Addictive Behaviors 78 (2018) 173–177

Contents lists available at ScienceDirect

Addictive Behaviors

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

# Parachuting psychoactive substances: Pharmacokinetic clues for harm reduction

Amélie Daveluy[a,b,*], Hélène Géniaux[a], Marie Baumevieille[a,b,c], Louis Létinier[b], Marie-Noëlle Matta[d], Aurélie Lazès-Charmetant[e], Françoise Haramburu[a,b], Pascale Guéroult[d]

[a] Centre d'addictovigilance, Service de pharmacologie médicale, CHU Bordeaux, F-33000 Bordeaux, France
[b] Univ. Bordeaux, Inserm, Bordeaux Population Health Research Center, Team, Pharmacoepidemiology, UMR 1219, F-33000 Bordeaux, France
[c] Laboratoire de droit et économie pharmaceutiques, Univ. Bordeaux, F-33000 Bordeaux, France
[d] Laboratoire de technologies pharmaceutiques industrielles (LTPIB), Univ. Bordeaux, F-33000 Bordeaux, France
[e] Comité d'étude et d'information sur la drogue et les addictions (CEID-Addictions), F-33000 Bordeaux, France

## HIGHLIGHTS

- Parachuting is a way to ingest psychoactive substances wrapped into cigarette paper.
- Parachute acts as sustained-release form when made with a cigarette paper wrapper.
- Parachute acts as immediate release form in the presence of alcohol.
- This is a message for harm reduction to avoid overdose.
- Users must avoid taking another parachute in the absence of an immediate-effect.

## ARTICLE INFO

*Keywords:*
Harm reduction
Dosage forms
Parachuting
Pharmacokinetics
Substance-related disorders

## ABSTRACT

*Background:* Parachuting, also called bombing, is a way to ingest psychoactive substances wrapped into cigarette paper, toilet paper, *etc.* There is little data describing parachuting in terms of substances use, context of use and, most importantly, the motivations for using such wrappers, although some authors hypothesized that parachute could be used for pharmacokinetic reason. However, inconsistently, some authors report that parachutes are used for sustained-release whereas others report that users are looking for an immediate effect.
*Research design and methods:* Considering parachute as a "home-made" dosage form, we have applied the dissolution testing to characterize the dissolution performance of a substance wrapped into a parachute and to characterize whether a parachute represents an immediate-release form or not.
*Results:* This *in-vitro* study provides the first pharmacokinetic data for drugs wrapped in parachutes. It shows that parachute acts as sustained-release form when made with a cigarette paper wrapper, but as immediate release form in the presence of alcohol or if wrapped with toilet paper.
*Conclusions:* An important message to harm reduction is that users must be aware that a parachute can have unexpected pharmacokinetics and have to avoid taking another parachute in the absence of an immediate-effect to avoid overdose.

## 1. Introduction

Parachuting, also called bombing or hammer is a way to ingest powdered or crystallized psychoactive substances wrapped into cigarette paper, toilet paper, *etc.* Used in the early 2000s almost exclusively for amphetamines (EROWID, 2012), parachuting has been more recently used for many other psychoactive substances, particularly 3,4-methylenedioxymethamphetamine (MDMA) and research chemicals (Boels et al., 2017; Daveluy et al., 2016; Winstock et al., 2011). In France, the changes in the psychoactive substances market, with many of them available as powder, leaded to expanding parachute use during the last 5 years; it is used both for psychoactive substances, illicit or not and for some psychotropic prescription medicines. This practice is recognized (Boels et al., 2017; Daveluy et al., 2016; Hendrickson, Horowitz, Norton, & Notenboom, 2006; Kenerson & Lear-Kaul, 2012), but there is little data describing parachuting in terms of substances

* Corresponding author at: ORCID: 0000-0003-1922-8630, Centre d'Addictovigilance, Service de Pharmacologie Médicale, Hôpital Pellegrin, CHU, F-33076 Bordeaux Cedex, France.
*E-mail address:* amelie.daveluy@u-bordeaux.fr (A. Daveluy).

https://doi.org/10.1016/j.addbeh.2017.11.021
Received 24 July 2017; Received in revised form 10 November 2017; Accepted 12 November 2017
Available online 16 November 2017

used (Boels et al., 2017; Daveluy et al., 2016), context of use and, most importantly, the motivations for using such wrappers, although some authors hypothesized that parachute could be used for pharmacokinetic reasons (Boels et al., 2017; Daveluy et al., 2016; Hendrickson et al., 2006; Kenerson & Lear-Kaul, 2012). However, inconsistently, some authors report that parachutes are used for sustained-release (Boels et al., 2017; Kenerson & Lear-Kaul, 2012) whereas others report that users are looking for an immediate effect (Daveluy et al., 2016). No pharmacokinetic study has been conducted until yet to test this hypothesis.

Dissolution testing is an *in vitro* test, used to establish drug release characteristics of solid dosage units, into a dissolution medium under standardized experimental conditions representing the gastrointestinal tract environment as closely as possible (European Directorate for the Quality of Medicines and Healthcare, 2015).

In the present study, we have applied the dissolution testing to characterize the dissolution performance of a substance wrapped into this "home-made" dosage form and therefore to characterize whether a parachute represents an immediate-release form or not, the influence of the particle size, alcohol intake and the nature of the wrapper on drug release. Acetylsalicylic acid (ASA) was chosen as the active substance of reference as this dissolution testing had been standardized for this substance before (European Directorate for the Quality of Medicines and Healthcare, 2015).

## 2. Methods

The active substance of reference (ASA) was chosen in pulverized (pASA) and crystallized (cASA) forms (COOPER; cooperation pharmaceutique française (Melun); batches no 11020051/A and 12090118/B) and put in capsules or in parachutes.

Parachutes users, who were recruited in addiction centres, were asked to make ready-to-use parachutes with cigarette paper and cASA, with no limitation in ASA quantity (users-parachutes). They were also asked to show how to make parachutes; for the rest of the study, parachutes were made within the laboratory, by the same person, with 150 mg of ASA using cigarette or toilet paper as wrapper (lab-parachutes).

The release tests were carried out using PharmaTest dissolution apparatus (apparatus II, European Pharmacopeia) at a rotation speed of 75 rpm and a temperature of 37 ± 0.5 °C. In order to simulate the gastric fluid, the experiment was carried out over 2 h in buffer pH 2 (NaCl 0.2 M, HCl 0.2 M).

Dissolution tests with capsules (size no.4), containing 150 mg of cASA and with lab-parachutes containing cASA were performed. These two tests were considered as references.

The influence of the particle size was measured by testing lab-parachutes of pASA and cASA. The influence of the wrapper was measured by testing lab-parachutes using 11 different brands of cigarette papers (cASA) measured and toilet papers (cASA). The influence of the parachute maker was measured by comparing lab-parachutes and users-parachutes. The influence of the effects of alcohol on the release of the active substance from lab-parachute was measured after addition of 40% ethanol in the dissolution medium. This limit represents a standard strength of spirits. It is recognized that, *in vivo*, the ingestion of spirits in such concentration will be subject to immediate dilution by the residual volume of the stomach (typically 50 mL in the fasting state) with further dilution over time due to gastric secretion, the intake of food and fluid and the absorption and metabolism of ethanol in the stomach (Walden, Nicholls, Smith, & Tucker, 2007). Thus, *in vitro* experiments with concentrations of 40% ethanol over a 2 h period are expected to be representative of the most extreme conditions likely to be encountered *in vivo* (Anand, Yu, Conner, & Davit, 2011; Food and Drug Administration (FDA), 2014).

In order to simulate the gastro-intestinal transit conditions, the drug release of parachutes with cASA was carried out for 2 h in buffer pH 2, then 3 h in buffer pH 7.

Every 15 min, 2 mL of the sample was withdrawn. Drug releases in different dissolution media were analyzed spectrophotometrically (Spectophotometer UVIKON XL Seconam), using UV detection at a wavelength of 278 nm (buffer pH 2) and 269 nm (buffer pH 7).

According to European Pharmacopeia, immediate-release form is considered when at least 80% of the active pharmaceutical ingredient is dissolved within 120 min (European Directorate for the Quality of Medicines and Healthcare, 2015).

### 2.1. Statistical analysis

Main analysis was to compare *in vitro* release profile between lab parachutes and other parachutes forms or capsules at time = 15 min and 120 min. The non-parametric Mann Whitney Wilcoxon test was used.

Furthermore, in order to compare the different brands of cigarette, the Kruskal-Wallis test was used (time = 120).

## 3. Results

Twelve parachutes were made by 9 parachutes users (Fig. 1). There was a great variability among conception of parachutes by users in term of sizes, shapes, quantity of substance: two users remove the "queue" of the parachute before ingestion (no. 1 & no.7) whereas others swallow the entire parachute. The no. 9 was bigger than the other parachutes and made with two sheets of cigarette paper.

As psychoactive substances put in parachute can be of different granular forms (powder, crystal, *etc.*) (Daveluy et al., 2016), the *in vitro* release profile of ASA in pulverized and crystallized forms was determined; At T = 15 and at T = 120, there was no statistical difference between the two granular forms (Table 1). After 2 h, pASA release from parachutes was approximately 35.1% *vs.* 26.0% of cASA, indicating that whatever the granular form of the substance was, parachute does not act as an immediate-release form.

To assess if lab-parachutes can be used as parachutes of reference, the cASA release profiles from lab-parachutes and users-parachutes in pH 2 buffer were measured. At T = 15 and at T = 120, there was no difference between the two forms of parachutes (Table 1).

The cASA release profiles from these lab-parachutes and from capsules in pH 2 buffer were measured. At T = 15 and at T = 120, there was no difference between the two forms of parachutes (Table 1). After 2 h, cASA release from lab-parachutes was 26.0% *vs.* 90.5% from capsules (Fig. 2), classifying capsules as an immediate-release form contrary to lab-parachutes.

To see if the wrapper could modify the results, the same experiment was conducted with cigarette paper and toilet paper wrappers. At T = 15 and at T = 120, there was a difference between cigarette paper and toilet paper (Table 1). < 45% of cASA was dissolved after 2 h with cigarette paper wrappers, whereas 100% were dissolved at this time with toilet paper wrapper, indicating that parachutes made with toilet-paper wrapper acted as an immediate-release form. There was no difference between the eleven brands of cigarette papers (p-value: 0.87).

The influence of alcohol on parachutes with cigarette paper wrapper was studied. At T = 120, there was a difference in the dissolution of lab-parachutes with and without ethanol (Table 1, Fig. 3), At T = 15 there was no significant statistical difference (p = 0.053). After 2 h in a dissolution medium with ethanol, 100% of ASA was released *versus* < 30% in the absence of ethanol. In presence of alcohol, parachute with cigarette paper wrapper acts as an immediate-release form (Fig. 3).

The results are summarized in Table 2.

Finally, to evaluate the complete dissolution time of the parachute, cASA release profile from lab-parachutes in media simulating the gastrointestinal transit conditions (2 h in buffer pH 2 then 3 h in alkaline buffer pH 7, obtained by adding to buffer pH 2: tris-(hydroxymethyl)-amino-methane, citric acid anhydrous and sodium acetate anhydrous) was conducted (Fig. 4). In these conditions, nearly all the cASA contained in the parachutes was dissolved after 5 h.