Chapter 4
Case Studies of Emerging Drugs: Salvia, Bath Salts, and Bromo-DragonFly

In order to offer more insight into the novel and emerging drug phenomenon, a series of case studies are presented in the following pages that intricately explore the recreational use, media coverage, and regulation of three emerging psychoactive substances with diverse effects and unique histories. First, a short-acting dissociative plant in the mint family, *Salvia divinorum,* is described as an example of an extant drug that somewhat suddenly became linked to recreational use after the natural product was chemically enhanced, mass produced, and packaged for retail sale by a handful of organizations. This drug is also an excellent example of state-led drug regulation as opposed to federal oversight. Second, the chapter examines the appearance of psychoactive synthetic stimulants marketed as "bath salts." This category of substances received significant media attention and was quickly scheduled at the federal level in most countries. Finally, we present the recreational use of a recently synthesized research chemical that has yet to become a widespread drug of abuse. Bromo-DragonFly is a powerful and long-acting hallucinogen when taken recreationally.

4.1 Case Study 1: Salvia divinorum

Salvia divinorum, or commonly referred to by users and law enforcement by its genus name "salvia," has emerged as a new drug of concern in the last decade in the USA. Salvia has also been called the "diviner's sage," "magic mint," and "Sally D" and may be referred to by some as Purple Sticky, the name of a popular brand of fortified salvia product. Its use as a psychoactive drug, however, is far from a new phenomenon and likely preceded colonization of the Americas. Salvia is a naturally occurring plant in certain regions of Mexico, but it is considered an emerging drug since it is now being altered, marketed, transported, and administered in new ways and is reaching a larger base of potential recreational users.

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4.1.1 Historic Use of Salvia

Gordon Wasson authored one of the first academic references to salvia as a psychoactive drug in 1962. Wasson and colleagues had been annually exploring the Oaxaca region of Mexico throughout the previous decade to investigate the natives' use of psychoactive mushrooms in religious ceremonies. During their investigations, they learned of a plant occasionally used for its psychoactive properties when hallucinogenic mushrooms were unavailable. Wasson (1962, p. 77) reported that the Mazatec Indians considered salvia, referred to as *ska Pastora* in Mazatec culture, a "less desirable substitute" to mushrooms, but that they took some effort in cultivating the plant.

Within the Mazatec Indian culture, salvia was administered to the unhealthy by a *curandero* (a shaman or folk healer). In a way, salvia was a diagnostic tool that they believed could help determine the source of an illness. Wasson (1962) reported that the Mazatec Indians believed that an individual that drinks water containing the leaves would reveal the source of their malady during the ensuing semi-delirious state. As such, friends and family would observe the individual while they were under the influence and listen to their comments. Its use in this form led to salvia being referred to as the "diviner's sage."

4.1.2 Modern Salvia Use

The use of salvia did not appear to extend much beyond this form until the 1990s and then was only rarely consumed by recreational drug users (Appel and Kim-Appel 2007). Recreational users would choose to smoke dried leaves rather than drinking a water-based salvia mixture or holding leaves in one's cheek as was the custom in Mazatec religious and healing ceremonies. Additionally, recreational users often purchase modified salvia products in which the concentration of salvinorn A (the active ingredient) had been artificially increased through a modified growing process or the leaves being chemically impregnated with its own extract after being harvested.

When salvia is smoked using a tobacco or marijuana pipe, users experience a relatively short, but very potent high. The typical high from smoking lasts fewer than 30 min (Prisinzano 2005; González et al. 2006). Some recreational users choose to chew the leaves and experience a more "subtle" version of the plant's effects. When administered in this way, the salvia's effects, although weaker, can last an hour or more (Baggott et al. 2004). Salvia users most frequently report disorientation and an intense dissociative sensation that almost immediately follows the administration (Prisinzano 2005; González et al. 2006). Other reports seem to liken salvia's effects to those of LSD claiming mystical insights, psychedelic visual distortions, hallucinations, and mood alterations (Zawilska and Wojcieszak 2013), but these appear to be far rarer. Loss of consciousness and out-of-body experiences have also been associated with salvia use (González et al. 2006).

Initial reports in the USA suggested that salvia use was rare and sporadic, but did note that it might become a problematic drug in the future. In 2003, the Drug Enforcement Administration (DEA) did not have cause to believe that salvia was likely to become a club drug and decided to label it a "drug of concern" rather than scheduling it. At that time, they suggested that its use in the USA was and would continue to be limited to adolescents and young adults that regularly shop at "head shops." These outlets are likely a source of information for potential salvia users and later studies (i.e., Khey et al. 2008) would implicate them as a major source of recreational salvia. Internet searches for "legal high," "herbal high," or "safe legal high" would often return lists of websites selling salvia (Dennehy et al. 2005), and many offered different versions of their product with different concentrations of salvinorin A, the psychoactive compound responsible for the plant's effects. However, as previously mentioned, Internet purchasing does not appear to serve as a substantial source for users to acquire emerging drugs, including salvia (Khey et al. 2008).

4.1.3 Media Coverage and Regulation of Salvia

Much of the focus on salvia in the mid-2000s can be attributed to its label as a "legal high," arguably the first of its breed in the USA. The legal availability of salvia drew the interest of concerned groups while media outlets easily gathered the attention of the public by describing salvia as a scary new drug right at children's fingertips. In fact, initial media coverage may have actually spread curiosity about salvia among adolescents and young adults and facilitated increased experimentation during this time.

Salvia-focused media attention increased significantly when Delaware teen Brett Chidester committed suicide after having used the substance on January 23, 2006. Though his use of salvia may not have been the direct cause of his suicide, or even contributed to it, the media's portrayal of the event sparked a panic that led to some states banning salvia possession. The resulting Delaware legislation was even labeled "Brett's Law" (Griffin et al. 2008). Use of salvia, however, was not considered a cause of death in the Chidester case and was only retrospectively added after reports of previous salvia use were found in his personal journal (presumably due to political pressure). In the journal, Chidester described the drug as exposing him to new dimensions and feelings of emptiness. Chidester's autopsy did not find salvia in his system, but his family continues to attribute his death to salvia (Spring 2009). This may be an overwhelming oversimplification of complex behavior (Khey et al. 2008). In a situation like this where a young person dies at an early age, it may be easier to vilify a tangible product than unravel the full sequence of events that contributed to the saddening outcome. Being a relatively unknown and rare drug, salvia may have been ripe for vilification. Whereas the public would instantly deny that caffeine, tobacco, or marijuana was the leading cause of a suicide, they are unlikely to similarly question personal stories of a drug about which they know little. Where there are few users, high-profile cases may heavily influence public opinion. The family maintains a blog "Brett Chidester—Stolen Angel" to honor his memory and promote salvia regulation.

Prior to Chidester's death, Louisiana and Missouri were the only two states that had banned the use or possession of salvia. Whereas Louisiana enacted a specific law that prohibited growing, manufacturing, or distributing salvia in 2005, Missouri had simply added *S. divinorum* and salvinorin A to its list of controlled substances. A little over a month after Chidester's death, Delaware Senator Karen Peterson sponsored "Brett's Law" and the state classified salvia Schedule I just 14 weeks after the tragedy. By mid-2012, 27 states had scheduled salvia or passed a law that effectively banned possession while three others prevented its sale to minors (Stogner et al. 2012). Yet, salvia remains legal in most of the western and northeastern states. Thus, salvia regulation continues to be interesting in that the federal government has not acted and has completely left its legal status in the hands of state legislatures. This model is more consistent with drug regulation policies prior to the Second World War than the last several decades.

Years after the Chidester case, salvia once again received national attention when Jared Loughner opened fire with a semi-automatic handgun in Tucson, Arizona killing six people and injuring Congresswoman Gabrielle Giffords. Shortly after the horrific incident, the television news program Nightline reported on Loughner's recurrent use of salvia and introduced it as a possible cause of his delusions and concern with existential realities. Unlike Chidester's case, the Arizona shooting was not followed by a wave of states regulating salvia. Even Arizona refrained from modifying its policies. Though it may be simply the case of the states willing to regulate salvia, already having enacted legislation, it seems that the Loughner case was co-opted by those that favor gun control that quickly generated their own narrative to push the issues they believe in. In other words, for political gain (or other reasons), the Loughner shooting was tied to the issue of gun control. Therefore, access to the gun may have served the function of being the villain eliminating the need for salvia to serve that role. Salvia may have avoided further infamy since the tragic event had already been blamed on something. To be clear, it is likely that neither case was directly driven by salvia; the distinction is that the Chidester family and news outlets pushed the salvia connection more so than those covering the Arizona shooting. Regardless, each tragic event increased public awareness of salvia and depicted it in a negative light.

4.1.4 The Scope of Salvia Use

Initial reports of salvia use and its effects when smoked came from case studies or small samples of users (Bücheler et al. 2005; González et al. 2006). For example, González and his colleagues surveyed 32 admitted salvia users in Spain. Members of their sample were frequent users of other drugs, but fewer than half expected to use salvia regularly in the future. It appears that they viewed their experience as somewhat positive citing the euphoria and dissociation as pleasurable outcomes, but disliked the ensuing lack of control and unpleasant after-effects (González et al. 2006). While studies like this one and Baggott's web-based survey of users (Baggott

et al. 2004) were helpful in understanding the perceptions of salvia, its effects, and its utility among those strongly involved with drug use in general, they could neither be used to estimate the prevalence or frequency of use in the population nor were they able to detail less frequent drug users' reaction to salvia. For these issues, randomized samples of the population (or select portions of it) are necessary.

Due to ease of access to subjects and the fact that drug use is common during the collegiate years, many early assessments of salvia use relied on samples of university students. James Lange and his colleagues were among the first to evaluate the prevalence of salvia use. They found that 4.4 % of students at a southern California university had used salvia and argued that males, whites, and individuals that use other drugs used salvia more often. Later, David Khey et al. (2008) found that only 22.6 % of University of Florida students had even heard of salvia, but that a third of these (6.7 % of the total sample) had used salvia in their lifetime. Their results further suggested that continued use of salvia was rare.

S. divinorum was added to the National Survey of Drug Use and Health (NSDUH) in 2006. The NSDUH, sponsored by the Substance Abuse and Mental Health Services Administration (SAMHSA 2007), surveys 70,000 randomly selected individuals annually to provide national and state-level statistical information on drug use. According to the NSDUH in 2006, only 0.9 % of teens (12–17 years old) had ever used salvia and even fewer had used in the last month (0.1 %). These rates slowly grew over the next 4 years reaching 1.6 % in 2010. A larger portion of young adults (18–25 years old) reported use (3.6 % in 2006), but few older adults (26 and older) reported use (0.2 %). Adult salvia use also substantially increased between 2006 and 2010. In 2010, 8.8 % of young adults and 0.9 % of older adults reported ever using the substance. The past year and month rates suggest that the majority of those that have experimented with salvia do not continue to use over a long period of time. Recent findings from the NSDUH suggest that the prevalence of salvia use has been relatively stable since 2010 (SAMHSA 2012).

Salvia was not added to the USA's annual national study of high school students (Monitoring the Future [MTF]) until 2009, so the study has limited utility in tracking trends in use throughout the salvia's emergent period. It, however, will be helpful in tracking salvia trends once several years of data have been collected, and it also does help to clarify and confirm estimates from the NSDUH. Given that the average age of participants in its sample are older than that of NSDUH's youth subsample, it is not surprising that its estimates of salvia use are higher. The most recent MTF results noted that salvia use was reported by 1.4 % of 8th graders, 2.5 % of 10th graders, and 4.4 % of 12th graders. It also appears from the MTF data that fewer high school students view salvia as harmful as compared to normal drugs. This could be problematic and indicate that users overestimate the drug's safety. In MTF, data do suggest that use may be decreasing among youth. There was a statistically significant drop in reported salvia use between 2011 and 2012. Whereas approximately 3.6 % of students reported using in 2011, only 2.7 % reported the behavior in 2012. This decrease in use may be the product of increased legal controls or simply the substance falling out of favor.

While this text largely focuses on the USA, it should be noted that salvia has been used throughout the world and many countries encountered salvia use before the USA. For example, Spain (González et al. 2006), Italy (Pavarin 2006), and Switzerland (Giroud et al. 2000), all had issues with salvia before the first US state regulated the substance. Additionally, even though *S. divinorum* is native only to Mexico, it seems to be grown throughout the world. Most smoked salvia is adulterated or fortified in some way to increase its potency, but its base is still the organic plant. As early as the late 1990s, salvia was discovered in indoor marijuana-growing facilities in Switzerland (Giroud et al. 2000).

4.1.5 Salvia: An Internet Phenomenon?

Some early reports suggest that the spread of salvia use was largely facilitated by its prominence on the Internet (Hoover et al. 2008). A fear promoted by media outlets looking to capitalize on parents' and other concerned citizens' protective impulses was that children and teens would learn of salvia, discover its legality, purchase the drug, and learn how to use it from online webpages established to promote salvia use. There is no question that salvia was readily available online and that several websites were established promoting its use (Dennehy et al. 2005). Additionally, heavily trafficked drug user forums such as Erowid.org and Lycæum.org often offered positive reviews of the substance.

Valerie Hoover et al. (2008) completed a complex review of salvia's web presence over a 2-year period. They suggested that salvia was an ideal Internet drug because of its legality in some states, the public's limited awareness of its effects and dangers, its potency, and the ease of cultivation/manufacturing and, therefore, assessed salvia-related web content. Their research found that approximately 60 % of sites returned on Google and Yahoo! using the search term "*Salvia divinorum*" either offered to sell the substance or linked directly to a website that did. Over three-quarters promoted salvia use in some way and only 2 % classified it as a treatment or anti-drug. Further, this study indicated that many sites misinterpreted scientific evidence or interpreted the lack of scientific evidence on toxicity, health impairments, addictive potential, or other consequences as positive evidence of its safety. This implies that potential users, likely teens and young adults, may not appropriately question the pro-salvia arguments or realize that the limited evidence of toxicity does not equate to a confirmation of safety. Further, these researchers found that salvia-promoting sites are inconsistent in their analogies: Many likened it to a legal substitute to cannabis, others to hallucinogens, and still others (very inaccurately) to opioid analgesics.

Research on young adult populations suggests that friends played a much greater role in transferring information about salvia prior to scheduling than did the Internet. Very few respondents from general surveys reported learning of the drug online and less than 10 % reported ever purchasing it online (Khey et al. 2008). Friends were much more often the key source of information, and "head shops" were the overwhelmingly most common mode of acquisition. Additional evaluations of young

adult populations suggest that friends continue to be the most common information source, and salvia was rarely purchased online (Stogner et al. 2012). It appears that while pro-salvia information is readily available on the Internet, it actually is used infrequently, viewed skeptically, or only used by young adults to supplement the information passed along by their friends.

Salvia's favorable reviews and availability on the Internet likely had little to do with its legality. While some users may have been motivated to post messages and create websites in order to assist with the continued legality of salvia, the most common motivations are likely profit. As most sites offered to sell salvia or were associated with a site that did, they profited from giving positive reviews of the product. The promotion of a psychoactive substance for sale online is certainly not linked to the legality of the drug. Numerous rogue pharmacies claiming to sell prescription opioids and other scheduled pharmaceuticals exist online. Similarly, sites claiming to legitimately sell pharmaceuticals but failing to require adequate prescriptions or meet pharmaceutical standards are common on the Internet. Thus, the issue of Internet drug promotion or sales is not linked to a drug's legal status or unique to salvia, but is a larger issue shared by many drugs. We must also consider that simply because a substance is being advertised and is available for purchase online does not mean that it will reach the consumer. These websites may be utilized only sparingly or rarely deliver the product after purchase. Investigations into illicit pharmacies have suggested that those sites frequently charge potential consumers for drugs that they never ship or deliver (Chandra and Cupps 2002). As these victims are violating the law, they are unlikely to report not receiving their expected shipments. In this case, sales of salvia to states in which it is banned may be more an issue of fraud than substance use.

The Internet has aided our understanding of salvia use in several ways as well. In addition to web-based surveys, academics have gathered a great deal of information online via YouTube. Many groups have recorded and posted videos of individuals using salvia. Lange and others completed a detailed systematic observation of these posted videos and significantly improved our understanding of the effects that the drug has on individuals in a nonclinical setting (Lange et al. 2010). Their assessment helped clarify the delay of symptom onset and duration of effects in a typical drug-use setting. They noted the frequency of symptoms such as hypo- and hyper-movement, speech impairment, excitation, fear, and overheating which suggests that clinical effects may be subtler than effects observed outside a laboratory.

4.1.6 Typology of Salvia Users

Academic and anecdotal evidence would suggest that salvia is used in different ways and in different contexts. It appears that most use, and most users, could be classified as one of three types. First, there are "experimental users." These individuals use once or twice when in the company of friends and do not progress to habitual use. The use of these individuals may have been facilitated by salvia's legal status (and

continue to be facilitated in those states where it's legal), but use may have occurred regardless. Use of salvia may be a rite of passage in certain groups or be an informal type of hazing. Members of the group may persuade new members to use so that they can witness and laugh at their high. Additionally, it appears that some individuals enjoy having the experience of using salvia, but show little interest in using again. Thus, in a way it may be perceived as part of a checklist of risky behaviors to be completed as a young adult. These individuals likely view themselves as someone who has used salvia rather than a salvia user.

Another type of salvia use is connected to those more involved in drug use and the drug using culture. Those that consider marijuana or psychedelics as their primary drug(s) of choice are particularly likely to experiment with salvia. Salvia itself appears to be used not as a drug of choice, but as one drug among many that the individual uses. It is unlikely that salvia acts as any type of a gateway agent for these users. Their drug use is likely diverse and frequent, and they may even pride themselves in the number of drugs they have tried or their knowledge about drug use. Their use may have originated with seeing a new product in a "head shop" they frequented and the desire to remain current with "advances" in drug use. For them, salvia is just another piece of the drug puzzle. Much like the experimental salvia users, the "avid drug users" appear unlikely to advance to habitual or regular use although they may occasionally or intermittently use. Given that they are more likely to be identified as drug/salvia users and they frequent locations and websites associated with drug use, these users are likely overrepresented in focused samples (i.e., González et al. 2006; Baggott et al. 2004).

A very small subset of salvia users may progress to become "ritualistic users." Although this appears to be very rare, there are individuals who may select salvia as their drug of choice and define the dissociative experience produced by the substance as pleasurable. This group is likely to tie salvia use to its origins in mystic religions and use the substance (and other psychoactive drugs) as a form of meditation or self-exploration. The ritualistic user would be very knowledgeable about the effects of the drug and be most likely to use it in its traditional forms (chewed as a leaf or mixed into a drink). This group would likely not be deterred by the illicit status of salvia, but unlike avid drug users they are less likely to have drug-related problems given their more structured use.

If this typology accurately represents salvia users, the scheduling of salvia may have very limited utility. The avid drug users are likely to continue to desire and use salvia regardless of its legality just as they use other illicit drugs. The scheduling may make salvia more challenging to obtain, but these individuals would likely be motivated enough to expand their drug experiences that they would be willing to violate the law and navigate obstacles. Ritualistic use of salvia would likely be similarly unaltered. Since experimental users are likely to only use a limited number of times, scheduling salvia would have little effect on drug-related harms experienced by this group. Once the substance is scheduled, this type of individual may not ever use salvia. Members of this group may not be willing to go through the hassle of obtaining salvia given that more pleasurable drugs may be more easily obtained. However, given that salvia has not been directly linked to automobile accidents or

short-term negative health outcomes, a small reduction in use likely has negligible benefits at best. However, if salvia is truly acting as a rite of passage or risky behavior for the sake of experience in young adult peer groups, it is possible that another more dangerous substance or behavior will fill this void. As noted by Stogner et al. (2012), due to it being minimally reinforcing, salvia’s role may have simply run its course with individuals becoming less interested after its novelty wore off and newer drugs became available.

4.1.7 Lessons from Salvia Use in the USA

S. divinorum, as an emerging drug, is an interesting case. As it is typically viewed as less reinforcing and less pleasurable than other psychoactive drugs, it may never have become even remotely popular if “head shops” were not able to legally sell it and if media did not sensationalize it as a “legal high.” However, as noted previously, salvia regulation may not be as useful as one would suspect. Additionally, salvia is an excellent example of how a long-existing substance can spark an emerging drug threat following enhanced manufacturing, marketing, and distribution. The case of salvia also provides evidence of how a single event, perhaps even only tangentially related to the drug, can significantly affect willingness to regulate and possibly more importantly, public perception. This model mirrors events that have heavily influenced perceptions of other drugs such as the act of attempted cannibalism that was (inaccurately) linked to “bath salts” in Florida in 2012. Finally, salvia’s Internet presence may have been erroneously blamed for its spread in the mid-2000s. This case suggests that the presence of pro-drug websites may only be marginally important in comparison to peers.

4.2 Case Study 2: Synthetic Stimulants Called “Bath Salts”

The term “bath salts” has been used to refer to a diverse group of commercially produced synthetic stimulants that reached drug-using populations in the last decade. These stimulants were produced as drugs for the purpose of euphoria and increased energy. As previously mentioned and contrary to their tacit claims, these products were never intended as a bathing aid or even sold in stores specializing in bath products. Some forms were instead labeled as “stain removers,” “insect repellent,” “plant food,” or even “ladybug attractant” to similarly bypass regulations, but the name bath salts is typically used by the law enforcement, the media, and users to collectively refer to synthetic stimulants marketed in this way.

Though some legitimate consumers of bathing aids may have been concerned after initial reports of bath salts as a psychoactive substance prior to bans, there was little chance of accidental purchase of psychoactive bath salts. Rather than being sold in major retail outlets and stores specializing in spa and bath aids, these synthetic

stimulants were most commonly sold over the Internet and in "head shops," tattoo parlors, pawnshops, discount tobacco outlets, truck stops, and some independent gas stations (Fass et al. 2012; Spiller et al. 2011). Additionally, rather than having a soothing title as one would expect for a bath product, psychoactive bath salts were often labeled in a way that reflected their intense and stimulating effects: "Blitz," "Zoom," "Atomic," "Hurricane Charlie," "White Lightning," "Spark," "Charge+," "White Rush," and "Scarface." Though the fear that a person may accidentally purchase psychoactive bath salts may have contributed to public outrage at their initial legal status, it was unrealistic.

Substances falling into the category of bath salts likely contain one or more compounds that mimic the effect of cathinone, an amphetamine-like alkaloid found in leaves of the *Catha edulis* (khat) that naturally grows near the Red and Arabian Seas (Prosser and Nelson 2012). The compounds most commonly labeled as bath salts are Methylenedioxypyrovalerone (MDPV), mephedrone, methylone, 4-Methoxymethcathinone, and 4-Fluoromethcathinone, but products may also contain butylone, dimethylcathinone, ethcathinone, ethylone, or 3-fluoromethcathinone. These chemicals act as powerful central nervous system stimulants by inhibiting the reuptake of monoamine neurotransmitters. For example, MDPV primarily inhibits norepinephrine–dopamine reuptake (Westphal et al. 2009; Baumann et al. 2012; Lehner and Baumann 2013) while mephedrone mostly inhibits serotonin reuptake (Dybdal-Hargreaves et al. 2013).

4.2.1 Bath Salts and the Body

The typical use of bath salts occurs after the purchase of a packet of 50 mg or more of a white (sometimes tan or brown) powder that costs between US$ 25 and 50 (Fass et al. 2012). Most reports suggest that the most common route of administration is nasal insufflation (inhalation through the nose), but intravenous injection (likely after dissolving the powder in water) and ingestion also appear to be common (Murray et al. 2012). Additionally, there have been reports of bath salts being smoked (Wright et al. 2012), administered rectally (Khan et al. 2013), and taken sublingually (Coppola and Mondola 2011) but it is unknown how frequently, or even if, bath salts are utilized in each of these ways. The case reports offered by Winder et al. (2013) suggest that some brands can be smoked, but most melt or burn when heat is applied. The speed at which intoxication appears is, of course, linked to the form of administration, but even with ingestion, the effects peak in less than 2 h (Ross et al. 2011). Symptom onset is more rapid with other common forms of administration and the most notable effects last approximately 3–4 h (Fass et al. 2012).

As previously mentioned, bath salts' effects are more similar to cocaine, amphetamines, and methamphetamines than other drugs. Most users experience increased energy, heightened alertness, increased libido, and euphoria. Bath salts also increase blood pressure and heart rate, decrease appetite, and prevent sleep. Users may become agitated and anxious or develop muscle spasms and nosebleeds. Some

experience untoward symptoms such as severe paranoia, panic attacks, delusions, and extreme hallucinations that have been linked to hazardous and unpredictable behavior. Further, while under the influence of bath salts, many individuals become aggressive, violent, and combative. As such, bath salt use presents a significant danger to both users and the general public. Hyperthermia is also common which may explain why some users remove their clothing after taking bath salts. In the most problematic instances, bath salts have driven liver failure, kidney failure, seizures, and death (Meyer et al. 2010; Schifano et al. 2011; Murray et al. 2012; Fass et al. 2012; Adebamiro and Perazella 2012).

Many users of bath salts re-dose during a single drug episode. That is, they administer more of the drug to intensify or extend the high (Coppola and Mondola 2011; Streur et al. 2011; Schifano et al. 2011). This is not unlike how users go on a "binge" or "run" with more common stimulants. Heavy users also may develop a tolerance to bath salts (Freeman et al. 2012). As with other stimulants, bath salt users also report symptoms associated with psychological dependence after ceasing long-term use. Those quitting use report fatigue, reduced energy, depression, anhedonia, anxiety, craving, and insomnia that continue for a long period of time after the last use (Winstock et al. 2011; Winder et al. 2013). However, as is the case with most drugs that are only used by a small portion of the population, most of the knowledge of bath salts' effects and potential for dependence is reliant on case studies and reports consisting of few users (Antonowicz et al. 2011; Penders and Gestring 2011). Additionally, the reported number of deaths may be an overestimate of deaths actually caused by bath salts since many involved multiple drugs (Prosser and Nelson 2012). However, a preponderance of reports link bath salts to problematic outcomes and suggest that it should receive greater attention than most other emerging drugs.

4.2.2 The Emergence of Bath Salt Use

In terms of bath salt use, the USA lagged behind Europe, Australia, and other parts of the world. Mephedrone, marketed as a bath salt, became increasingly popular in the UK during 2008–2009. Winstock et al. (2010) found that over 40 % of 2,295 visitors to a popular UK dance music website had used mephedrone. An overwhelming majority of these users had used it in the last month. This study also assessed MDPV use, but found it to be much rarer (1.9 %) in the sample. Dargan et al. (2010) explored use in a more representative sample of young adults (one thousand Scottish students) noting that 20.3 % had used at least once and 4.4 % used mephedrone on a daily basis. Additionally, a number of bath salt-related Swedish deaths were identified as early as 2009 (Gustavsson and Escher 2009). Further, over 14 % of urine samples from an Irish heroin treatment clinic were found to contain evidence of mephedrone (McNamara et al. 2010), and a Finnish study identified MDPV in 8.6 % of samples taken from individuals suspected of intoxicated driving (Kriikku et al. 2011). Several other studies also suggested that bath salts were being increasingly used in Europe (Brandt et al. 2011; McElrath and O'Neill 2011; Prosser and Nelson 2012).

Though the UK and many nearby countries regulated mephedrone in 2010, its use continued. Winstock et al. (2010) reported that 63 % of their UK sample of mephedrone users continued to use, but complained that the price had more than doubled as a result of the ban. Alternatively, Carhart-Harris et al.'s (2011) research suggests that the majority of these users at least reduced their use as a result of the ban. Several bath salt-related deaths were also reported in the UK, which confirmed its presence in the region (Fass et al. 2012).

Around the time the UK banned bath salts in 2010, use reached the USA (Spiller et al. 2011). Initially, the only clear evidence that bath salt use was becoming more frequent was an increasing number of calls to poison control centers focused on managing the effects of bath salts (Johnston et al. 2013) and it being identified in a handful of laboratories (DEA 2013). Several deaths had been attributed to the drug (Johnson 2011; Murray et al. 2012; Wright et al. 2012), and the media had announced several cases of suspected bath salt use, but Spiller and colleagues provided the first truly insightful look into US bath salt in 2011. They retrospectively reviewed 236 cases of bath salt intoxication reported to poison centers and identified common symptoms, results, and laboratory findings (Spiller et al. 2011). Though bath salts were first federally restricted in 2011, very little additional information is known about the extent of bath salt use in the USA. Questions about bath salts were added to the national Monitoring the Future study in 2012, and it was found that 0.8, 0.6, and 1.3 % of 8th, 10th, and 12th graders, respectively, had used bath salts at least once (Johnston et al. 2013). Stogner and Miller's (2013) later research noted that 1.1 % of a large collegiate sample had used bath salts in their lifetime.

One thing that does appear clear is that the main psychoactive compound in products marketed as bath salts in the USA is MDPV (Spiller et al. 2011). This is in contrast to European bath salts, which were primarily mephedrone or, less commonly, methylone. It is not clear whether this distinction was driven by convenience, avoidance of regulation, market forces, consumer preferences, or producers moving on from a product that had already been stigmatized in another country. That being said, the composition of bath salt products in a given country is likely to vary, as is their potency. As such, users cannot be confident that they are taking the same substance that they took in the past or had seen others take.

It appears that bath salt users are more entrenched in the drug using culture than those that experiment with previously mentioned novel drugs like salvia or synthetic cannabinoids. Most are males and have an extensive history of drug use or at the very least use other substances (Fass et al. 2012; Stogner and Miller 2013; Porrovecchio 2011). Many apparently experimented with bath salts as a replacement for cocaine or another stimulant due to supplies of the previously used drug becoming limited, to avoid legal repercussions, or to avoid a positive drug test (Karila and Reynaud 2011). It seems that bath salts are more of an alternate or replacement stimulant as opposed to the so-called gateway drug.

4.2.3 US Media and Cultural Panics Linked to Bath Salt Use

Beginning in 2011, several prominent reports of aggressive and bizarre behavior attributed to bath salt use initiated what might be labeled a minor modern drug panic. Many of the stories that reached the national stage may have been sensationalized, and each vilified bath salt use. Two major stories aired in April 2011. ABC News covered the overdose and death of a Florida bath salt user, and a military officer was involved in a murder-suicide. Sergeant David Stewart allegedly suffocated his 5-year-old son, led law enforcement on a high-speed chase, shot his wife, and took his own life under the influence of "bath salts" (ABC News 2011; ABC24 2011; Johnson 2011). This horrific act led many members of the public to fear not only the direct effects of bath salts but also being violently victimized by a bath salt user. A month later, a West Virginia man was arrested after he was found wearing women's lingerie in his bedroom with a goat that he had allegedly raped and killed (Sheridan 2011), and a man in Tennessee reportedly attempted to perform surgery on himself under the influence of "bath salts" (ABC24 2011). However, as *The Economist* (2012) noted, "few things command attention like a random act of cannibalism."

The panic reached a precipice in May 2012 when a naked Rudy Eugene cannibalistically attacked Ronald Poppo in Miami. Eugene, who removed both of Poppo's eyes and most of his nose during the attack, was shot and killed by police responding to the incident. His behavior was attributed to "bath salts" (Dahl 2012) despite later reports that indicated that Eugene did not have MDPV or synthetic cathinones in his system (Hiaasesn and Green 2012). Media outlets dubbed him the "Causeway Cannibal" and bath salts the "zombie drug." Even a year after the incident and after reports that Eugene had only used marijuana, the majority of the populace primarily associates bath salts with cannibalism. We interviewed numerous law enforcement officers, educators, and military personnel about their knowledge and opinions related to emerging drugs (not yet published). The overwhelming majority of those that had heard of bath salts linked it to the cannibalistic Miami attack when asked what they knew about the drug.

Bath salts continue to be linked to bizarre behavior. A month after the Miami incident, a naked Pamela McCarthy choked her 3-year-old before running into the streets of Munnsville, New York and attempting to strangle her dog. She died of cardiac arrest after a conflict with police that led to her being tasered (Nelson 2012). While McCarthy had a history of bath salt use and was likely under the drug's influence, there has been no indication of bath salt use by Jett McBride, the Tacoma man who while claiming to be Jesus drove his car into pedestrians and began assaulting them until stopped by Caleb "Kai the hitchhiker" McGillivary. The lack of confirmation that McBride was a bath salt user, however, did not keep the members of the media (such as former ESPN host Jim Rome) from making assumptions about McBride's substance use that may have further exacerbated concern over bath salts (Rome 2013).

Each of these incidents, and even more so, the group as a collective, fanned the flame of public outrage. Bath salts appeared to be a growing menace moving in terms of public awareness from unheard of to repeatedly causing unexpected and violent

behaviors in less than 2 years. Even though their use is still somewhat rare, the media implied bath salt use had "exploded" (Roff 2012), "runs rampant" (Cross 2012), and even had hit "epidemic proportions" (Erickson 2011). This may have initiated or exacerbated the concern of the public that they were just starting to sense the initial effects of a bath salt outbreak. The forms of bizarre behavior reported may also have furthered public panic in that many people fear the unpredictable. While other psychoactive drugs cause them concern, they may take some comfort in knowing what happens after someone uses marijuana, LSD, or heroin. The nondrug using population is likely to know very little about an emerging substance like bath salts and fear the unknown. Similarly, in the absence of other information, they are likely to believe media reports that only focus on the most sensationalistic cases of bath salt use (or even sensational events that do not involve bath salts).

While the previous paragraphs should clearly present the opinion that bath salt coverage was inaccurate, sensationalized, and led to a misinformed population, readers should not infer that the reports and public concern failed to yield positive effects. As described in previous sections, MDPV, mephedrone, and other compounds labeled as bath salts are quite dangerous. Whether the public supported regulation because they inaccurately believed bath salts drove cannibalism or because they were well informed about its toxicity, link to violence, and potential for psychological dependence may be somewhat politically unimportant. In both circumstances, they support regulation and removal from store shelves. Ideally, voters and politicians should make the "right" decision for the "right" reasons, but implementing the "right" policy for the "wrong" reason is likely far better than taking no action at all or enacting problematic legislation. While regulation may not eliminate use, it would likely cause an increase in price (Winstock et al. 2010) and decrease in frequency of use (Carhart-Harris et al. 2011) as was reported in the UK.

4.2.4 Regulation of Bath Salts and Results

As use of bath salts in the UK preceded their use in the USA, it would be expected that the UK would ban mephedrone and other cathinone derivatives prior to the USA. They regulated them on April 16, 2010 under the 1971 Misuse of Drugs Act and the Republic of Ireland soon followed suit. Other European countries followed as did more than half of the US states. The US Federal Government placed a 1-year ban on MDPV, mephedrone, and methylone in the fall of 2011. This temporary emergency scheduling was chosen to allow the DEA time to collect data and evaluate the substances before placing them in a schedule, which may limit scientific research or interfere with individual liberties. In July of 2012, President Obama signed the Synthetic Drug Abuse Prevention Act of 2012 and the Food and Drug Safety and Innovation Act, 2012 that made MDPV and all synthetic cathinones Schedule I drugs under the Controlled Substances Act (1970). While some suggest that regulation may fail to decrease harms or may actually increase harms due to potential users turning to black market providers who may use adulterated products (McElrath and O'Neill 2011), it is too early to assess the efficacy of this regulation.

4.2.5 Lessons from Bath Salts and the Future

One of the most interesting aspects of bath salts' emergence was the speed of the spread of information, use, and regulation. Within 2 years of its first regular reported use in a country, it caught the public's attention and was regulated. This is very much unlike salvia, which for several years has remained in federal limbo being labeled a "drug of concern," and has remained unscheduled. While its strong effects created great pressure for immediate action, one must question whether the current scheduling system and bath salts' placement in Schedule I could prevent or delay the discovery of therapeutic uses for chemicals in this category.

The use of the term bath salts to represent an array of psychoactive chemicals is itself interesting and affects both policy and research. The term originates from marketing and labeling practices shared by multiple drugs in the same general category. Whereas European clinicians and law enforcement should connect the term to mephedrone, their US equivalents should believe it to primarily represent MDPV. This distinction may be of minimal importance due to the drugs sharing many pharmacological similarities, but this may not always be the case for drugs grouped by marketing practices. The bath salts term is derived from a marketing strategy designed to circumvent the law. Future successful attempts at bypassing regulation by appearing as some other legitimate product will likely be mirrored by other novel drug producers using the same label. If the drug effects are distinct (e.g., a stimulant and a cannabinoid), confusion with deadly repercussions may arise among users, law enforcement officials, and clinicians.

Once again, the media response to an emerging drug was sensationalistic and focused only on cases with horrific outcomes. In this case, coverage promoted regulation that was likely beneficial due to the nature of the drugs' effect. However, the media could better serve the population in the future by producing accurate and nonbiased reports. Future drugs with limited potential for harm may be inappropriately vilified if the pattern seen for salvia and bath salts continues. Particular insight should be derived from the Rudy Eugene and Jett McBride cases; not all bizarre and horrific behavior can be attributed to drug use. Mental health issues may be responsible for some acts, and it is therefore best to avoid linking a drug to an event until toxicology reports confirm the presence of that drug or its metabolites. Even further, use of the drug does not necessarily indicate the drug is responsible for the act. The behavior of an individual with mental health issues who uses a drug may be more the result of those issues (which may have also influenced their drug use) as opposed to the drug itself.

Finally, bath salt use presented a particular challenge for clinicians due to its rapid emergence. Given that only a limited number of case studies had explored the effects and reported appropriate treatment for someone suffering from the effects of bath salts, there was a clear lack of training among clinicians and those in public health as the number of users began to grow (Simonato et al. 2013). Since they are not regularly detected in drug screens, clinicians may be unaware that they are dealing with a patient under the influence of synthetic bath salts (Kyle et al. 2011).

Additionally, as manufacturers change the psychoactive compounds in emerging drugs to stay one step ahead of the law, they are also staying a step ahead of clinicians. The new products tweaked to avoid regulatory control may not respond to the same therapy or be as easily identified. It may take years to create tests, evaluate cases, and develop best practices by which time manufacturers will likely have switched to new formulations to skirt the law.

4.3 Case Study 3: Bromo-DragonFly, a Powerful Hallucinogen

While emerging drugs like salvia, bath salts, and synthetic cannabinoids appear to dominate media coverage, numerous other psychoactive substances have reached drug-using populations in the last several years. In some instances, the term "research chemicals" is used since the drugs may be involved in legitimate research and purchased from legitimate chemical providers. In other instances, it may be used since manufacturers label it a "research supply" to avoid regulation. One research chemical in the former category that has yet to attract mass attention is a phenethylamine called Bromo-DragonFly. This benzodifuran phenethylamine analogue (Dargan and Wood 2010) owes its name to the diagram of its chemical structure resembling a fly's body and is also referred to as spamfly, placid, and BDF.

Bromo-DragonFly was first synthesized as part of a project at Purdue University in the 1990s and appears to have transitioned to recreation use shortly after the turn of the century. At present, there are no solid assessments of its prevalence among drug users, but records of fatalities (Andreasen et al. 2009; Nielsen et al. 2010), seizures of the product (EMCDDA 2012), and Internet forums suggest that use extends beyond a handful of cases. Bromo-DragonFly is typically produced as a white or pinkish powder, but is sometimes transformed and marketed as tablets, liquid, or in blotter paper to recreational users (Dargan and Wood 2010). Coppola and Mondola (2012) suggest that the most common form of recreational use involves impregnated paper, but that insufflation, ingestion, and intravenous injection also occur.

Bromo-DragonFly's effects can most easily be compared to LSD. It is a quite potent hallucinogen with effects that can last over 24 h (Corazza et al. 2011). Users have reported that it causes euphoria, hallucinations, distorted time and space perceptions, brighter colors, sexual enhancement, diarrhea, headache, nausea, confusion, and muscle spasms (Coppola and Mondola 2012). More problematic effects have also been noted such as seizures, liver failure, renal failure, hyperpyrexia, ischemia, and death (Andreasen et al. 2009; Wood et al. 2009; Personne and Hulten 2008; Thorlacius et al. 2008). Bromo-DragonFly use seems to be limited to avid drug users, and they may use the substance in conjunction with a diverse array of other psychoactive substances (Coppola and Mondola 2012b).

Even avid drug users experience flashbacks and have claimed that the drug is too intense, too powerful, and too long-lasting (Corazza et al. 2011). Given their hesitance to promote Bromo-DragonFly to the same degree as other drugs discussed in online forums, it is questionable as to whether use will grow among drug users in

the future. LSD, the drug's traditional analogue, has become less popular in recent years partially because its long action does not mesh with the demands of an increasingly interconnected modern society. With Bromo-DragonFly's effects lasting even longer than LSD's, the drug may not ever garner significant interest from casual drug users. As such, the "shadow industry" may not view the drug as being as potentially profitable as the shorter acting and more reinforcing cathinones and cannabinoids. Their market assessment may have led them to decline to invest in the production and advertisement of the product. While it may be that a negative financial assessment of the potential market prevented expenditures on Bromo-DragonFly marketing, and thus limited information reaching consumers, the lack of production could also indicate an ethical decision by producers of "legal highs." They may have chosen to withhold a product that was too potent, too dangerous, or too unpredictable. While we view this hypothesis skeptically given the inherent dangers and mass production of synthetic cathinones, it is nonetheless appropriate to question whether some form of ethics affects decision making within the "shadow industry." Regardless, it seems that there are relatively few producers and retailers of the drug (excluding those legitimate research companies only selling it in large laboratory quantities at prices well beyond the reach of individual users). Anecdotal evidence suggests that Bromo-DragonFly is far more challenging to acquire than other emerging synthetics; rather than finding it in the local "head shop," users have had to actively seek the drug to obtain it and may lack the proper lab credentials or financial means.

Given that recreational use initiated over a decade ago and has yet to become an expansive problem, Bromo-DragonFly may never be more than a chemical that a select group of avid drug users experiment with. This, however, does not imply that regulation is completely unwarranted. Only a handful of countries (e.g., Denmark, Sweden, Norway, Australia, and Romania), Oklahoma, where a young child died as a result of accidentally consuming the compound, and a few other states have expressly regulated Bromo-DragonFly (Corazza et al. 2011). Many countries such as the USA and the UK have regulations that prevent possession or use of analogues of regulated substances, but it remains to be seen whether Bromo-DragonFly is chemically similar enough to those drugs to qualify as an analogue, and it remains difficult to prosecute cases in which substances are not outright-banned. Regardless, a full ban of the substance seems imprudent given its utility in research and the security demands of working with a scheduled substance. Therefore and in light of the apparent limited recreational use, it appears that at this time an alternative approach such as product registration may be more sensible.

Bromo-DragonFly demonstrates a few insights into the novel drug phenomenon. First, unlike synthetic cannabinoids, bath salts, salvia, and other high profile novel drugs emerging around the same time, Bromo-DragonFly has never truly been a focus of popular media outlets. Other than an incident in Oklahoma that was mistakenly attributed to another drug in early reports (News9.com 2011) and a segment on "The Dr. Oz Show" (Lee 2011), the drug is largely absent from public discussion. While it could be hypothesized that the lack of media coverage is a reason use never reached quantifiable proportions, it is more likely that the undesirable extended

effects deterred individuals from experimenting which, in turn, decreased the likelihood that the drug would catch the media's attention. Second, Bromo-DragonFly as a recreational drug remains underresearched despite a decade of use. Most of our understanding of the drug's recreational effects comes from the handful of cases that required medical attention or led to death. Clinicians that do deal with Bromo-DragonFly overdoses are vastly undertrained. Since there is so much unknown about Bromo-DragonFly in the recreational context, we cannot be certain that use will not escalate beyond its present scope. As such, we may not be prepared for the challenges of the future. It seems prudent to investigate emerging psychoactive substances when they first begin to reach potential drug users because we cannot be certain whether use will become relatively common as was the case for synthetic cannabinoids or remain limited as it appears was the case for the first decade of Bromo-DragonFly's recreational history.

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