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Mexico's precursor chemical controls: Emergence of less potent types of methamphetamine in the United States

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ABSTRACT

Background: This study examines whether Mexico's controls on ephedrine and pseudoephedrine, the two precursor chemicals that yield the most potent form of methamphetamine, *d*-methamphetamine, impacted the prevalence/availability of less potent types of methamphetamine in the United States–types associated with the alternative precursor chemical P2P.

Method: Using ARIMA-intervention time series analysis of monthly drug exhibits (a prevalence/availability indicator) from the System to Retrieve Information from Drug Evidence (STRIDE), we tested whether Mexico's controls, which began in 2005, were associated with growth/decline in *d*-methamphetamine and growth/decline in P2P-associated, less potent *l*-methamphetamine, racemic methamphetamine (a 50:50 ratio of *d*- and *l*-isomers), and mixed isomer methamphetamine (an unequal ratio of *d*- and *l*-isomers). Heroin, cocaine and marijuana exhibits were used for quasi-control (01/2000–04/2011).

Results: Mixed-isomer exhibits constituted about 4% of the methamphetamine exhibits before Mexico's controls, then rose sharply in association with them and remained elevated, constituting about 37% of methamphetamine exhibits in 2010. *d*-Methamphetamine exhibits dropped sharply; *l*-methamphetamine and racemic methamphetamine exhibits had small rises. *d*-Methamphetamine exhibits partially recovered in the US West, but little recovery occurred in the US Central/South. Quasi-control series were generally unaffected.

Conclusion: The US methamphetamine market changed. Widespread emergence of less potent methamphetamine occurred in conjunction with Mexico's controls. And prevalence/availability of the most potent type of the drug, *d*-methamphetamine, declined, a partial recovery in the West notwithstanding. Granting that lower potency drugs typically engender less dependence and attendant problems, these findings suggest that, following Mexico's controls, the potential harm of a sizeable amount of the US methamphetamine supply decreased.

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1. Introduction

The control of ephedrine and pseudoephedrine, the precursor chemicals commonly used to synthesize methamphetamine, has become one of the foremost environmental prevention policies in the field of illicit drugs (environmental prevention targets the user's environment rather than the user; EMCDDA, 2008; Rhodes, 2009). Its strategy is straightforward: reduce methamphetamine production/availability by limiting access to ephedrine/pseudoephedrine, and declines in methamphetamine consequences including hospitalizations, treatment admissions, and arrests should follow (Callaghan et al., 2009; Cunningham and Liu, 2003, 2005, 2008; Cunningham et al., 2008, 2009, 2010a; Maxwell and Brecht, 2011; McKetin et al., 2011).

Historically, methamphetamine producers have attempted to circumvent ephedrine/pseudoephedrine controls by finding

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alternative sources for the chemicals. The controls, however, are becoming increasingly restrictive (Cunningham et al., 2010a). If they were to effectively end ready access to ephedrine/pseudoephedrine, it is reasonable to expect that producers would seek alternative precursor chemicals, particularly 1-phenyl-2-propanone (P2P) (Mendelson et al., 2006). While relatively little licit P2P is manufactured, it can be readily produced using phenylacetic acid, which is widely traded as a licit substance and not well controlled (INCB, 2008, 2011, 2012). Moreover, esters of phenylacetic acid (e.g., methyl phenylacetate and ethyl phenylacetate) are also widely available and readily converted to phenylacetic acid (UNODC, 2011). Producers would likely turn to P2P reluctantly, however, as it results in a less potent type of methamphetamine (Mendelson et al., 2006). (Potency here refers to the ability of a drug to produce intoxication and a "high.")

This study examines whether recent ephedrine/pseudoephedrine controls implemented by Mexico, North America's primary methamphetamine producer, are associated with the emergence of P2P-associated, less potent methamphetamine in the United States, the continent's primary methamphetamine consumer (UNODC, 2008).

1.1. Evolution of ephedrine/pseudoephedrine control in North America

The United States implemented ephedrine/pseudoephedrine import, domestic distribution, and export controls beginning in the late 1980s (Cunningham and Liu, 2003, 2005). These efforts, however, were challenged by the absence of comparable controls in Canada and Mexico, which helped render the two countries alternative sources for the chemicals (Cunningham et al., 2009, 2010a). Recognizing this, Canada implemented import, domestic distribution, and export ephedrine/pseudoephedrine controls in the early 2000s (Brouwer et al., 2006; Callaghan et al., 2009). Mexico remained a major alternative source for ephedrine/pseudoephedrine until implementing its own controls beginning in the mid-2000s (Cunningham et al., 2010a). Following Mexico's controls, producers may have had for the first time no remaining, ready alternative source for ephedrine/pseudoephedrine in North America.

1.2. Ephedrine/Pseudoephedrine controls in Mexico

A Mexico government analysis in 2004 found that the country's pseudoephedrine imports far exceeded domestic need, and in 2005 Mexico began the gradual implementation of a series of efforts to better control precursors, including unannounced inspections at ports and enhanced collaboration with ephedrine/pseudoephedrine exporting nations (INCB, 2006; NDIC, 2010). (Note that Mexico does not manufacture ephedrine/pseudoephedrine and thus must import it.) Pseudoephedrine imports were reduced from 132,826 kg in 2005 to 45,524 kg in 2006 (INCB, 2006). Monthly import data show that this reduction, which was thought to place imports in line with legitimate need (SFP, 2006), was achieved by consistently limiting imports to a range of 150–7000 kg per month, a pattern which began in November 2005 (COFEPRIS, 2007a). In comparison, during the preceding period of January–October 2005, imports ranged from 475–31,000 kg per month. In February 2006, Mexico required that pharmacies limit pseudoephedrine product sales; diversion/loss/theft/wastage or extraordinary sale of pseudoephedrine products be reported immediately; distributors maintain pseudoephedrine records and submit them to the government; and federal officials, upon request, be given immediate access to records created in the past year (COFEPRIS, 2006). In an update, prescriptions were required to obtain any pseudoephedrine product in a pharmacy beginning September 2007 (Cordova Villalobos, 2007; Fármacos, 2008).

In March 2007, government officials searched the Mexico City home of the head of Unimed Pharm Chem de México (a commercial chemical company) and seized more than $200 million cash in US currency plus additional cash in other currencies, possibly the largest single drug-cash seizure in history (McCampbell, 2007). The company was accused of illicitly importing 60+ tons of pseudoephedrine (PGR, 2007). Its ability to continue massive pseudoephedrine smuggling (assuming accurate charges) was probably compromised significantly, if not ended, when the search was conducted and the cash was seized. Subsequent to this, in September 2007 the government filed 41 criminal complaints involving multiple companies for the falsification of 161 import permits related to pseudoephedrine and other health supplies (COFEPRIS, 2007b).

In July 2008, Mexico banned pseudoephedrine and ephedrine from the country, excepting as needed in federally approved research, surveillance and toxicological analysis (Consejo, 2008). In so doing, Mexico superseded its prior import and pharmaceutical restrictions and became the first North American country to ban the chemicals.

1.3. Precursors and methamphetamine potency

If Mexico's ephedrine/pseudoephedrine controls were to push some producers to P2P, isomeric composition of the methamphetamine produced should change. Consider that the methamphetamine molecule exists as 2 isomers (enantiomers), *d*-methamphetamine and *l*-methamphetamine (Cody and Schwarzhoff, 1993; Fowler et al., 2007). Methamphetamine synthesized using ephedrine or pseudoephedrine consists of *d*-methamphetamine only. But methamphetamine synthesized using P2P typically results in racemic methamphetamine, a 50:50 mixture of *d*-methamphetamine and *l*-methamphetamine (Mendelson et al., 2006). And racemic methamphetamine can be reprocessed to alter the ratio of *d*-methamphetamine and *l*-methamphetamine (DEA, 2012).

With a P2P-associated change in isomers, methamphetamine potency should change as well. Mendelson et al. (2006) compared *d*-methamphetamine, *l*-methamphetamine, racemic methamphetamine and a placebo regarding ability to produce intoxication and a "high." Twelve methamphetamine abusers received intravenous administrations of each in a 6-session, double-blind, balanced crossover design. Using a 100-point scale, the subjects assigned ratings for intoxication resulting in the following mean scores: *d*-methamphetamine: 46.0 (SD 35.3); *l*-methamphetamine: 30.3 (24.9); racemic methamphetamine: 24.7 (27.4); and placebo 1.7 (4.7). The mean scores for a "high" were *d*-methamphetamine: 46.5 (SD 35.0); *l*-methamphetamine: 31.0 (25.9), racemic methamphetamine: 25.4 (28.4); and placebo 1.5 (3.7).

The ratings for *d*-methamphetamine were significantly higher than all other conditions, while the placebo's ratings were significantly lower than all other conditions. Racemic methamphetamine ratings were below those for *l*-methamphetamine, but the difference was not statistically significant. These findings indicate that *l*-methamphetamine and racemic methamphetamine both produce intoxication and a high, but neither is as potent as *d*-methamphetamine. They also indicate that although racemic methamphetamine includes the more potent *d*-methamphetamine, racemic methamphetamine's potency is no greater than that of *l*-methamphetamine, and possibly less.

The potency of methamphetamine that consists of unequal *d*-methamphetamine and *l*-methamphetamine ratios has received little or no study. However, given the above findings, it is reasonable to assume that such methamphetamine, referred to

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