SYNTHETIC DESIGNER DRUGS

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Department of Psychiatry
Harvard Medical School
Modern Drugs Were Isolated from Plants

Digitalis 1875

Aspirin 1853

Atropine 1831

Quinine 1820
Goals

• What are Designer Drugs?
• What Drives Designer Drug Markets?
• Trends?
• Are Designer Drugs Legal?
• Who Uses “Bath Salts”, Synthetic Cannabinoids, and Why?
• Effects and Harmful Effects?
• Summary
What Are Designer Drugs? 
Categories

• **Bath salts**: stimulants hallucinogens, entactogens, “empathogens”
  • These are not bath salts!!!!!!! They are chemicals.

• **“Spice”, “K2” Cannabinoids**: marijuana-like chemicals

• **“Dragonflys”**: Hallucinogens

• **Morphine-like**: Krokodil

• **Tryptamines**: Hallucinogens
National Trends: Unique Type of Synthetic Drugs

NFLIS (2010-2012)

Source: US DEA, Office of Division Control, National Forensic Laboratory Information System, 2012
What Are Designer Drugs?
Bath salts

Phenethylamine (PEA)

Amphetamine

Methamphetamine

MDMA or ecstasy

Cathinone

Mephedrone

Methylene

Pyrovalerone

Naphyrone

MDPV or methylenedioxymethylenedioxymethamphetamine

ARE NOT
Skin cleansers, perfumes or soothing lotions
Bath salts: how to recognize

- If sold as “Bath salts” warning signs:
  - Is it in a small packet?
  - Is it labeled: “not for human consumption”?
  - Is it labeled “not illegal”?
  - Is it labeled “adults only”?

- If sold as “plant food”, “fertilizer”
What Are Designer Drugs? Marijuana-like

THC: phyto-cannabinoid
made by plant Cannabis sativa

JWH-018: synthetic cannabinoid
made in chemistry laboratory

Anandamide: endocannabinoid
made by brain cells
What Are Designer Drugs?  
Dragonfly

Phenethylamine (PEA)

2C^Bfly

Br^Dragonfly
Krokodil

- **Desmorphine**: Russian, response to tight heroin supply
- **Synthesis**: Simple with codeine, iodine, red phosphorus.
- **Purity**: Highly impure, contaminated with toxic, corrosive byproducts
- **Psychoactive effects**: Similar to heroin, shorter duration; brain damage
- **Notoriety**: produces severe tissue damage, phlebitis, gangrene
- **Life expectancies**: short
Where Did Designer Drugs Come From?

Dr. David Nichols

Dr. John W Huffman

Dr. Alexander Shulgin

ACS Chemical Neuroscience

Extensive Rigid Analogue Design Maps the Binding Conformation of Potent N-Benzylphenethylamine 5-HT₂A Serotonin Receptor Agonist Ligands

Jose U. Tovar-M., Jr., Martin Hansen, Lisa A. Bremes, Juan Pablo Caoza, Rebecca M. Holeman, John D. McCoy, Duhong Ma, Lisa A. Bremes, Markus A. L.R.B, and David E. Nichols

Department of Medicinal Chemistry and Molecular Pharmacology, College of Pharmacy, Purdue University, West Lafayette, Indiana, USA

Supporting Information

1-Pentyl-3-phenylacetylindoles and JWH-018 share in vivo cannabinoid profiles in mice

Jenny L. Wiley,*, Julie A. Marusich,*, Billy R. Martin, and John W. Huffman

Department of Chemistry, Virginia Commonwealth University, Richmond, VA 23284-0012, USA

Supporting Information

Drug and Alcohol Dependence

Contents lists available at SceienceDirect

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journal homepage: www.elsevier.com/locate/druid

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Supporting Information
Why do Medicinal Chemists Compounds?

- New medications
- Basic science
- Publish research
- Publish patents
Marijuana distribution (CB₁) in Human Brain

Red, yellow regions have high concentrations of CB1 cannabinoid receptor
PET image CB1 MRI defines anatomy MRI, PET combined

Terry et al., Quantitation of cannabinoid CB₁ receptors in healthy human brain using positron emission tomography and an inverse agonist radioligand. Neuroimage 48 362, 2009
How Did Legitimate Chemical Research Evolve into Illegal Drug Production?

Extensive Rigid Analogue Design Maps the Binding Conformation of Potent N-Benzylphenethylamine 5-HT_{2A} Serotonin Receptor Agonist Ligands

José I. Jácome, Jr., Martin Hansen, Lisa A. Barnes, Juan Pablo Carre, Rebecca Madhusko, James D. McCawey, Danuta Macrina-Lewicka, Markus A. LIE, and David E. Nichols

Department of Medicinal Chemistry and Molecular Pharmacology, College of Pharmacy, Purdue University, West Lafayette, Indiana 47907, United States

ABSTRACT: Based on the structure of the agonist 5-HT_{2A} receptor agonist, 5-methoxy-D,L-tryptophan-methylamine, and modified with the benzyl group, we designed and synthesized a small library of constrained analogues to identify the optimal arrangement of the pharmacophore elements of the agonist. Studies consisted of docking, molecular dynamics, and radioligand-binding experiments. We found that 5-HT_{2A} receptor agonist activity in COC-400, which showed the highest affinity of the series, we propose an optimal binding conformation. COC-400 also displayed low affinity for the 5-HT_{2C} receptor. We found that the most selective 5-HT_{2A} receptor agonist is also a potent mGlu7 receptor antagonist.

KEYWORDS: serotonin, 5-HT_{2A} agonist, rigid analogue, hallucinogen, molecular model

Drug and Alcohol Dependence

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Contents data available at ScienceDirect

Journal homepage: www.elsevier.com/locate/drugalcdep

1

\[
\begin{align*}
& \text{R} = 4-\text{CH}_3 (\text{RS}) \\
& \text{b} \ R = 4-\text{CH}_3 (\text{S}) \\
& \text{c} \ R = 4-\text{CH}_3 (\text{R}) \\
& \text{d} \ R = \text{H} \\
& \text{e} \ R = 4-\text{F}
\end{align*}
\]
What Drives Designer Drugs?

- Internet: sales, production, information
- Deceptive Marketing
- Grey zone legal status
- Evade drug tests
To have novel
- feelings
- sensations
- experiences

AND

To share them

Vivian Felsen
To evade drug testing
To evade legal issues
A Human Experiment without Informed Consent

Marketed to teens and young adults

- Unknown composition of matter
- No consistency in manufacturing
- Not tested for human consumption
- Unknown actions in brain or body
- Unknown dosage, drug interactions
> 200 discussion forums, social media, online shops, websites (YouTube, eBay, Google, Google Insight)

> 410 substances/products

Information is valuable, as scientific data are scarce

“Spice”, mephedrone, naphyrone, MDAI, MDPV were tracked from single source country to spread

After made illegal, online searches decrease
Trends: Synthetic Marijuana, Bath Salts?
High School Students

Source: Monitoring the Future, Dec 2012

- **Synthetic marijuana**
  - **10th, 12th graders**: 2nd most widely used drug after marijuana
  - **8th graders**: 3rd most widely used drug after marijuana, inhalants

Bar chart showing usage rates for 12th, 10th, and 8th graders.
Adapted by CESAR from Stogner, J.M. and Miller, B.L., “A Spicy Kind of High: A Profile of Synthetic Cannabinoid Users,” *Journal of Substance Use*, Advance online publication (doi:10.3109/14659891.2013.770571), 2013. For more information, contact Dr. Stogner at stogner@email.unc.edu.
1. Actual or potential for abuse, addiction
2. Significant psychoactive effects
3. Risk to public health
   • Driving under influence, suicides, homicides, drugs abused to evade drug screens, overdose illness, deaths
4. Analogs currently controlled, same reasons
• October 2011: DEA controlled three synthetics, mephedrone, 3, 4-methylenedioxypyrovalerone (MDPV), and methylone, sold as “bath salts” “plant food”.

• March 1 2012: DEA extended control of five “fake marijuana” products (JWH-018, JWH-073, JWH-200, CP-47,497, cannabicyclopentanol).

• June 2012: 26 synthetic drugs, including 15 synthetic cannabinoids, placed under Controlled Substance Act.

• Possession, sale of these chemicals, or products that contain them, illegal in the United States.
New Jersey: bans six chemicals used to make designer drug ‘bath salts’

AR K AN S AS: STATE HEAL TH OFFICER ACTS TO BAN DESIGNER DRUG

Nebraska: ban on synthetic designer drugs advances

Ohio: Senator Burke working to ban designer drugs.

Florida: House Committee Passes Bill to Ban 27 Substances Used in Designer Drugs

Michigan: Bills banning synthetic designer drugs headed to Gov. Snyder
Calls to Poison Control Centers Decline After Drugs Scheduled (FL)

Illegal Status Reduces Use

Number of calls
“Bath Salts”
<table>
<thead>
<tr>
<th>DRUG NAME</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mephedrone</td>
<td>4-methyl-methcathinone; “Miaow” Similar to cocaine and MDMA (ecstasy)</td>
</tr>
<tr>
<td>Methylone</td>
<td>β-MDMA: 3,4-methylenedioxymethcathinone; “Explosion” Similar to cocaine and MDMA (ecstasy)</td>
</tr>
<tr>
<td>MDPV</td>
<td>3,4-methylenedioxypyrovalerone; MDPV; “NRG-1” (Brandt, 2010); “Ivory Wave” Stimulant with rapid onset; 2-4 hour duration of action</td>
</tr>
<tr>
<td>BZP</td>
<td>1-benzyl-piperazone Similar to amphetamine 1/10 potency of d-methamphetamine</td>
</tr>
</tbody>
</table>

Cathinones Trends: Calls to Poison Control Centers Jan 2010 – June 2011

- National Counts of Exposure Calls: Synthetic Cathinones

Graph showing the trend of calls to poison control centers from January 2010 to June 2011 for synthetic cathinones. The data shows a significant increase in calls from March 2011 onwards.
“Bath Salts” Affect Many Organs

- Brain
- Eyes, ears, nose, throat
- Lungs
- Heart, blood vessels
- Kidney, hormones
- Digestive tract
- Reproduction

- Palpitations
- Shortness Of Breathe
- Chest Pain
- Dry Mouth
- Abdominal Pain
- Anorexia
- Vomiting
- Erectile Dysfunction
- Skin Discoloration
- Muscular Tension
"Bath Salts", Psychoactive Effects

- **Psychoactive effects**: Aggression, dizziness, memory loss, seizures, blurred vision, anxiety, hallucinations, depression, dysphoria, euphoria, fatigue, increased energy and decreased concentration, panic and paranoia.

- **Addiction**: Mephedrone user survey; 50% considered it addictive, ~ 50% reported continuous use for > 48 h, and > 30% fulfilled 3+ criteria for abuse/addiction (DSM-IV).

- **Addiction**: Another survey (n=1,006); 17.5% of users reported addiction symptoms
  - highest frequency of daily use falling in the 11-15 year old age range.
“Bath Salts” Case Reports

- Man repeatedly stabs himself in face
- University student runs head-on into traffic and killed
- Daughter attacks 71 year old mother with machete
- Mother leaves 2 year old on highway median and carries 5 year old
- Man runs into police station thinking someone hiding under his car
- Man jumps from 3rd story window fleeing from non-existent person
- Couple destroy home walls trying to stab imaginary people
- Man flees car he thinks is melting and chased by electricity
- 19 year old man arrested pointing 3 rifles at family members
- Woman driving with toddler arrested after banging head on steering wheel
- Man arrested for disorderly conduct eats dirt while handcuffed
- Man rams stolen car into front door of store and steals bath salts
- Man arrested at grocery store after damage and drinking hand sanitizer
- Man makes 911 call being chased by people with rifles
# Bath Salts: Medical Effects

<table>
<thead>
<tr>
<th>Organ system</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>Palpitations, tachycardia, chest pain, vasoconstriction, myocardial infarct.</td>
</tr>
<tr>
<td>Psychological</td>
<td>Aggression, anger, anxiety, agitation, auditory visual hallucinations, depression, dysphoria, empathy, euphoria, fatigue</td>
</tr>
<tr>
<td>Neurological</td>
<td>Seizures, tremor, dizziness, memory loss, cerebral edema, headaches, lightheaded</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Arthralgia, coldness, numbness, discoloration, numbness, tingling of limbs, muscular tension, cramping</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Abdominal pain, anorexia, nausea, vomiting</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Shortness of breathe</td>
</tr>
<tr>
<td>Ears, nose, throat</td>
<td>Dry mouth, nasal pain, tinnitus</td>
</tr>
</tbody>
</table>
### Clinical Symptoms in Patients Admitted to ED (n=236)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Agitation</td>
<td>82%</td>
</tr>
<tr>
<td>Combative/Violent behavior</td>
<td>57%</td>
</tr>
<tr>
<td><strong>Tachycardia</strong></td>
<td>56%</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>40%</td>
</tr>
<tr>
<td>Paranoia</td>
<td>36%</td>
</tr>
<tr>
<td>Confusion</td>
<td>34%</td>
</tr>
<tr>
<td>Myoclonus/Movement disorders</td>
<td>19%</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>17%</td>
</tr>
<tr>
<td>Chest pain</td>
<td>17%</td>
</tr>
<tr>
<td>CPK elevations</td>
<td>9%</td>
</tr>
</tbody>
</table>

Biology of “Bath Salts”

- Bath salt drug
- Transporter
- Brain message
Bath Salts Likely Affects Many Brain Regions

**HYPOTHALAMUS**
Controls appetite, hormonal levels and sexual behavior

**NEOCORTEX**
Responsible for higher cognitive functions and the integration of sensory information

**BASAL GANGLIA**
Involved in motor control and planning, as well as the initiation and termination of action

**HIPPOCAMPUS**
Important for memory and the learning of facts, sequences and places

**VENTRAL STRIATUM**
Involved in the prediction and feeling of reward

**AMYGDALA**
Responsible for anxiety, emotion and fear

**CEREBELLUM**
Center for motor control and coordination

**BRAIN STEM AND SPINAL CORD**
Important in the vomiting reflex and the sensation of pain
“Bath Salts”: Summary

- Cathinones do not all confer same effects or health risks.
- They engender risks and adverse consequences:
  - (a) emergency department mentions
  - (b) persistence of effects after 24 hours
  - (c) addictive potential
  - (d) psychiatric, cardiovascular effects
  - (e) deaths
Synthetic Cannabinoids (Marijuana) 
K2; Spice

Bliss
Black Mamba
Blaze
Bombay Blue
Genie
Spice
JWH -018
JWH -073, -250
“herbal smoking mixture”
“incense”
“herbal blends”
“air freshener”
“not for human consumption”.

Calls to Poison Control Center for Synthetic Cannabinoids Jan 2010-June 2011

Source: DEA
K2, Spice overview

• **What**: Synthetic forms of marijuana

• **What**: Mixture of dried, shredded plants sprayed with THC-like chemicals; THC is the most active constituent of marijuana. Strong clove smell

• **Onset time**: 5-15 minutes (smoked)

• **Duration**: 1-8+ hours

• **Effects**: Many

• **Comparison with marijuana**: effects may be extreme of smoked marijuana *or* different.
## Comparison of Marijuana and Synthetic Cannabinoids

<table>
<thead>
<tr>
<th>Cannabis  ~=} Synthetic Cannabinoids</th>
<th>Symptoms More Typical of Synthetics</th>
</tr>
</thead>
<tbody>
<tr>
<td>• High heart rate</td>
<td>• Seizures</td>
</tr>
<tr>
<td>• Red eyes</td>
<td>• Low blood potassium</td>
</tr>
<tr>
<td>• Anxiety</td>
<td>• High blood pressure</td>
</tr>
<tr>
<td>• Mild sedation</td>
<td>• Nausea/vomiting</td>
</tr>
<tr>
<td>• Hallucinations</td>
<td>• Agitation</td>
</tr>
<tr>
<td>• Acute psychosis</td>
<td>• Violent behavior</td>
</tr>
<tr>
<td>• Memory deficits</td>
<td>• Coma</td>
</tr>
</tbody>
</table>

Positive Psychoactive Effects

- Pleasant
- Euphoria
- Relaxation
- Sedation

Negative Psychoactive Effects

- Severe paranoia, endangering self, others
- Agitation, delirium
- Headaches
- Anxiety, panic attacks
- Loss of control
- Confusion, hallucinations, psychosis
- Suicidal thoughts
- Seizures, tremors
- Impaired short-term memory concentration
- Persistent psychosis
“K2, Spice” Affect Many Organs

- Brain
- Eyes, ears, nose, throat
- Lungs
- Heart, blood vessels
- Kidney, hormones
- Digestive tract
- Reproduction

- Vomiting, nausea
- Eye soreness
- Profuse sweating
- Severe GI symptoms
- Muscle spasms
- Increased blood pressure, heart rate
- Chest Pain
- Serious injury or death
### Adverse effects of cannabinoids

- Abusers in ER seek treatment for addiction
- Multiple deaths associated with these alone or combined

<table>
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<tr>
<th>Organ system</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychological</td>
<td>Anxiety, aggression, agitation, confusions, dysphoria, paranoia, irritation, panic attack, hallucinations</td>
</tr>
<tr>
<td>Neurological</td>
<td>Seizures, loss of consciousness</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Tachycardia, hypertension, chest pain, cardiac ischemia</td>
</tr>
<tr>
<td>Metabolic</td>
<td>Hypokalemia, hyperglycemia</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Nausea, vomiting</td>
</tr>
<tr>
<td>Autonomic, other</td>
<td>Fever, mydriasis, conjunctivitis,</td>
</tr>
</tbody>
</table>
Acute Kidney Injury Associated with Synthetic Cannabinoid Use

CDC: Multiple States, 2012 MMWR Weekly February 15, 2013 / 62(06);93-98
Marijuana plant makes ~80 phytocannabinoids
THC = #1

Brain, other organs make Endocannabinoids
Anandamide: arachidonylethanolamide
2-AG: 2-arachidonoylglycerol
7 or more made in brain and in other tissues

Synthetic cannabinoids: 1,000s made by chemists
Δ9-THC (Gaoni & Mechoulam, 1964)
Δ9-THC, others, endocannabinoids target similar cannabinoid receptors

Endocannabinoid
made by the brain

Anandamide

Drug
THC made by the plant, Cannabis Sativa
Brain Cannabinoid System
Controls Communication

- Modulates brain communication by reducing chemical messages
- Critical for brain development
- Controls chemical messages critical for pleasure, mood, pain, appetite, motivation, memory

- THC, synthetics affect anandamide control of brain signals
- THC, synthetics‘ effects are prolonged, more powerful, different
Addiction

• Addiction to JWH-018, JWH-200, JWH-073, CP-47,497, cannabicyclohexanol: physiological and psychological dependence liability similar to that of marijuana and THC.

• Physical and psychological withdrawal: elevated blood pressure, restlessness, drug craving, nightmares, sweating, nausea, tremor and headache, palpitation, insomnia, headache, diarrhea, vomiting.
“Spice” and “K2”, widely used by high school and college students, are emerging public health challenges.

Their rapid rise in popularity,

• ready access from multiple sources
• production of acute psychological distress
• toxicity
• potentially long term harmful effects
• ability to evade standard drug tests, require a massive public education campaign and strategies for deterrence in healthcare systems are needed to respond to this emerging threat.
1. Phenethylamines: similar to mescaline
2. Dragonfly: 2C-Bfly, Br-fly, Br-dragonfly)
3. SalvinorinA: 5.9% among 12th graders
4. Smiles:
5. Dissociative anesthetics: methoxetamine, ketamine, PCP
6. DMAA (1,3-dimethylamylamine): “party pills”, weight loss, sports performance supplements.
“Smiles” or "25-I“: analog of 2C-B: drug is the newest of "research chemicals" available for purchase online.

25-I's chemical makeup varies from batch to batch, effects similar to LSD, 2C-I, and 2C-B, all banned under federal law.

Psychoactive effects: hallucinations, in some cases severe brain hemorrhaging, death.

Trend in Connecticut: among high school and college students.

Public awareness: Unaware of potentially fatal side effects.
Figure 1  2C-Phenethylamine and Tryptamine Reports to NFLIS, 2006-2010

- Tryptamines
- 2C-Phenethylamines
<table>
<thead>
<tr>
<th>2C</th>
<th>Chemical name</th>
<th>Dosage</th>
<th>Duration (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2C-B</td>
<td>4-Bromo-2,5-dimethoxyphenethylamine</td>
<td>12–24 mg</td>
<td>4–8</td>
</tr>
<tr>
<td>2C-C</td>
<td>4-Chloro-2,5-dimethoxyphenethylamine</td>
<td>20–40 mg</td>
<td>4–8</td>
</tr>
<tr>
<td>2C-D</td>
<td>4-Methyl-2,5-dimethoxyphenethylamine</td>
<td>20–60 g</td>
<td>4–6</td>
</tr>
<tr>
<td>2C-E</td>
<td>4-Ethyl-2,5-dimethoxyphenethylamine</td>
<td>10–25 mg</td>
<td>8–12</td>
</tr>
<tr>
<td>2C-G</td>
<td>3,4-Dimethyl-2,5-dimethoxyphenethylamine</td>
<td>20–35 mg</td>
<td>18–30</td>
</tr>
<tr>
<td>2C-G-3</td>
<td>3,4-Trimethylene-2,5-dimethoxyphenethylamine</td>
<td>16–25 mg</td>
<td>12–24</td>
</tr>
<tr>
<td>2C-G-5</td>
<td>3,4-Norbornyl-2,5-dimethoxyphenethylamine</td>
<td>10–16 mg</td>
<td>32–48</td>
</tr>
<tr>
<td>2C-I</td>
<td>4-Iodo-2,5-dimethoxyphenethylamine</td>
<td>14–22 mg</td>
<td>6–10</td>
</tr>
<tr>
<td>2C-N</td>
<td>4-Nitro-2,5-dimethoxyphenethylamine</td>
<td>100–150 mg</td>
<td>4–6</td>
</tr>
<tr>
<td>2C-P</td>
<td>4-Propyl-2,5-dimethoxyphenethylamine</td>
<td>6–10 mg</td>
<td>10–16</td>
</tr>
<tr>
<td>2C-SE</td>
<td>4-Methylseleno-2,5-dimethoxyphenethylamine</td>
<td>~100 mg</td>
<td>6–8</td>
</tr>
<tr>
<td>2C-T</td>
<td>4-Methylthio-2,5-dimethoxyphenethylamine</td>
<td>60–100 mg</td>
<td>3–5</td>
</tr>
<tr>
<td>2C-T-2</td>
<td>4-Ethylthio-2,5-dimethoxyphenethylamine</td>
<td>12–25 mg</td>
<td>6–8</td>
</tr>
<tr>
<td>2C-T-4</td>
<td>4-Isopropylthio-2,5-dimethoxyphenethylamine</td>
<td>8–20 mg</td>
<td>12–18</td>
</tr>
<tr>
<td>2C-T-7</td>
<td>4-Propylthio-2,5-dimethoxyphenethylamine</td>
<td>10–30 mg</td>
<td>8–15</td>
</tr>
<tr>
<td>2C-T-8</td>
<td>4-Cyclopropylthio-2,5-dimethoxyphenethylamine</td>
<td>30–50 mg</td>
<td>10–15</td>
</tr>
<tr>
<td>2C-T-9</td>
<td>4-(t)-Butylthio-2,5-dimethoxyphenethylamine</td>
<td>60–100 mg</td>
<td>12–18</td>
</tr>
<tr>
<td>2C-T-13</td>
<td>4-(2-Methoxyethylthio)-2,5-dimethoxyphenethylamine</td>
<td>25–40 mg</td>
<td>6–8</td>
</tr>
<tr>
<td>2C-T-15</td>
<td>4-Cyclopropylthio-2,5-dimethoxyphenethylamine</td>
<td>&gt;30 mg</td>
<td>Several hours</td>
</tr>
<tr>
<td>2C-T-17</td>
<td>4-(s)-Butylthio-2,5-dimethoxyphenethylamine</td>
<td>60–100 mg</td>
<td>10–15</td>
</tr>
<tr>
<td>2C-T-21</td>
<td>4-(2-Fluoroethylthio)-2,5-dimethoxyphenethylamine</td>
<td>8–12 mg</td>
<td>7–10</td>
</tr>
</tbody>
</table>
Dragonfly Deaths

- **2Cs** are designer drugs emerging as new drugs of abuse.
- The published literature concerning 2Cs is limited; a few 2Cs have been studied, i.e., 2C-T-7, 2C-B, and 2C-E, limited information.
- A syndrome consistent with excited delirium including severe agitation, aggression, violence, seizures, and hyperthermia is consistently depicted in lethal 2C cases.
- No antidotes for 2C intoxication.
- Treatment is limited to supportive care but should include rapid sedation, aggressive treatment of severe hyperthermia and excited delirium.

<table>
<thead>
<tr>
<th>Age/sex</th>
<th>Agent</th>
<th>Route</th>
<th>Dose</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-year-old male</td>
<td>2C-T-7</td>
<td>Snorted</td>
<td>35 mg</td>
<td>Vomiting, hallucinations, agitation, violence/ aggression, nasal bleeding, possible seizure activity, pulmonary edema, cardio/pulmonary arrest</td>
</tr>
<tr>
<td>17-year-old male</td>
<td>2C-T-7</td>
<td>Snorted</td>
<td>Unknown</td>
<td>Agitation, violence, aggression, possible laryngeal edema, cardio-pulmonary arrest</td>
</tr>
<tr>
<td>Unknown male [37]</td>
<td>2C-T-7; 200 mg MDMA</td>
<td>unknown</td>
<td>unknown</td>
<td>Agitation, aggression, violence, seizures, hallucinations, cardio/pulmonary arrest, cerebral edema</td>
</tr>
<tr>
<td>22-year-old male [38]</td>
<td>2C-T-21</td>
<td>Ingestion</td>
<td>Unknown (dipped tip of tongue into powder)</td>
<td>Hyperthermia (108 °C), seizures, coma</td>
</tr>
<tr>
<td>19-year-old male [34, 44]</td>
<td>2C-E</td>
<td>Snorted</td>
<td>Unknown</td>
<td>Aggressive/agitation, hyperthermia, DIC, multi-organ failure</td>
</tr>
<tr>
<td>17-year-old male [39, 40]</td>
<td>2C-L-NBOMe</td>
<td>Ingestion</td>
<td>Unknown, mixed with chocolate</td>
<td>Hyperventilation, foaming at the mouth</td>
</tr>
<tr>
<td>18-year-old male [39, 40]</td>
<td>2C-L-NBOMe</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

Information is taken from that reported in the media and therefore accuracy cannot be verified.
# Methoxamine and methylhexanamine

<table>
<thead>
<tr>
<th>Methoxamine</th>
<th>Methylhexanamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 2011</td>
<td>• Stimulant</td>
</tr>
<tr>
<td>• Dissociative, pain suppression</td>
<td>• Dietary supplement market</td>
</tr>
<tr>
<td>• Sold as ketamine derivative</td>
<td>• Cathinone replacement</td>
</tr>
<tr>
<td>• Similar to PCP</td>
<td>• DMAA FDA challenges for safety evidence</td>
</tr>
<tr>
<td>• 5-7 hour duration</td>
<td>• Deaths</td>
</tr>
<tr>
<td>• Deaths</td>
<td></td>
</tr>
</tbody>
</table>
Methoxetamine and 3,4-methoxy analogues of PCP target NMDA receptors

Summary

Designer drugs: a rapidly expanding threat to public health

- A vast array of new drugs are being introduced
- Contents, doses of substances unknown
- Drug interactions unknown
- Short-, long-term effects unknown
- Toxicity reports are increasing rapidly
- Effects on developing brain unknown
- Routine drug testing currently not feasible
- Legal status for many uncertain
Designer drugs: a rapidly expanding threat to public health

- Impact on brain function, behavior, organ systems, is unacceptably high
- Preclinical research on each drug (100’s) is not feasible unless massive scale-up of research funding
- Drug combinations challenge research
- We are engaged in a massive human experiment, which will require years to resolve
What Concerned People Can Counsel

• Avoid consuming drugs that affect thinking, feelings, judgment.

• The adolescent brain is fragile as it is not fully formed.

• No one knows what a street drug contains, how much, impurities, toxins.

• Intoxication is risky, for health, for making unsafe or unhealthy choices.

• Any drug, legal or not, if not prescribed / used for medical purposes, can be unsafe.

• No one knows long term effects of designer drugs.
Faustian Bargains
Drug Use and Drug Policy

Pleasure
Full, legal access

Pain
Medical, social, economic, legal, costs
Death Rates 3-5 Times Higher in Addicted Patients

Standardized Mortality Rates of Patients with a Primary Substance Use Disorder (SUD)

1 = no added risk