RUNNING HEAD: On-site testing of ecstasy tablets

The Marquis reaction as a harm reduction element in party atmospheres: an assessment of the on-site testing of ecstasy tablets

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Abstract

Background: The main aim of this study was to evaluate the reliability (sensitivity and specificity) of pill testing (Marquis reaction) in order to detect MDMA in ecstasy tablets. The second aim was to highlight the linear relation between MDMA concentration and the intensity of the Marquis reaction. **Methods:** Between 2000 and 2001, a total of 66 ecstasy tablets were collected and analyzed using a double-blind procedure involving gas chromatography and the Marquis reaction. The level of agreement between the results of the laboratory analysis and the *in situ* pill testing was then verified. **Results:** Pill testing detects MDMA in all tablets containing this substance (sensitivity and specificity = 100%, $p<0.00001$). The linear trend was also significant ($F_{1,50}= p<0.003$) and showed that the more intense the Marquis reaction is, the higher the MDMA concentration. **Conclusion:** This study shows that the Marquis reaction is a very valuable test for the purposes of harm reduction because of the high quality of screening it provides for MDMA in ecstasy tablets. Moreover, due to the linear relation between the MDMA concentration and the Marquis reaction, this test allows workers in the prevention field to communicate more specifically customized harm reduction messages. The present study should be considered as the first stage in the evaluation of this testing.

Keywords: harm reduction, ecstasy, MDMA, pill testing

Introduction

Over the last ten years, France has witnessed a constant increase in both the availability and use of stimulant substances (1). As far as ecstasy is concerned, however, consumption appears to have reached a stable level as a result of its everyday acceptance in party environments and a relatively high proportion of the French population has experience of this substance (2 % of those aged 18-64 years). However, the corresponding level is twice as high among the 18-25 year-olds and is of the order of 1.4 % over a year. Young males consume more than females, with 4.2 % stating that they have used the substance at least once in their lives compared to 2.8 % among females (2). As far as mortality levels associated with the consumption of ecstasy are concerned, five deaths were reported in 2005 (3).

Ecstasy, or MDMA, is the most widespread substance in use in party environments after cannabis because, according to users, it is "essential for a successful evening ". In 2003-2004, 70 % of all people who attended techno parties experimented with ecstasy (4). Although it is primarily taken orally, a significant increase in injections was observed between 2003 and 2006 (up from 13 % to 19 %) (5, 6). There has also been an increase in ecstasy sniffing (from 15% in 2003 to 18% in 2006). These latter modes of administration are primarily due to the search for more intense effects. There has also been a net reduction in the price of ecstasy (7, 8) due, in particular, to the "gross" purchase of tablets.

Although the use of ecstasy is primarily restricted to party environments, the emergence and increasing popularity of injection and sniffing as modes of administration may represent the first step towards more hazardous practices and, in particular, the consumption of heroin and cocaine which are becoming increasingly prevalent and available in free parties and teknivals.

Harm reduction mechanisms for use in party environments exist in France. Several associations, and in particular "Médecins du Monde", provide flyers, sterile kits, ear plugs and condom during rave parties, free parties or teknivals. These mechanisms are enhanced by the possibility of analyzing the ecstasy tablets at the user's request by means of thin-layer chromatography. These analyses also give us with an idea of the current "quality" of ecstasy and provide "field" data for the SINTES mechanism (National System for the Identification of Toxins and Substances). However, this

is a relatively time-consuming operation which takes an hour before the results are known. This delay tends to discourage users who thus eventually consume their tablets without any certainty that they actually contain MDMA or of the concentration.

This drug analysis plan can only be effective in terms of prevention provided that all the analysis tools are gathered together: marquis reaction, thin-layer chromatography, laboratory analysis with the SINTES mechanism (9).

Nevertheless, although questioned since its appearance in France in the 90s and finally banned in 2005 without having been properly assessed, testing makes an essential contribution to harm prevention, and in particular makes it possible to establish a dialogue between prevention workers and users. In the case of the so-called Marquis reaction, the testing consists of taking a pinhead size powder sample of the substance and adding a drop of the Marquis reagent (a mixture of formalin and sulfuric acid) to it. Depending on the colour of the reaction, this method makes it possible to surmise whether or not substances derived from the methylenedioxyamphetamines (MDMA), from amphetamines or from hallucinogens of type 2CB are present. However, the technique provides no information about blended products.

In particular, as far as amphetamines and MDMA family derivatives are concerned, the joint Inserm assessment (9) showed that tablets sold under the naming "ecstasy" were of a very variable composition, with rates of MDMA varying between 12 and 194 mg depending on the tablet. However, the toxic caused by ecstasy is dose-dependant and the minimal lethal dose is situated between 140 and 200 mg. Furthermore, within the harm reduction perspective, if users wish to consume the substance despite the prevention messages they are exposed to, then prevention workers must give them advice adapted to the substance that is to be consumed, i.e. the tablet of ecstasy for testing. It is within this framework that testing appears to be unavoidable.

The main aim of this study is to answer the criticisms that have been made concerning the quality of testing in terms of the reliability of presumed MDMA recognition. The second aim is based on observations made by prevention workers concerning a possible dose-effect relation between MDMA concentration and the intensity of the Marquis reaction.

Method

Procedure

Between 2000 and 2001, 100 samples of ecstasy were collected in party environments within the framework of the SINTES mechanism (2003). These were sent to a Pharmacology and Drug Dependency Laboratory for a qualitative and quantitative analysis.

Before being packaged and sent, every sample was tested by the same tester. The laboratory had no information concerning the results obtained during this testing.

Analysis of the products

To determine the nature and the concentration of the substances present in the ecstasy samples, the analytical laboratory used a gas layer chromatography method.

As far as testing is concerned, the nature of the observed reaction was described in terms of two reaction factors to make it possible to rate the Marquis reaction.

- appearance of coloured patches:
    - purple / black: assumption is the presence of the MDMA family
    - brown / orangey colour: assumption is the presence of amphetamines
    - yellow / green: assumption is the presence of type 2CB hallucinogens
- appearance of a cloud of white smoke

Intensity criteria were also rated for these two reaction factors:

- speed of appearance of the coloured patches: absence, slow, fast, instantaneous appearance
- size and concentration of the coloured patches: small scattered patches, single large patch
- presence of a cloud of white smoke

The initial coding obtained in this way is presented in table 1.

This initial coding was then simplified (because it must be practical and capable of utilization by all harm reduction workers without the need for any particular training) by only taking account of the criterion of the intensity of the observed patches. The coding which was finally defined contains four modalities and is presented in table 2.

Statistical analyses

To respond to our first objective, i.e. to estimate the reliability of the presumed recognition of methylenedoxyamphetamines, amphetamines and typical 2CB hallucinogens by means of testing, we conducted a test equivalent to the Chi-square but suitable for small samples. This precisely corresponded to the Fisher test.

To reveal a dose-effect relation between the concentration of MDMA and the reaction to testing, we performed an ANOVA with a test of linear tendency. All these analyses were performed using the SPSS 11 package for Mac OS X.

Results

Descriptive statistics

The final sample consisted of 66 ecstasy tablets. The laboratory results showed that 58 of them contained MDMA or families, 2 of them amphetamines and 6 of them other products (these were chloroquine, buflomedine, thiocolchicoside, prazepam, while two tablets contained no toxic substances). Given the very low number of ecstasy tablets containing amphetamines and the absence of tablets containing hallucinogens, we conducted analyses only for the 58 tablets containing MDMA. The average MDMA dosage was 58.6 mg (ET=5.5).

Reliability of MDMA detection

No significant difference ($p < 0.0001$) was observed between the results obtained for the laboratory analyses and those revealed by the Marquis reaction. Furthermore, as far as the detection of the presence of MDMA in the ecstasy tablets is concerned, we found that the testing exhibited a sensitivity and specificity of 100% in our sample, both in terms of positive and negative predictive values.

Revealing of a dose-effect relation

To verify the existence of a dose-effect relation between MDMA concentration and intensity of the reaction to testing, we first compared the average MDMA dosages as a function of the level of intensity of the reaction to testing. The results of the ANOVA showed that these average dosages were very significantly different as a function of the obtained reaction to testing ($F_{4,50}=2.854$; $p=0.033$). Furthermore, the test of linear tendency ($F_{1,50}= p < 0.003$) showed that the more intense and faster the reaction to testing was, the higher the MDMA dosage (graph 1).

Discussion

This study is one of the few European studies to evaluate the efficiency of testing both in terms of MDMA detection and the consequences for harm prevention (10-12). These preliminary results make it possible to confirm the diagnostic qualities of testing with regard to the detection of the presence of MDMA in the samples of ecstasy taken (sensitivity and specificity of 100%). These initial results greatly encourage us to verify whether these qualities are the same with regard to the detection of amphetamines and type 2CB hallucinogens. At the same time, this is the first study to reveal the existence of a significant linear relation between MDMA concentration and the intensity of the Marquis reaction. These preliminary results are therefore of interest for two main reasons. The first is that this method permits the quick, easy definition of the nature of the ecstasy in circulation in any given place or at any given time. The second advantage of this method is to improve and, more especially, to adapt the harm reduction message as a function of the substance that is actually going to be consumed by the user, i.e. it makes this message more individualized, closer to the reality experienced by a particular consumer and thus more effective than a standardized discourse.

However, the sample used for the purposes of this study was "collected" only by a single team from "Médecins du Monde". Although the sample is probably representative of ecstasy tablets in circulation in party environments, it would be interesting to repeat these analyses with samples collected by different teams, in different places and at different times.

Another comment has to be considered both at the level of the obtained results and at the level of the practice of testing. The coding of the intensity of the reaction to the Marquis test is based solely on the observation of physical reactions and performed by a single individual. It would seem to be necessary to check whether this coding would be the same if it were performed by one or more other testers. In effect, it must be possible for testing to be performed easily and reliably by any operator. It would thus be desirable to reproduce this study with several independent testers and to verify whether

the indications chosen for the coding (physical reactions, reaction speed) are indeed appropriate in order to validate this scale using a method of inter-rater reliability (Kappa coefficient).

Despite these reservations, this study clearly shows that testing is a simple and inexpensive tool which appears to be an essential aid for all harm reduction workers. permits the quick and reliable (sensitivity and specificity of 100%) verification of the presence and concentration of MDMA in ecstasy tablets. It is thus necessary to continue to test the properties of this tool in order to enhance its usefulness and to re-establish testing as part of the practice and policy of harm reduction in party environments.

Conflicts of interest : none declared

Keypoints : This article supplies first data in favour of the efficiency of the on-site testing to detect and quantify presence of MDMA in ecstasy tablets. It also defendes the point of view that on-site testing of ecstasy tablets is an inescapable tool in public health practice concerning risk reduction in substance use.

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Table 1: Initial coding of the intensity of the Marquis reaction

Coding	Intensity	Observation
0	No reaction	
1	Low intensity reaction	Slow appearance of scattered purple/blackish patches of total duration greater than 10 seconds
2	Intermediate/low intensity reaction	Slow appearance of scattered purple/blackish patches of total duration between 5 and 10 seconds
3	Intermediate/high intensity reaction	Semi-rapid of appearance of scattered purple/blackish patches which then agglomerate and of total duration between 2 and 5 seconds
4	High intensity reaction	Fast appearance of a generalized purple/blackish patch of duration about 1 second
5	Very high intensity reaction	Joint sudden appearance (for a fraction of a second) of generalized purple/blackish patch and a cloud of white smoke. Presence of intense effervescence

Table 2: Final coding of the intensity of the Marquis reaction

Initial Coding	**Final coding**	**Reaction**	**Observations**
0	**0**	None	No patch
1	**1**	Low	Scattered patches
2			Slow appearance
3	**2**	Intermediate	Scattered patches
			Semi-rapid appearance
4	**3**	High	Single patch
5			

Graph 1: Graphic representation of the dose-effect relation between MDMA concentration and intensity of the reaction to testing