

THE SYNTHETIC DRUG PHENOMENON

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Global overview of synthetic drug markets

The illicit manufacture, trafficking and non-medical use of synthetic drugs are not new global challenges. Developments in the pharmaceutical and chemical industries have contributed to the continued discovery and proliferation of synthetic drugs. Since the early twentieth century, new pharmaceuticals, such as synthetic tranquillizers, stimulants and anaesthetics, have advanced medicine but also expanded opportunities f or the non-authorized supply and use of new mind-altering substances. The adoption of the Convention on Psychotropic Substances of 1971, in which Member States agreed to extend controls over some new synthetic drugs, many of which were pharmaceutical in origin, was testimony to the harm caused by the non-medical use of synthetic drugs in the twentieth century.^{2,3}

Synthetic drugs have proliferated in drug markets in the last decade. However, only a few synthetic drugs – mainly ATS, in particular methamphetamine and MDMA – have established robust global markets. Methamphetamine is probably the most widely used and supplied synthetic drug worldwide, and its manufacture and use continue to expand in South-East Asia, North America, South-West Asia, Africa and Europe.⁴ Synthetic cannabinoids encompass a wide class of ever-changing compounds, which continue to be found in drug markets across the globe.^{5, 6, 7}

Markets for other synthetic drugs are concentrated regionally, including synthetic opioids such as fentanyl in North America and tramadol in North and West Africa and parts of Central Asia. In Eastern Europe and Central Asia, a multitude of synthetic drugs

(including internationally controlled drugs and NPS that are not subject to control) have reshaped a drug market once dominated by heroin. Amphetamine in the form of "captagon" is the drug of main concern in the Near and Middle East. Meanwhile, drug markets in South America have witnessed the growing distribution of synthetic drugs, including ketamine and other NPS stimulants and hallucinogens.

Profit-maximizing criminals

In general, the illicit trade in drugs operates much like that in other commodities, with supply dominated by profit-driven individuals and organizations. However, one critical difference is that the activities involved in the drug trade are prohibited and subject to criminal penalties. Drug suppliers face not only standard business risks (e.g. lost investments and inventory), but also risks that stem from the nature of the illegal activity (e.g. risk of arrest and prosecution and risk of violence). They compensate for these risks by increasing markups at each transaction level, ultimately leading to substantially higher prices than if the manufacture of the commodities were legal.¹² From an operational and financial standpoint, trafficking organizations, like other businesses, seek to reduce operating costs and are therefore motivated by finding means of reducing risk or improving production efficiency. If successful, that cost saving, coupled with competitive market pressures, can translate over time into reductions in the price of drugs sold at the retail level. Declining retail prices are associated with increasing quantities consumed, as existing users consume more and new initiates enter the market, expanding the overall pool of consumers.13,14

Compared with plant-based drugs, some synthetic drugs offer greater means of reducing the risks and operational costs faced by criminal actors. Manufacture involves chemicals that, for some synthetic drugs, are readily available or substitutable, and improved synthesis methods can reduce the scale or nature of manufacture, boost yields or lead to the development of new compounds that are more potent than traditional drugs or can escape existing controls and detection capabilities. Additionally, suppliers can benefit by processing or distributing synthetic drugs as retail formulations, e.g. tablets, which may be appealing to new users or those averse to injection.^{15, 16}

The manufacture of synthetic drugs can offer two other important advantages for suppliers: timeliness and geographical flexibility. The large-scale production of most plant-based drugs requires so much space that it cannot easily be hidden, and can therefore only be pursued in places where State control is compromised or severely limited. In contrast, synthesizing illegal drugs usually requires little space, and so can be done almost anywhere. Furthermore, crops take time to grow – particularly coca, which comes from a bush that can take several years to mature to peak productivity.

Illicit crops can be destroyed by eradication or natural factors, such as drought or blight, resulting in substantial product loss in the course of a season. Large quantities of plant-based drugs seized through interdiction may represent considerable investment losses in the form of the time and labour involved in producing, for example, cocaine or heroin. Conversely, synthesizing drugs usually takes hours or days, so sudden unexpected shortages can be made up for comparatively quickly.

The advantages offered by synthetic drugs have not gone unnoticed by criminal suppliers. When fentanyl and several of its analogues first emerged on heroin markets in parts of the United States as early as 1979, some posited that suppliers were exploring cheaper "designer" drugs that could be made from readily available inputs and circumvent drug laws.¹⁷ However, the supply of synthetic drugs has, until more recently, been constrained by knowledge of chemical synthesis being limited to a handful of trained chemists, restricted access to precursor chemicals or related equipment and connections to existing distribution networks to get products to market. Many of those barriers have been drastically reduced in recent decades.

Defining drugs of natural and synthetic origin



Organic or naturally derived

- Occur naturally, often in plants (but also in fungi and animals)
- Alkaloid concentrations generally limited by rudimentary extraction/refinement procedures
- May be altered by humans to generate new (semi-synthetic) compounds of greater potency
- Discovery of new compounds occurs in nature and is slow



Synthetic

- Manufactured artificially by humans using chemicals (although some can be made from plant-based inputs)
- Producers can manufacture products of higher purity given improvements to synthesis and refinement processes
- Potency can vary but is often much higher than in naturally occurring alternatives
- New compounds are discovered rapidly in the laboratory or on the computer

Increasing availability of inexpensive inputs needed for synthetic drug manufacture

The global pharmaceutical and chemical sectors have developed very rapidly in the last four decades, in particular in Asia, 18, 19 where industry growth since the end of the twentieth century has resulted in the proliferation of firms and an increase in the number of individuals with the requisite knowledge of chemical synthesis and pharmacology. 20, 21 WHO estimates that China is the world's largest single producer of active pharmaceutical ingredients by volume, manufacturing over 2,000 products and comprising a quarter of global output, with annual production close to 2 million tons.²² Industry analysis indicates that the share of production of active pharmaceutical ingredients by India is slightly smaller.²³ The extent of these sectors and their rapid growth makes it challenging for regulators to ensure that manufacturers and vendors abide by handling restrictions and other regulations aimed at limiting the diversion of psychoactive substances and related precursor chemicals. 24, 25, 26, 27

Limited oversight of large industries or the absence of specific regulations covering the advertising and distribution of precursors increases the accessibility of a wide range of inputs needed to manufacture drugs. 28, 29 The manufacture and sale of basic chemicals, sometimes called pre-precursors, are difficult to control given the variety of legitimate uses of such chemicals. Additionally, some firms manufacture "designer" or masked precursors that are intended to fall outside of control or trade restrictions.30 Many of those chemicals are inexpensive. Prior analysis by UNODC has shown that the total value of all legal sales of controlled precursors and other chemicals needed in the manufacture of drugs is very small, at \$9 billion globally in 2012.31 The prices of some non-controlled precursor chemicals advertised by vendors in Asia are extremely low, and orders can be placed online and fulfilled by commercial shipment or post.³²

The illegal manufacture of synthetic drugs is also facilitated by access to other equipment needed to manufacture substances at an industrial scale (e.g. from bespoke commercial-grade reaction vessels to off-the-shelf glassware and commercial-grade

automated tableting machines).³³ Although international conventions call on Governments to adopt appropriate measures to prevent the diversion of materials and equipment to facilitate illegal drug manufacture, few countries have put in place effective regulations on the sale, transfer or possession of tableting machines or other similar apparatus.³⁴ Criminals have been found to use such equipment, sometimes finding vendors on the Internet, to illegally manufacture tablets containing synthetic drugs such as ATS, unapproved benzodiazepines or fentanyl.^{35, 36, 37, 38}

Analysis of significant seizures of fentanyl and tramadol shows that both South and East Asia are sources for finished pharmaceutical drugs destined for the illicit market as well as the precursors needed in the manufacture of finished drugs.

Improvement of manufacturing techniques

Coupled with increased access to chemicals and related equipment, the movement of goods and people and the expansion of Internet-based communications and encryption technologies have provided new means by which criminal organizations and drug suppliers can trade and exchange information and trade with end users.39 This has facilitated the trade in drugs and chemicals, especially newer or "designer" compounds that may not arouse the suspicions of customs authorities or other law enforcement agencies. 40, 41 Criminal organizations are reportedly using online platforms on the open web to identify vendors of precursor chemicals or suppliers of other equipment needed to produce or process synthetic drugs. 42,43 This is not the case for most plant-based drugs, apart from cannabis. Poppy and coca cultivators largely sell or trade their harvests directly to criminal groups.

Likewise, the ability to make use of findings from patents and medical literature on new synthetic drug discoveries, which are accessible online, allows clandestine chemists to consider and manufacture new drugs that were researched as potential medications but later shelved due to undesirable effects or abuse potential. This appears to be the case with several synthetic cannabinoids developed in the 1990s and

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MAP 1 Significant individual Fentanyl and Tramadol seizures over 1 kg in weight, 2017-2022

The boundaries and names shown and the designations used on this map do not imply official endorsement or acceptance by the United Nations. Dotted line represents approximately the Line of Control in Jammu and Kashmir agreed upon by India and Pakistan. The final status of Jammu and Kashmir has not yet been agreed upon by the parties. Final boundary between the Republic of Sudan and the Republic of South Sudan has not yet been determined.

Source: UNODC Drugs Monitoring Platform.

Note: Member States have reported higher quantities of tramadol seized than is suggested by the map. On the basis of recent annual report questionnaire submissions, there appears to be a route for tramadol from countries in the Sahel region to North Africa and the Middle East.

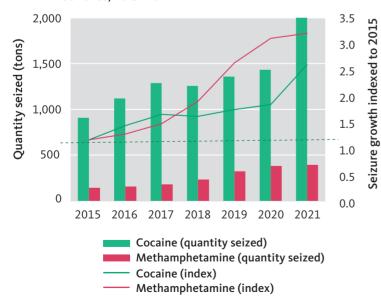
synthetic opioids developed in the 1970s, which later emerged on illegal drug markets or in brick-and-mortar stores selling NPS.^{44, 45}

The Internet-based sharing of information related to synthesis and new drug discoveries also provides knowhow for the synthetic manufacture of various drugs using plant-based inputs. The increasing availability of novel, semi-synthetic cannabis-derived compounds, such as hexahydrocannabinol (HHC), that serve to circumvent national and international controls may be related to the publication and promotion of simple synthesis routes that utilize CBD found in hemp as a starting material. In addition to synthesis routes found in peer-reviewed literature, simple Internet searches return easy step-by-step instructions on Internet forums and in video tutorials on how to extract and convert the primary inputs to finished psychoactive products. 46,47

Alternative chemicals that are not monitored or are less dangerous can facilitate new means of manufacture. For example, a review of the literature on the continuous development of synthesis routes for fentanyl has shown that those involved in the illegal manufacture of the drug are learning from published research and patents. 48 Enhanced synthesis routes for synthetic drugs offer shorter or simpler methods of manufacture for criminals who are not classically trained in chemistry. The analysis of fentanyl seizures has shown, for example, that in Mexico alternative synthesis routes have been employed that are sometimes operationally easier or utilize non-controlled chemicals.⁴⁹ Advances in the illegal manufacture of methamphetamine from P-2-P using tartaric acid refinement to boost potency, a method that has been used in Mexico since 2009, were reported in Europe for the first time in 2019.50 Changes in the methods used to illegally manufacture methamphetamine might also be occurring in South-East Asia, with the use of P-2-P, which is increasingly being seized, or of tartaric acid in conjunction with other chemicals to yield ephedrine.^{51, 52} Afghanistan has recently become a reported source of methamphetamine manufactured using a variety of potential precursor inputs, including *Ephedra* and diverted cold medication; however, several recent large seizures of formic acid, totalling more than 5,800 litres, suggest an evolution in illegal manufacture towards smuggled industrial-grade precursors.^{53, 54}

While global seizures of both methamphetamine and cocaine have increased in recent years, the increase in methamphetamine seizures has been much larger, indicating the scalability and diffusion of the synthetic drug's manufacture. Global cocaine seizures roughly doubled between 2015 and 2021, while methamphetamine seizures almost tripled over the same period. Although other factors are likely to be at play in relation to trends in seizures – better interdiction efforts, expanding markets, etc. – the production of most plant-based drugs cannot readily expand as rapidly or widely given that harvesting and processing take time and are sometimes limited to certain geographical locations.

FIG. 1 Global growth of methamphetamine and cocaine seizures, 2015–2021



Source: UNODC, responses to the annual report questionnaire.

Pharmacology and demand-related factors

The pharmacology of synthetic drugs can offer advantages to criminal suppliers and might be attractive to some people who use drugs. Several synthetic drugs are substantially more potent than the plant-based products they mimic. This is especially true of fentanyl and heroin. Fentanyl is perhaps 25 to 50 times more potent than heroin.55 This translates into reduced legal risk and, therefore, costs, as traffickers can more easily conceal smaller quantities of pure fentanyl in place of larger volumes of heroin. It has been estimated that as little as a few tons of pure fentanyl would be needed to satisfy the annual consumption of illegally sourced opioids in the United States, in contrast to about 50 metric tons of heroin. 56 Smaller quantities can reduce risks to smugglers; however, high-purity, high-potency synthetic drugs are sometimes sent through legal channels. For example, prior to 2019, law enforcement in the United States frequently reported high-purity seizures of minute amounts, sometimes as small as a single gram, of fentanyl in the international postal and courier systems.57

Fentanyl's high potency relative to heroin means that smuggling even small quantities of low purity through a variety of means is sufficient to meet demand. The advantages of a higher-potency product suggest that trafficking organizations can spread the risk of interdiction over a large number of single pedestrians or vehicles. This could make many synthetic drugs resilient to interdiction, translating into reduced retail prices. As evidence of this, the purity-adjusted low-level wholesale price of illegally manufactured fentanyl powder in the United States fell by more than 50 per cent between 2016 and 2021.⁵⁸

Similarly, methamphetamine has a longer duration of action than cocaine.⁵⁹ This can translate into less frequent redosing, which could be attractive to some buyers. There are other pharmacological aspects of methamphetamine that make it appealing to some. Unlike cocaine, which merely blocks dopamine reuptake, methamphetamine increases dopamine release while blocking its reuptake, thus providing a stronger stimulant effect.⁶⁰

More productive sources of methamphetamine manufacture, coupled with the drug's greater potency and lower cost per dose, as reported in Western and Central Europe, South-East Asia and North America, signal an expansion of the prevalence of the substance. ^{61, 62, 63} In Western and Central Europe, where amphetamine has traditionally been more common, methamphetamine supply is increasing according to early warning and drug services monitoring systems. ⁶⁴

The market dynamics of single drugs are determined by a combination of supply and demand factors. Users – especially price-sensitive heavy users – typically seek purer or cheaper drugs. ^{65, 66, 67} Novice users may be less reluctant to try cheap drugs that appear in tablet form, especially if they appear to have been diverted from the pharmaceutical system and do not need to be smoked, snorted or injected. ⁶⁸ Synthetic drugs can be manufactured and distributed at lower costs per dose ^{69,70} and formulated in ways that satisfy existing user behaviours and preferences, such as the practice of taking tablets.

Manufacturers of synthetic drugs can easily adjust combinations to respond to supply or demand dynamics. Analysis of tablet seizures in the United States indicates that some drugs, including drugs made to look like diverted medicines, contain illegally manufactured fentanyl instead of pharmaceutical drugs. In Afghanistan, tablets sold as MDMA often contain methamphetamine. In other instances in the United States, tablets sold as MDMA or diverted pharmaceutical stimulants, such as Adderall, have reportedly contained methamphetamine. Tablets containing amphetamine are often sold as "captagon" of pharmaceutical origin in the Near and Middle East.

While drugs sold on illegal markets often contain other adulterants or diluents, suppliers had a narrower range of choices in earlier years. Long-term analysis of impurities in heroin and cocaine sold in Europe and North America shows increasing variety in additives. Previously, additives were generally limited to caffeine, procaine or sugars; sometimes, other tranquillizers were added, but mostly in the form of approved benzodiazepines or other barbiturates. To approved benzodiazepines or other barbiturates. To approved drug cocktails in order to offer various qualitative and

psychoactive effects, often concealing the risks to buyers, with severe health-related consequences. In some opioid markets in North America, an increasing share of drug seizures contain mixtures of fentanyl with unapproved benzodiazepines, xylazine or veterinary tranquillizers.^{77,78}

Similarly, pharmacological factors, such as duration and mechanism of action, might be more variable for synthetic drugs, and appeal to different demand niches. Several synthetic ATS, such as MDMA or MDA, can produce varying psychoactive effects, unlike many plant-based drugs.^{79,80} The ease with which synthetic drugs can be rapidly modified to generate new psychoactive effects far outpaces the discovery of new naturally occurring drugs. For example, the synthetic cathinone mephedrone, which quickly gained entry to and prominence on some drug markets in Europe during the late 2000s and early 2010s, was reported by users to be similar but preferable to cocaine.^{81,82,83}

Synthesis allows suppliers to explore new "research chemicals" that are designed to mimic the effects of existing drugs or to sell cheaper alternatives to unsuspecting buyers. A Such buyers include those looking for wholly new drug-induced experiences unlike those provided by typical drugs on offer (e.g. psychonauts), those on certain dance or party scenes seeking to enhance their lifestyles (e.g. persons engaging in chemsex), or those who want a drug-induced experience but wish to avoid detection (e.g. individuals subject to drug screening). S, & Of the hundreds of NPS currently monitored by national authorities and international bodies, only a handful are plant-based.

Different supply and revenue structures for naturally occurring and synthetic drugs

Table 1 and figure 2 summarize the significant differences in the supply of drugs of synthetic versus natural origin. In many respects, synthetic drug manufacture offers structural benefits to criminal groups in the form of shorter supply chains, reduced risk and lower costs associated with risk and production when compared with drugs of natural origin.

 TABLE 1
 Comparison of drugs of natural and synthetic origin

| | Drugs of natural origin | Drugs of synthetic origin | |
|----------------------------------|--|--|--|
| Emergence of new drugs | Rare; would require discovery of new naturally occurring compounds; slow and limited | Chemical development; rapid by comparison and nearly unlimited | |
| Inputs and materials | Crops or other natural inputs that require certain climates or environments; limited State control over growing areas; other related chemicals needed in processing | Precursor chemicals, some of which are controlled, at least in theory. Others can easily be masked or designed to circumvent controls | |
| Scale and scope of production | Large, low-skilled labour supply dedicated to cultivating and harvesting large areas of illicit crops; geographically fixed production centres; extraction and refinement of alkaloids in rudimentary clandestine labs | Only requires a few individuals with knowledge of chemistry or means of carrying out chemical reactions in concealed and small locations; production can be mobile or easily relocated and scaled up or down as needed | |
| Production time | Months. Some illicit crops are harvested only a few times a year, while some have staggered harvests; some plants may take years to reach maturity | Hours or days for reactions and processing | |
| End products | Extracted/isolated and refined alkaloids (cocaine, morphine) or processed plant matter (cannabis, khat, kratom) | A wide array of psychoactive compounds can be produced using a range of precursor inputs | |
| Trafficking | Often involves larger quantities of primary inputs and finished products transported over vast distances or through remote areas, sometimes crossing several borders, which enables the authorities to detect and seize such drugs | Can be manufactured close to end markets; small quantities can be posted to end buyers | |
| Forms of administration | Most often injected, snorted or smoked, sometimes ingested | Can be smoked, snorted or injected, but a considerable share is tableted | |
| Pharmacology | Largely understood | Not always known or predictable, even if the chemical structure is known; some new compounds may appeal to different user groups | |

Synthetic drug manufacture represents a technological advancement, possibly disrupting markets and traditional supply chains. The supply structure for traditional plant-based drugs can be thought of as having an hour-glass shape, with many cultivators and farmers at the top. The labour supply for each subsequent layer gets smaller until it reaches exporters and importers, as drugs make their way, often across international borders, from areas where they are produced to areas where they are consumed. After that point, the number of people involved increases, up to the many retailers who supply products to users. In contrast, synthetic drug manufacture removes much of the top half of the supply chain.

The manufacture of synthetic drugs can be scaled more easily; that is, the marginal return for an additional chemist is much greater than for an additional farmer. This has been the case with several synthetic drugs, such as methamphetamine and ketamine, whose manufacture has moved from small, "cottage industry" laboratories to larger and more professional industrial-scale laboratories in North America, Asia and Europe. 91, 92, 93 From there onward, the number of

individuals involved in each level of the supply chain gets larger with each subsequent layer.

In economic terms, the synthesis of drugs is a capital-intensive means of production compared with labour-intensive plant-based drugs, although even for synthetic drugs, the capital involved can be small. Simply put, chemical synthesis obviates the need for tens of thousands of hectares of arable land and a large supply of unskilled labour. The illicit cultivation of plant-based drugs generally relies on poor farmers and their families living in remote locations. ⁹⁴ The nature of this means of production incurs additional costs for criminal groups. Many plant-based drugs are cultivated in areas with weak rule of law and governance and their production often requires non-State actors, who may also be violent, to control the production and transport of key inputs such as coca or poppy.

In contrast, synthesis offers suppliers several advantages. Clandestine synthesis can occur in facilities that are easier to conceal from authorities, including single residences, warehouses or laboratories in remote areas, ports or cities. The large-scale manufacturing

Producers and chemists

Producers and processors

Exporters

Importers

Wholesalers

Retailers

Retailers

FIG. 2 Labour supply for drugs of natural and synthetic origin

Sources: Kilmer, B. and Reuter, P., 2009. DOPED. Foreign Policy, (175), p.34.; and Reuter, P., Pardo, B. and Taylor, J., 2021, "Imagining a fentanyl future: Some consequences of synthetic opioids replacing heroin", International Journal of Drug Policy, 94, p.103086.

of synthetic drugs has endured in areas with weak rule of law, but also happens in countries with strong rule of law; MDMA, amphetamine and methamphetamine, for example, are manufactured in Europe, as is a small share of cathinones, mostly to meet local or regional demand.95,96 Authorities in Europe have noted the increasing manufacture of synthetic drugs within the continent and their trafficking to other regions. 97 Compared with the production of plant-based drugs, which prioritizes control over territory and rural populations, the manufacture of synthetic drugs can be easily relocated, sometimes closer to end markets or to major commercial hubs with access to imported chemicals or export routes, and chemists or cooks can be rotated from one laboratory to another, further reducing the risk of detection.

Shorter supply chains for synthetic drugs can reduce or eliminate some risks, especially if synthesis laboratories are relocated within a country in order to avoid the crossing of borders. In recent years, Canadian and United States authorities have detected and dismantled fentanyl synthesis laboratories, sometimes located not far from end markets. 98, 99 Similarly, since the early 2010s, the illegal manufacture of "captagon" has shifted from East and South-Eastern Europe to end markets in the Middle East.¹⁰⁰ European authorities have recently seized increasing amounts of chemical precursors and detected clandestine laboratories for several synthetic drugs, such as cathinones, gamma-butyrolactone (GBL), *qamma*-hydroxybutyric acid (GHB) and ketamine, suggesting a shift in production to meet demand on the continent.101 Prior to 2020, many of these synthetic drugs came from Asia. 102

In other instances, criminal producers have expanded operations to other emerging markets or countries that have limited capacity to detect drugs or screen imports for a growing range of precursors. For example, the illegal manufacture of methamphetamine has recently been reported in countries in Africa, including South Africa and Nigeria, 103, 104 using precursor inputs from Asia 105 and intended for regional and global markets. In recent years, several large-scale ketamine laboratories using industrial-grade equipment and employing teams of foreign cooks have been dismantled in Cambodia. 106 Countries in Central Asia have also recently reported marked increases in the

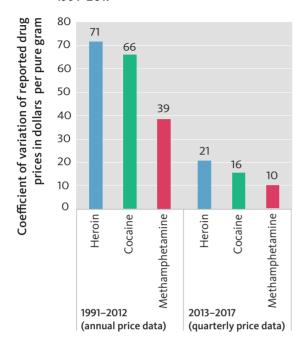
detection of domestic laboratories used for the manufacture of synthetic drugs, which was not previously the case. Authorities in Kazakhstan reported a 50 per cent increase in laboratory detections between 2020 and 2021, detecting, in 2021, 36 laboratories manufacturing mephedrone and *alpha*-PVP using increasingly sophisticated techniques and equipment.¹⁰⁷

The synthesis of drugs can be honed to better guarantee product consistency and prices. The productivity of coca or poppy crops may vary from one harvest to another.¹⁰⁸ Economic analyses of illegal drug markets reveal that commodity prices for plant-based drugs suffer from chaotic or periodic fluctuations given the agricultural nature of inputs and because distributors are unlikely to hold much inventory in order to avoid risk.¹⁰⁹ Synthetic drugs have lower price volatility as they are guaranteed to have more consistent purity, and because synthesis takes a short amount of time, producers are more likely to be able to respond to demand signals and reduce the risk associated with holding inventory. In fact, data from the United States show that the price volatility of cocaine and heroin was much higher than that of methamphetamine. 110

Furthermore, the processing of many drugs for retail markets requires diluting and repackaging the product, often near the point of retail sale.^{111, 112} Generally, wholesale distributors take illegal imports and dilute them further, contributing to price volatility in retail markets as buyers are unable to determine the quality of the product until after consumption.¹¹³ The retail distribution of powder imported in bulk allows local retailers to compete through product differentiation and branding in order to attract customers.¹¹⁴ Dilution, repackaging and retail-level branding are common aspects of drug markets, especially for products sold in powder form.

Synthetic drugs can appear in tablet form, which has not generally been the case for plant-based drugs. From the supplier's standpoint, tableting can be automated and can ensure greater product consistency. Large-scale commercial tableting machines can run uninterrupted and require only a few skilled technicians to produce tens or hundreds of thousands of tablets a day. 115, 116 While dosing in tablets may be inconsistent across different suppliers, 117 large-scale manufacture

FIG. 3 Price volatility of heroin, cocaine and methamphetamine in the United States, 1991–2017



Source: UNODC calculations based on ONDCP, National Drug Control Strategy, Data Supplement 2016 and DEA, 2019 National Drug Threat Assessment (December 2019).

Note: The coefficient of variation is defined as the standard deviation of a time series divided by its mean and multiplied by 100.

may reduce heterogeneity in dosing within a single batch. The Furthermore, such processing for retail can occur at the point of manufacture, where risks are lower than immediately before final sale, given that the product has not yet been traded or trafficked. Moreover, the industrial- or large-scale tableting of synthetic drugs allows criminal groups to control branding using stamps, dies and colours, adding value to the product and possibly increasing export revenues by consolidating several layers of the supply chain.

Drug synthesis and tableting can shift revenue retention along the supply chain. Most of the price markups and revenue generated by the supply of illegal drugs occurs at the stages closest to retail, compensating for the risks incurred along the supply route. This is true for drugs of synthetic origin, but with traditional

plant-based drugs, many (transnational) trafficking groups tend to focus on one segment of the supply chain and do not control the entire chain from seed to sale. For example, a consignment of cocaine or heroin is subject to multiple trades as the product is transported from the mountains of Colombia or Afghanistan to retail street markets in destination countries.¹²⁰

Outlook

From a criminal perspective, barriers to entry are lower for the supply of synthetic drugs than for plant-based drugs, and their production capacity ceilings much higher. Going forward, supply reduction efforts may be increasingly challenging as criminal suppliers employ new means of manufacture that are easier to conceal, use chemicals that fall outside of existing controls, or procure inputs from a global and expanding chemical and pharmaceutical sector. Additionally, traffickers stand to benefit from the shorter production times and higher potency offered by some synthetic drugs that reduce or overcome risks.

While synthetic drug manufacture provides a means of reducing production costs, declining revenues in the form of reduced retail and wholesale prices might affect illegal business operations. The way in which criminal groups will respond to declining revenues is unknown, but it may encourage adaptation in the form of new products aimed at new markets, or diversification into non-drug-related types of criminal enterprise. Expansion along the supply chain (either upward towards synthesis, or downward towards retail through tableting) is a possible response to the shifting nature of production costs, associated supply risks and revenue generated.

Beyond the manufacturing-related benefits enjoyed by criminal producers, new drug discoveries involving synthetic substances far outpace the emergence of new plant-based drugs. Chemists can design new compounds that could become quite popular for certain user groups based on their pharmacology. Many new synthetic drugs fall outside the scope of existing controls. While most new compounds fail to gain market share, they can sometimes cause harm during their

introduction to drug markets, especially if their potency is much greater than the drugs they replace.

In that regard, consumers face several challenges. In some instances, synthetic drugs are so new that their pharmacology and the harm that they cause are not entirely understood or documented. Likewise, there may be fewer available treatments, therapies or antagonists for some new drugs. The growing availability of a wider range of psychoactive substances allows suppliers to create ever-more dangerous cocktails, as evidenced by the growing number of tranquillizers, including unapproved benzodiazepines, mixed with other drugs that are showing up in the drug supply.

Although drugs of synthetic origin create certain economic and cost-cutting benefits for profit-maximizing criminals, they are unlikely to displace all plant-based drugs on every occasion and in every place. User tastes and preferences will continue to shape markets. Sociocultural contexts are important drivers, and some markets or individuals may opt for traditional plantbased drugs, such as cannabis or cocaine, because they appear to be more natural (i.e. they are considered to be less harmful), produce the desired psychoactive effect or are regarded more highly than their synthetic counterparts. In some instances, plant-based drugs such as cocaine¹²¹ are for now, still more cost-effective than the synthesis of some key compounds. For these reasons, criminal groups are likely to continue to supply certain plant-based drugs.

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