toluene</u>

Zolpidem (and Zaleplon, Zopiclone)

Biographical Sketches of Lead Authors and Main Contributors

Phencyclidine (PCP)

PCP is a white, crystalline powder (contaminants may cause tan to brown color), or a clear, yellowish liquid.

Synonyms: 1-phenylcyclohexylpiperidine; amp, angel dust, animal tranquilizer, dips, dust, elephant, embalming fluid, formaldehyde, fry, hog, ozone, peace pill, rocket fuel, Sernyl, Sernylan, super kools, TicTac, tranq, water, wet.

Source: Synthetic chemical made in clandestine laboratories, or diverted from veterinary sources. PCP is currently a Schedule II controlled substance. In illicit synthesis, piperidine is reacted with cyanide and cyclohexanone to make piperidinocyclohexanecarbonitrile (PCC), which is then reacted with phenylmagnesium bromide to make PCP. PCP can be mixed with dyes and sold in a variety of tablets, capsules and colored powders. PCP is also sold as a liquid in small shaker bottles. PCP analogs are also available: cyclohexamine (PCE), phenylcyclohexylpyrrolidine (PHP), phenylcyclopentylpiperidine (PCPP), and thienylcyclohexylpiperidine (TCP).

Drug Class: Hallucinogen, dissociative anesthetic, psychotomimetic, sedativehypnotic.

Medical and Recreational Uses: Formerly used as a surgical anesthetic, however, there is no current legitimate medical use in humans. Used as a veterinary anesthetic or tranquilizer. Recreationally used as a psychedelic and hallucinogen.

Potency, Purity and Dose: A light dose typically consists of 3-5 mg; a common dose is 5-10 mg; while a strong dose is greater than 10 mg. Lighter doses are usually smoked, intravenously or intranasally administered, while heavier doses are commonly ingested orally. The liquid can be sprinkled on tobacco or marijuana then smoked, or the cigarettes or joints themselves can be dipped in PCP solution; the resulting PCP dose can therefore vary widely. Due to difficulty of synthesis, street preparations have highly variable concentrations of PCP and byproducts. PCC, the PCP precursor, is found in approximately 20% of illicit samples and is more toxic than PCP as it releases cyanide. Abuse of PCP precursors or analog chemicals leads to similar or more devastating pharmacological effects than PCP. PCP is often administered or mixed with other drugs such as crack cocaine ("beam me up"), cocaine hydrochloride ("lovelies"), and marijuana ("crystal supergrass", "donk", "killer joints", "sherms", "wacky weed", "wicky stick").

Route of Administration: Smoked, intravenous injection, snorted, added as eye drops, oral ingestion, and transdermal absorption.

Pharmacodynamics: Dopaminergic, anticholinergic and opiate-like activities exist. PCP is a non-competitive NMDA-receptor antagonist, and blocks dopamine reuptake and elevates synaptic dopamine levels. It has high affinity to sites in the cortex and limbic structures.

Pharmacokinetics: Well absorbed following all routes of administration, although ~ 50% of PCP in cigarette smoke is converted to an inactive thermal degradation product. PCP is highly lipid soluble and is stored in fat and brain tissue. The plasma binding of PCP is 65% and its half-life ranges from 7-46 hours (average 21 hours). PCP is extensively metabolized to inactive metabolites by a variety of metabolic routes.

Molecular Interaction / Receptor Chemistry: The cytochrome P450 3A isoenzyme plays a major role in PCP biotransformation. Potential inhibitors of this isoenzyme could decrease the rate of PCP elimination if administered concurrently, while potential inducers could increase the rate of elimination. PCP itself may inhibit 2B1 and 2C11 isoforms.

Blood to Plasma Concentration Ratio: 0.94 and 1.0 reported.

Interpretation of Blood Concentrations: There is no direct correlation between PCP concentration and behavioral or physical findings. Blood levels peak 1-4 hours after ingestion. Average peak plasma concentrations of 2.7 and 2.9 ng/mL were achieved after a 1 mg oral and intravenous dose, respectively. PCP concentrations ranged from 0.3 to 143 ng/mL in 63 patients presenting at a psychiatric hospital emergency room and were associated with a wide variety of psychotic clinical pictures resembling mania, depression or schizophrenia. All these patients had at least one manifestation of toxic psychosis and/or acute delirium, in addition to other symptoms. Similarly, plasma PCP concentrations ranged up to 812 ng/mL in 22 patients with nonfatal PCP intoxication. The most common physical findings were combativeness-agitation (64%), depressed level of consciousness (50%), hypertension (43%), miosis (43%) and tachycardia (43%). Blood PCP concentrations ranged from 12 to 118 ng/mL in 26 individuals arrested for public intoxication.

Interpretation of Urine Test Results: Elimination of PCP in 72 hours urine ranges from 4 to 19% for unchanged drug and 25 to 30% for conjugated metabolites. Approximately 97% of a dose is excreted in 10 days, and PCP use can be detected in urine by immunoassay up to a week following a high dose. Urine PCP concentrations ranged from 0.4-340 mg/L in 19 intoxicated patients.

Effects:

Psychological: Effects are usually dose dependent, and include euphoria, calmness, feelings of strength and invulnerability, lethargy, disorientation, loss of coordination, distinct changes in body awareness, distorted sensory perceptions, impaired concentration, disordered thinking, illusions and hallucinations, agitation, combativeness or violence, memory loss, bizarre behavior, sedation, and stupor.

Physiological: Rise in blood pressure and heart rate, flushing, profuse sweating, generalized numbness of extremities, blurred vision, grimacing facial expression, speech difficulties, ataxia, muscular incoordination, marked analgesia, nystagmus, and anesthesia. In the anesthetized state, the patient remains conscious with a staring gaze and rigid muscles.

Side Effect Profile: Excessive salivation, nausea, vomiting, amnesia, combativeness, severe anxiety, paranoia, flashbacks, seizures, coma, and death. PCP can simulate schizophrenic-like symptomatology such as flattened affect, dissociative thought disorder, depersonalization and catatonic states. Long periods of

use may lead to memory loss, difficulties with speech and thinking, depression, weight loss, liver function abnormalities, and rhabdomyolysis.

Duration of Effects: Onset of effects is very rapid when smoked or injected

(1-5 minutes) and are delayed when snorted or orally ingested (30 minutes), with a gradual decline of major effects over 4-6 hours. A return to 'normal' may take up to 24 hours. Consciousness is regained within 10-60 minutes following intravenous administration, with a prolonged recovery period of 3-18 hours. Long-term psychological effects are possible and PCP may precipitate a psychotic reaction lasting a month or more that clinically appears like schizophrenia.

Tolerance, Dependence and Withdrawal Effects: Most PCP users administer the drug intermittently, although daily use has been reported and tolerance may develop. There is evidence of tolerance to behavioral effects of PCP in animals. PCP can be addicting and use can lead to psychological dependence, craving and drug seeking behavior. There has been no demonstration of physical dependency in humans. Upon abrupt discontinuation, physical distress, lack of energy, and depression are reported. Long periods of use may lead to memory loss, difficulties with speech and thinking, depression, and weight loss. These can last up to a year after cessation of use.

Drug Interactions: Benzodiazepines can decrease hypertensive effects and reverse seizure activity of PCP. Chlorpromazine and PCP use can cause severe hypotension. PCP may enhance effects of other CNS depressants like barbiturates and alcohol.

Performance Effects: Laboratory studies have shown that PCP causes disorientation, drowsiness, dizziness, ataxia, double or blurred vision, body image changes, disorganization of thoughts, combativeness, impairment of eye-hand coordination, memory impairment, paresthesia, slowed reaction time, distorted perceptions of space. Effects generally occur within 1 hour post dose. Subjective sensation of intoxication has been reported up to 8 hours and slowed reaction time up to 14 hours.

Effects on Driving: Fifty-six (56) subjects were arrested for erratic driving and were evaluated by a drug recognition examiner. All subjects were judged to be driving under the influence of PCP, and blood PCP concentrations ranged from 12 to 188 ng/mL (mean 51 ng/mL). Similarly,blood PCP concentrations ranged from 10 to 180 ng/mL (mean

73 ng/mL) in 50 subjects arrested for driving under the influence of PCP.

DEC Category: Phencyclidine.

DEC Profile: Horizontal gaze nystagmus present; vertical gaze nystagmus present; lack of convergence present; pupil size normal; reaction to light normal; pulse rate elevated; blood pressure elevated; body temperature elevated. Other characteristic indicators may include rigid muscles, cyclic behavior, sudden turn to violence, lack of response to painful stimuli, trance-like state or blank stare, sweating, incomplete or delayed verbal responses.

Panel's Assessment of Driving Risks: The use of PCP is not compatible with skills required for safe driving. Severe impairment of mental and physical abilities can occur following single doses.

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