

LC-MS Investigation of RSDL® (Reactive Skin Decontamination Lotion Kit) Reactivity with the Synthetic Opioid Fentanyl

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Abstract

Fentanyl, classified as an incapacitating agent, is a potent synthetic opioid, with an estimated human lethal dose of 2 mg.¹⁻² Fentanyl is frequently manufactured in clandestine labs and illicitly sold by traffickers after it is mixed with narcotics such as heroin and cocaine.

A study was designed to investigate the surface decontamination of RSDL® (Reactive Skin Decontamination Lotion Kit) against fentanyl. An *in vitro* analytical method and validation procedure using liquid chromatography-mass spectrometry (LC-MS) with fentanyl interaction with RSD was developed. Using this LC-MS methodology, surface studies were conducted based on NATO standards using painted surface panels. In this investigation conducted in triplicate, the efficacy of RSDL in the surface decontamination of fentanyl was 99.86%. Subsequent investigation on the degradation kinetics of fentanyl will be performed in the near future.

Introduction

Fentanyl, chemically classified as a phenylpiperidine derivative, is a rapid-acting, synthetic opioid analgesic; fentanyl is estimated to be 80 times as potent as morphine and hundreds of times more potent than heroin.¹ Fentanyl can be absorbed into the body via inhalation, oral exposure or ingestion, or skin contact. The toxicology of fentanyl via inhalation or dermal absorption is highly debated and unclear; the specific dermal risk has not been well studied with "powders."

Fentanyl has become increasingly detected within illicit street drugs and often without the user's knowledge of its presence.² Fentanyl overdose may be fatal due to respiratory depression and the subsequent hypoxia that ensues.³ The respiratory depressant effects may be reversible systemically with the use of naloxone. However, if the exposure dose is large, the typical dose of naloxone utilized for typical opioid overdoses may be insufficient to reverse the respiratory depressant effects. The estimated lethal dose of fentanyl in humans is small and equivalent in size to two grains of salt.³

Fentanyl and First Responders

Fentanyl and its analogs, such as carfentanil and sufentanil, pose a potential hazard to first responders who could unknowingly come into contact with these drugs.^{4,5} The US Drug Enforcement Administration (DEA) recommends that police officers do not field test drugs if fentanyl is suspected.⁴ To minimize the exposure risk, first responders should wear personal protective equipment while handling and processing chemicals that may contain fentanyl.

The United Nations Office on Drugs and Crime noted that for first responders, "overdose may also result from handling strong synthetic opioids without precautions that prevent the substance from being inhaled or absorbed through the skin or mucous membranes. Contact with fentanyl and its analogues is so hazardous that both Canada and the US recorded incidents of hospitalization of law enforcement officers that carried out seizures due to physical exposure to such chemicals."⁶

Evaluation of RSDL Decontamination

The RSDL Kit, is intended to remove or neutralize chemical warfare agents and T-2 toxin from the skin.^{*}

Figure 1. Image of RSDL Kit



The kit is made of up a lotion impregnated sponge.

Neutralization

The RSDL lotion contains KBDO (reactive potassium oximate salt), the molecule responsible for the neutralization of the chemical warfare agents and T-2 toxin from the skin.

Physical Removal

The sponge is responsible for the carrier, delivery, and spreading mechanism for RSDL lotion in an open cell foam architecture with high surface area.

It is postulated that decontamination of fentanyl could occur based on the following two mechanisms of action (Figure 2):

1. Removal: rapid decontamination facilitated by solubilization of fentanyl via the RSDL solvent and removal by the sponge
2. Neutralization: nucleophilic reaction via potassium 2,3-butanedione monoximate (KBDO) interaction with the amide group of fentanyl

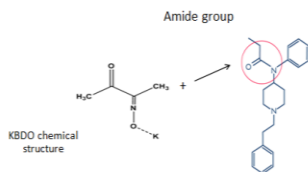
The study design for the evaluation of the RSDL Kit is being performed in the following three stages:

Stage 1: Analytical method development and validation

Stage 2: Decontamination from a surface material

Stage 3: Determination of degradation kinetics (not yet performed)

Figure 2. RSDL Postulated Mechanism of Action in Surface Decontamination of Fentanyl



Methods and Materials

Overview

- Matrix effects were studied and extraction solvent and mass spectrometry parameters were optimized to minimize interference.
- Calibration standards of derivatized fentanyl were prepared. Limit of detection and lower limit of quantification were derived.
- Recovery and accuracy were evaluated by application of a fixed amount of derivatized fentanyl citrate on chemical agent resistant (CARC) panels.

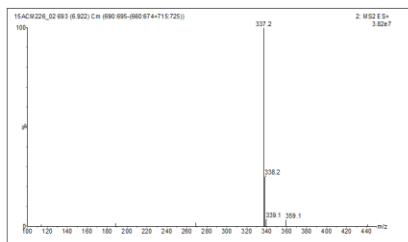
Materials and Standards

- Fentanyl citrate (Spruyt-Hillen BV, The Netherlands)
- Internal Standard: Chlorpromazine (Sigma Aldrich, The Netherlands)
- Acetonitrile (LC-MS grade, Sigma Aldrich, The Netherlands)
- Methanol (LC grade, Sigma Aldrich, The Netherlands)
- Formic acid (Fluka, The Netherlands)
- Milli-Q water (Milli-Q-system, Millipore, The Netherlands)

LC-MS Validation Procedure

- LC-pump: Acquity M-class
- Flow: 100 µl/min
- Injection volume: 1 µl (partial loop injection)

Figure 3. Full Scan MS of Fentanyl, Range 100-450 m/z, Time 0.5 s, Cone voltage 5V.



The mass spectrometer was operated in multi-reaction monitoring mode (MRM). Two transitions for fentanyl and one transition per internal standard (chlorpromazine) were monitored.

Table 1. MRM Dwell Times

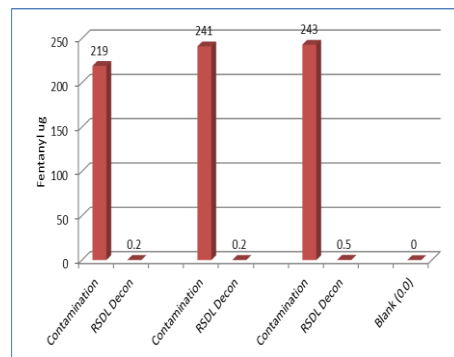
Compound	Precursor Ion MH ⁺	Transition 1	Transition 2	CE(V)	Cone (V)	Dwell Time(s)
Fentanyl citrate	337	188	105	30	40	0.2
Chlorpromazine	319	86	--	15	40	0.2

Surface Panel Study Method

- CARC painted panels (5x5 cm) were used and pre-conditioned according to standard protocols (STANAG 4360).
- Panels contaminated with fentanyl citrate by the application of evenly distributed drops to reach a total contamination level of 250 µg per panel.
- After 2 minutes, the contaminated panels were treated with RSDL for a 2-minute contact time for three replicates.
- Positive controls were panels that were contaminated but not treated by RSDL, and the negative control was a panel treated with RSDL only.

Surface Panel Study Results

Figure 4. RSDL Decontamination with Fentanyl citrate, 250 µg, applied on each CARC panel



Remaining fentanyl: 0.14%

Decontamination: 99.86%

Summary and Conclusions

- A significant number of deaths have been reported in the EU, Canada and the US following the exposure to illicitly synthesized fentanyl produced in clandestine labs.²
- The lethal dose of fentanyl in humans is exceedingly small (~2 mg in adults has been cited).
- First responders are at potential risk of inhalation and dermal exposure to fentanyl in these abused substances, many unknowingly contaminated by fentanyl.
- RSDL® (Reactive Skin Decontamination Lotion Kit) has been proven as an effective countermeasure to promptly remove or neutralize chemical warfare agents from the skin.
- Due to the chemical composition of fentanyl as a lipophilic phenylpiperidine moiety, it was hypothesized that RSDL may provide effective decontamination (i.e., removal and chemically neutralization) of fentanyl following dermal exposure by first responders.
- To test the hypothesis, an *in vitro* study was conducted to assess the efficacy of RSDL in the surface decontamination of fentanyl.
 - Analysis of fentanyl was conducted using LC-MS methodology.
 - Surface decontamination using RSDL was performed based on the NATO STANAG 4360 using fentanyl concentrations of 250 µg per CARC panel.
 - In this *in vitro* trial, the efficacy of RSDL (following 2-minute contact time) in surface decontamination of fentanyl was 99.86%. Clinical relevance unknown.**
- Degradation kinetics of fentanyl by RSDL will be assessed in the next phase of the trial.

*** RSDL is not cleared for use as skin decontamination of fentanyl.**

References

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