My Iowa State University creative component title page: A beta sample

by

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A creative component submitted to the graduate faculty

in partial fulfillment of the requirements for the degree of

MASTER OF SCIENCE

Major: Biomedical Sciences

Program of Study Committee:
Steve Carlson, Major Professor

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Iowa State University

Ames, Iowa

2023

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Breaking Bad Pharmacology and Biochemical Science

Breaking bad is an American crime drama television series created by Vince Gilligan. It is set in Albuquerque, New Mexico, following Walter White who is an underpaid, overqualified high school chemistry teacher. He turns to a life of crime with his former student and now partner Jesse Pinkman after finding out about his stage-three lung cancer diagnosis. Walter starts manufacturing and distributing methamphetamine to secure his family's financial future before he dies.

Amphetamines were the first kind of stimulant drug created in 1887 at the University of Berlin followed by methamphetamine. Belonging to the phenethylamine family it is a natural monoamine alkaloid acting as a CNS stimulant. Amphetamines are used in ADHD medication such as Adderall. It is most commonly used as a recreational drug by teenagers & young adults as a study drug to enhance focus, stay awake longer, and boost cognitive functioning. Amphetamine has many subtypes including that of methamphetamine. Although amphetamines & methamphetamines are similar in chemical composition, Methamphetamine has an extra methyl group attached to it causing it to be the stronger stimulant. Both drugs block the reuptake channel in the synapse not allowing the recycling of neurotransmitters like dopamine (The Freedom Center, 2021) Unlike cocaine & amphetamine, methamphetamine also opens pre-synaptic neuron channels allowing the flooding of even more neurotransmitters into the synapse (Figure1). The constant influx and lack of reuptake cause the half-life of methamphetamine to be 12 times that of amphetamine. Dopamine plays a role in the experience of pleasure, reward, motivation, as well as motor function. Its effects last six to twelve hours after ingesting, snorting, smoking, or injecting the drug. Immediate effects of the drug are seen when entering the bloodstream quickly in cases of snorting and smoking, unlike ingesting.

Methamphetamine is a psychostimulant on the central nervous system inducing a fight or flight response causing increased heart rate and blood pressure, vasoconstriction, bronchodilation, hyperglycemia. It creates increased focus, mental alertness, and a state of euphoria. Prolonged exposure can lead to paranoia, aggression, delusion, mood disturbances, and hallucinations. It is neurotoxic to dopaminergic nerve terminals (How Stimulants Affect the Brain and Behavior). Over dose can cause excessive heart rate and blood pressure causing stroke, heart, attack or even leading to death.

Methamphetamine was first reduced from ephedrine and pseudoephedrine extracted from the plant Ephedra (Figure 1). This occurred in Germany around 1893. It wasn't until 1919 that another chemist used phosphorus and iodine to reduce ephedrine into crystal meth. German drug companies started creating meth tablets to be used by those working the night shift to fight off fatigue, as well as in WW2 to enhance performance among soldiers. This ultimately led to it being sold as medicine to treat narcolepsy, depression, obesity, and ADHD. Eventually, they found negative side effects and risks of continued use which could cause addiction and lead to detrimental effects on essential organs like the brain, kidneys, heart, and skin (Campbell, 2017). Chronic abuse causes reduced motor skills, changes in emotion and memory, and psychotic features such as confusion, insomnia, paranoia, hallucinations, and delusions. It wasn't until 1970 under the controlled substances act that all forms of amphetamines were regulated regarding their manufacturing, possession, use, and distribution. However, ephedrine & pseudoephedrine pills weren't added as control substances until the early 1990s.

Methamphetamine is chiral, occurring in two enantiomers; D- methamphetamine, the stronger psychostimulant & L- methamphetamine (Figure 2), sold over the counter as a nasal decongestant. Due to being fat soluble it enters the brain faster and is more protected against

monoamine oxidase degradation. Desoxyn is a prescription drug containing D-methamphetamine as an active ingredient used to treat ADHD. It works to improve attention and lower impulsive/hyperactive behaviors. Benzphetamine is a drug that metabolizes to methamphetamine and is used short-term to suppress your appetite allowing weight loss in obese patients (United States Drug Testing Laboratories Inc.).

In the show breaking bad meth products occurred in various forms based on who was creating it. When using pseudoephedrine, it would form white meth known as glass. Methamphetamine is normally a colorless salt. Walter White's form was known as blue sky, his drug was highly pure but contained a light blue hue. There are several reasons for the color change. The first is trace impurities that occur during organic reactions or just the way the electrons absorb light. Other dealers in the show, such as Captain Cook, added chili powder to his meth, creating his own signature.

When Walter White first started producing meth, he used the Red phosphorous or Red-P method. The nasal decongestant pseudoephedrine is reduced with hydroiodic acid (HI) to yield methamphetamine. Pseudo is extracted from OTC cold medicine using water, alcohol, and coffee filters. Red phosphorus reduces elemental iodine (I2) to HI. Matchbook sticker pads & road flares are where recycled reformed I2 is collected. All components; pseudoephedrine, I2, and red phosphorous, are collected in a boiling flask, water is added, and heated. The organic solvent layer is removed and the D-isomer is precipitated as HCl crystals by bubbling HCl gas into the solution (Figure 4). The solution turns deep purple. During the heating process, it is important to take caution due to the toxic by-product of phosphine gas produced while heating (VICE, 2013).

In the show, Walter amplifies the production of phosphorus gas to kill two gangsters. He adds extra red phosphorus in presence of moisture and is accelerated by heat causing a large

increase in fumes & poisonous gas. Phosphorous is disproportionated to PH_3 and hypo phosphoric acid in the presence of water. PH_3 irritates the eyes, skin, and respiratory organs, causing difficulty breathing ultimately leading to suffocation (Hare, 2011).

After killing one of the gangsters, they are tasked with getting rid of the body. Walt takes a few large bottles of hydrofluoric acid (HF) from the high school to decompose the body. HF destroys tissues and decalcifies bone. HF is a strong acid that reacts with many metals, plastics, and glasses. The only plastics resistant to HF are fluorocarbons, the most known being Teflon (Helmenstine, 2018). Jesse, Walt's partner couldn't find a container large enough for the body. Instead, he puts the body in the bathtub and pours the acid in. Hours later he notices it has eaten through the bottom of the bath, through the floorboards and ceilings. The neutralization of HF is done best by using baking soda containing an alkaline pH. There are better methods for disposing a body than the one used in breaking bad. The best body-dissolving chemical is lye or sodium hydroxide, which is a base. Lye is used to unclog drains. The hydroxide anion is a strong proton acceptor helping strip hydrogen atoms off organic molecules creating simpler molecules. Tissues are dissolved into sludge that can be flushed down the toilet, leaving only brittle bones (Chemistry Stack Exchange).

The Red-P method was effective until the need for large-scale production came alone. Pseudoephedrine is bought in limited quantities due to government regulation, forcing Walter to switch to the P2P method. Using pseudo created a more potent product, unlike P2P which creates a racemic mixture. In this reaction phenylacetic acid and acetic acid are heated in a 70 mm tube furnace charged with thorium oxide (ThO_2) catalyst yielding phenylacetone. Phenylacetone plus methylamine undergo reductive amination in presence of aluminum amalgam yielding

methamphetamine. In order to acquire this methylamine, Walt has to break into a warehouse to steal the chemical (Figure 4).

In the show Walt states aqueous methylamine is water-based, it weighs slightly less than water. In the hunt to find available methylamine Walt's team finds out, there is a train loaded with barrels of it. They create tanks ready to siphon the methylamine into and replace it with water. They removed 1000 gallons of methylamine, they replaced it with 920 gallons of water. The issue with this scene is the idea that methylamine isn't water based, although they said it was. Methylamine becomes water soluble once it's sold in a solution in methanol or ethanol or even water, which is likely the case seen in the tanker. This allowed them to mix the methylamine with water to disguise their heist as the two won't separate. Methylamine is prepared by reacting ammonia with methanol in presence of an aluminosilicate catalyst yielding monomethylamine (MMA), dimethylamine (DMA), and trimethylamine (TMA). The most favored product is trimethylamine. It simply replaces one hydrogen atom in ammonia with a methyl or hydrocarbon group. Methylamine used in the P2P method to produce methamphetamine has other applications including being used in agricultural chemicals, paint industries, pharmaceuticals, etc. TMA is used in manufacturing choline chloride, a B-vitamin supplement used to feed chickens, swine, and turkeys. DMA is used as an herbicide and fungicide, as well as manufactured soaps, cosmetics, hand lotions, etc. TMA and MMA are insecticides with TMA being the most volatile (Airgas Specialty Products).

Walt was wary about his new business partner Tuco and made a plan on how to dispose of him before problems arise. Walt plans to poison Tuco with ricin. Ricin is naturally produced as a waste product by processing castor oil plant seeds. Inhalation of the bean would ultimately cause respiratory distress, low blood pressure, and sometimes death. Ingesting rather than

inhaling ricin significantly decreases the lethalness. Ricin is a macromolecule composed of two units connected by a disulfide bridge. The A-chain contains an N-glycosidic bond of an adenosine residue in 28S-rRNA. The ricin toxin causes deadenylation, degrading the ribosome and blocking the binding of elongation factors inhibiting protein synthesis. With the lack of essential proteins being made cell death occurs on a large scale. The B chain is responsible for binding carbohydrates on the surface of cells allowing the entry of toxins into the cell. Ricin is now being experimentally used in medicine to kill cancer cells. The United States as well as the Soviet Union have developed Ricin as a biological weapon as well (Facts About Ricin, 2018).

Ricin wasn't the only poison used by Walt. He also used the Lily of the Valley, a medicinal plant. It contains compounds like convallotoxin which is a cardioactive glycosides that are made into medication to treat heart problems, such as heart failure and irregular heartbeat. It acts on the heart muscle affecting contraction, heart rate, and excitability. Glycosides are chemical compounds where sugar is bound to a noncarbohydrate molecule. Calcium stores increase causing glycosides to increase the force they contract and the volume of blood pumped in the heart. Lily of the valley poisoning however causes cardiac arrhythmias and death when the incorrect dosage is given. Using Lily of the Valley is less suspicious than using ricin as someone could mistakenly eat the berries themselves and be poisoned. Lily of the Valley also isn't as poisonous as ricin, it has less of a risk of causing death (Soniak, 2011).

Selegiline is an irreversible monoamine oxidase inhibitor used in treating symptoms of Parkinson's disease. In veterinary medicine, it is used to treat pituitary-dependent Cushing's disease in canines. The drug increases the levels of dopamine in the brain & is a CNS stimulant. Its metabolites are l-methamphetamine, and l-amphetamine, with stereoisomers of d-methamphetamine and d-amphetamine which are psychostimulants. Within 24 hours the drug is

metabolized into meth any drug screening will show up as a false positive for methamphetamine. One study found that you can test the AM/MA ratio in the urine of those who received the drug vs meth abusers. Those receiving the drug had a much higher ratio which might be due to the way selegiline is metabolized. It has two pathways both ultimately yielding the metabolism into amphetamine (Kaewpunya, Nunthika, et al).

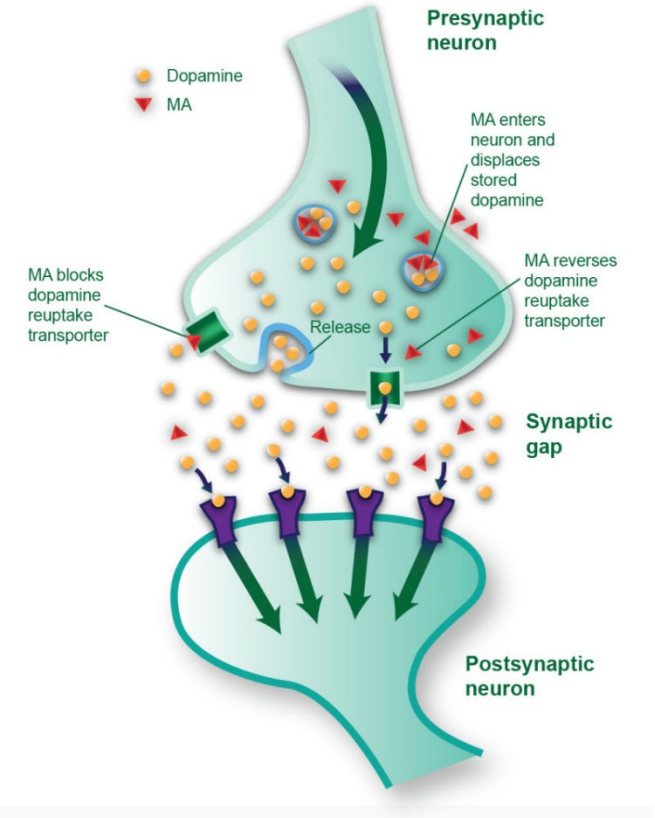


Figure 1: Dopamine Neuron Channel. "How Stimulants Affect the Brain and Behavior." *NCBI Bookshelf*, https://www.ncbi.nlm.nih.gov/books/NBK576548/.

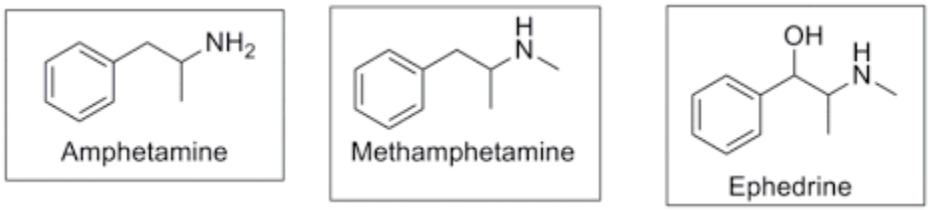


Figure 2: Ampetamine & Metampetamine synthesis from Ephedrine. Chiu, V. Schnek, J. (2012, September). *Chemical structures of amphetamine, methamphetamine, and...* (n.d.). Retrieved April 17, 2023, from https://www.researchgate.net/figure/Fig-1-Chemical-structures-of-amphetamine-methamphetamine-and-ephedrine_fig1_234077441

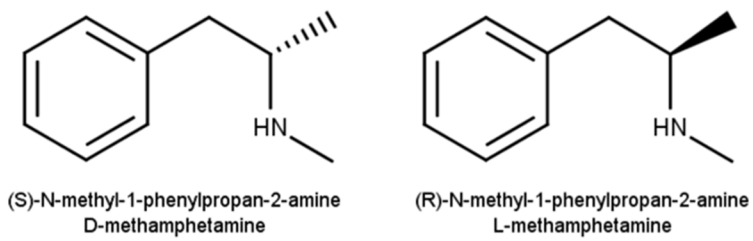
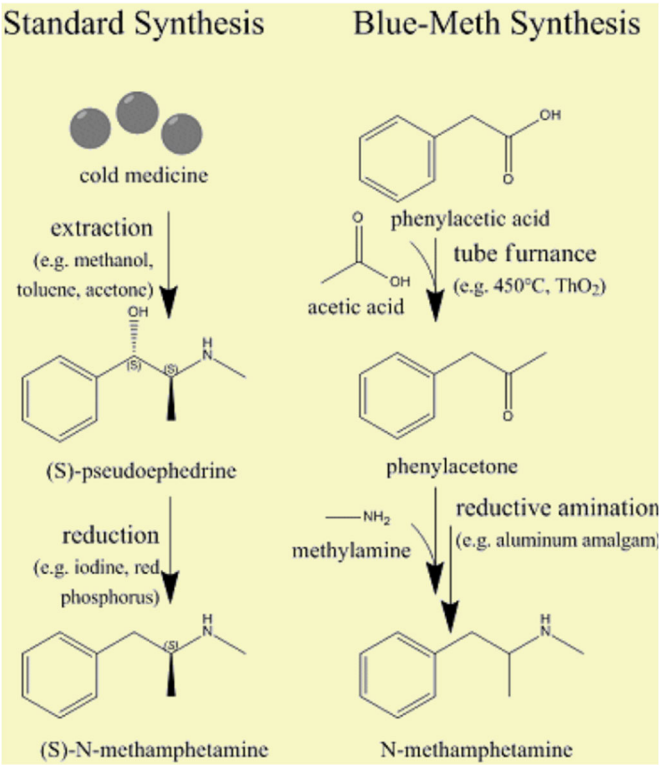


Figure 3: D vs L Isomer Methamphetamine, "D/L Methamphetamine Isomers Explained." *United States Drug Testing Laboratories Inc.*, 6 July 2022, https://www.usdtl.com/d-l-isomers.



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