HHS Public Access

Author manuscript

J Occup Environ Hyg. Author manuscript; available in PMC 2023 March 15.

Published in final edited form as:

J Occup Environ Hyg. 2020 September ; 17(9): 398–407. doi:10.1080/15459624.2020.1784426.

Fentanyl and carfentanil permeation through commercial disposable gloves

Lee Ann Greenawald[a], **Kent C. Hofacre**[b], **Edward M. Fisher**[a]

[a]National Institute for Occupational Safety and Health (NIOSH), National Personal Protective Technology Laboratory (NPPTL), Pittsburgh, Pennsylvania;

[b]CBRNE Defense, Battelle Memorial Institute, Columbus, Ohio

Abstract

In 2018, the Centers for Disease Control and Prevention reported that opioid overdose deaths (including fentanyl and carfentanil) comprised 46,802 (69%) of the 67,367 total drug overdose deaths. The opioid overdose epidemic affects Americans not only at home but also in the workplace. First responders may be at risk of opioid exposure during incidents such as vehicle searches and responses to overdose calls. To reduce direct exposure to opioids and other hazardous drugs, first responders rely in part on personal protective equipment (PPE) as their last line of defense. First responders seek guidance from the National Institute for Occupational Safety and Health (NIOSH) regarding appropriate PPE selection for potential opioid exposure. There is limited empirical glove performance data for illicit drugs. Empirical data are needed to validate NIOSH's current recommendations regarding gloves to help prevent exposure to illicit drugs (i.e., powder-free nitrile gloves with a minimum thickness of 5 ± 2 mil [0.127 ± 0.051 millimeters]); however, no industry standard or test method currently exists for specifically evaluating PPE performance against fentanyl and its analogs. To understand the permeation qualities of gloves when challenged against fentanyl and carfentanil solutions, the ASTM International (formerly American Society for Testing and Materials) ASTM D6978–19 standard for chemotherapy drug glove permeation was adapted to test fentanyl and carfentanil hydrochloride solution permeation through twelve disposable glove models, including five models in which the manufacturers claim fentanyl protection. No nitrile glove models showed fentanyl or carfentanil permeation rates above the chemotherapy drug threshold criterion of 0.01 μg/cm^2/min (i.e., thereby meeting the performance requirement) as calculated using the ASTM D6978–19 standard within the 240-min test. Latex and vinyl glove materials exhibited fentanyl and carfentanil permeation with permeation rates above this threshold. These findings are among the first empirical data to support NIOSH's current opioid glove recommendations and define procedures that could be used to support industry standards for evaluating opioid permeation through air-impermeable PPE materials.

✉**CONTACT** Lee A. Greenawald lgreenawald@cdc.gov National Institute for Occupational Safety and Health (NIOSH), National Personal Protective Technology Laboratory (NPPTL), 626 Cochrans Mill Road, Pittsburgh, PA 15236.

Keywords

PPE; permeation rate; opioids; test method

Background

Fentanyl—a synthetic opioid pain reliever—is 50–100 times more potent than morphine and 30–50 times more potent than heroin, whereas carfentanil is 100 times more potent than fentanyl (Suzuki and El-Haddad 2017). Heroin and cocaine have been reported to be laced with fentanyl for the purpose of "speedballing," which is combining a stimulant such as cocaine with a depressant such as fentanyl (Park et al. 2018; Department of Justice 2018a). Additionally, illicit fentanyl can also be found in the liquid form, such as in eye droppers or nasal sprays (Department of Justice 2018a; 2018b; Lexipol 2018). In 2018, the Centers for Disease Control and Prevention (CDC) reported that approximately 69% of the more than 67,367 drug overdose deaths in the U.S. involved an opioid (Centers for Disease Control and Prevention 2018; Hedegaard et al. 2020; Wilson et al. 2020; NIOSH 2015). An increase in opioid-related production, distribution, and arrests have increased the potential risk of first responders' exposure to these substances (RAND Corporation 2019). Consequently, first responders may be at an increased risk for coming into contact with opioids from both overdose cases and during tasks involving interventions at sites involved in the illicit manufacture or distribution of opioid-based drugs (Howard and Hornsby-Myers 2018). Permeation rates of opioids through skin are generally low and require extended exposure periods. It has been reported that it is unlikely that small, unintentional skin exposures to tablets or powdered fentanyl would cause significant opioid toxicity (Moss et al. 2018). However, variables in exposure conditions like the presence of solvents, such as alcohol, may contribute to some dermal permeation to first responders (Moss et al. 2018).

The National Institute for Occupational Safety and Health (NIOSH) has received numerous requests from first responders for advice about proper selection and use of PPE, including glove selection when exposed to opioid in powder or liquid form. Approximately 25% of the fentanyl-related public inquiries responded to by NIOSH's National Personal Protective Technology Laboratory (NPPTL) from 08/2016 to 12/2019 were related to glove selection. Unfortunately, there is limited empirical PPE performance data about the permeation of fentanyl or carfentanil solutions through gloves. In 2017, NIOSH developed opioid PPE recommendations for first responders, which include recommendations on respiratory and dermal protection (NIOSH 2020). Currently, the NIOSH glove recommendations for minimal and moderate anticipated illicit drug exposure are to wear nitrile gloves that are powder-free with a minimum thickness of 5 ± 2 mil (i.e., 0.127 ± 0.051 millimeters [mm]), unless manufacturer data provides performance breakthrough data for thinner gloves or gloves of a different material (NIOSH 2020). Some glove manufacturers have recently marketed their gloves claiming fentanyl protection (Ansell 2020); however, no industry-accepted standard test method exists for specifically evaluating PPE performance against fentanyl and its analogs.

The purpose of this study is to provide empirical data for the protective performance of selected commercial glove materials with varying thicknesses against permeation of liquid fentanyl and carfentanil solutions. To better understand the permeation of synthetic opioids through the selected gloves types, we sought to evaluate the effectiveness of adapting the American Society for Testing and Materials (ASTM) D6978–19, “Standard Practice for Assessment of Resistance of Medical Gloves to Permeation by Chemotherapy Drugs” for use with liquid synthetic opioids (ASTM International 2019).

Materials and methods

Permeation test method and sample collection

ASTM D6978–19 was adapted for use with fentanyl and carfentanil solutions. This ASTM standard in turn references ASTM F739–12 “Standard Practice for Resistance of Protective Clothing Materials to Permeation by Liquids or Gases Under Conditions of Continuous Contact,” where the chemotherapy drugs were replaced with fentanyl and carfentanil solutions (ASTM International 2012). Minor modifications to the commercial permeation test cell (Pesce Lab Sales, Kennett Square PA; Figure 1), as-received included: (1) replacing the 2-mm-thick paper support of the Teflon gasket with a comparably-sized Teflon support to eliminate any absorption of fentanyl solution and allow the support to be readily decontaminated; (2) Viton O-rings were added to the recess of the permeation cell reservoirs to ensure contact and a sufficient seal to the Teflon gasket since no O-rings were provided with the commercial product; and (3) a rubber O-ring replaced the supplied foam soft inserts between the metal flange and glass reservoir to ensure contact when the flanges were bolted together.

A closed permeation test cell, consisting of a 1-inch diameter glass cell, as referenced in ASTM F739–12 was used. The entire permeation cell system–comprising nine permeation cells–was secured in a vertical orientation on a shaker platform table to continuously agitate the fentanyl or carfentanil challenge solution in contact with the test material, which was placed in a fume hood. Eighteen milliliters of deionized water was added to each permeation cell to check test cell leakage. A sample of this collection reservoir water was designated as t_0=0 min to obtain a permeation cell background sample before the addition of the challenge solution to determine if any carryover existed from a previous test. Eighteen milliliters of challenge solution was added to the challenge reservoir of each permeation cell; this volume filled the reservoirs and was in contact with the glove specimen. The nine test cells were filled with this 18 mL challenge solution within 5 min such that the startup time was less than 2% of the overall test duration of 4 hours (hr) (i.e., 240 minutes [min]). A t = 0 for each test cell represented the completion of filling each cell with the fentanyl solution. A 0.1 mL aliquot was sampled for analysis every 30 min for up to 240 min in accordance with ASTM F739–12, totaling 8 aliquots sampled from each permeation cell. This equates to a total volume of solution removed of approximately 0.9 mL, representing about 5% of the total collection side volume. Collection samples were either analyzed within 12 hr or stored in the refrigerator and analyzed within 24 hr. Glove specimens were viewed and photographed upon completion of each test.

Each permeation cell was cleaned after each test using a series of water and methanol rinses. Challenge and collection components were kept separate to reduce cross-contamination.

Test parameters and conditions

Fentanyl hydrochloride (HCl) and carfentanil HCl salt were diluted separately in 19 mΩ Mili-Q deionized water (Millipore Sigma) to a concentration of 1 mg/mL; this concentration was a similar range of chemotherapy drugs concentrations tested in this standard. The fentanyl HCl and carfentanil HCl salt forms and concentrations used were based on discussions with personnel knowledgeable of first responders' potential exposures during opioid incidents. Fentanyl and carfentanil solutions were synthesized by Battelle with a purity of 94% determined by nuclear magnetic resonance analysis. Solutions were prepared and utilized the morning of each test or were stored in a refrigerator at a maximum temperature of 7°Celsius (°C) until utilized. In accordance with ASTM D6978–19, the tests were conducted at 35 ± 2 °C for a duration of 4 hr. In accordance with ASTM D3767–19 (used for thickness measurements) and ASTM F739–12, samples were pre-conditioned at 23 ± 3 °C, 50 ± 5% relative humidity (%RH) for at least 24 hr prior to testing. In accordance with ASTM D6978–19, the system was temperature controlled to 35 ± 2 °C (Innova Model 4000, New Brunswick Scientific). Test specimens and solutions were placed in the temperature-controlled environment prior to testing to equilibrate to the ambient environment.

Glove models and test specimen preparation

Twelve commercial glove models were selected for permeation testing and were purchased directly from the manufacturer or through a distributor. Market research was conducted to select a variety of glove models, differing in material composition, thickness, fentanyl manufacturer protection claims, and those that claimed accordance to standards (e.g., chemotherapy-rated). A summary of the glove models and their properties used for testing are shown in Table 1. Among these were five models with manufacturer claims for fentanyl protection where two manufacturer claimed resistance to fentanyl permeation in accordance with ASTM D6978–19. Five glove models claimed chemotherapy drug protection. Three product manufacturing lots were tested for each glove model, except for Glove Model 7 (G7), where only two different manufacturer lots were available, thus G7 Lot 1 was sampled twice and herein referred to as G7 L1B. Lots were randomized before glove sampling. For fentanyl permeation testing, 12 glove models and three manufacturing lots per model were tested. Three replicates were tested for each glove manufacturing lot for a total of 108 glove replicates (12 models × 3 lots × 3 replicates = 108 replicates per model). For carfentanil permeation, six of the 12 glove models were tested to determine if there was a difference in permeation between fentanyl and carfentanil. Three replicates were tested for each manufacturing lot, for a total of 54 glove replicates (6 models × 3 lots × 3 replicates = 54 replicates per model). All lots with available manufacturer dates (n = 29) were manufactured within the past four years (since 02/2016). All lots that listed an expiration date (n = 9) were within the shelf life.

Test specimens were cut from the glove palm in 5.1 centimeter (cm) diameter sizes, resulting in an area of 20.4 cm^2; the exposed area of each replicate in the 1-inch permeation cell was

5.1 cm^2. In accordance with ASTM 739–12, specimen thickness was measured at the palm for each glove tested (n = 3 replicates per glove where four gloves were tested per lot). An Ames Comparator Model BG2600–1-04 was used to measure each specimen to the nearest ± 20 microns (μm).

Analytical method

Fentanyl and carfentanil challenge and collection solutions were analyzed using an internal Battelle liquid chromatograph mass spectrometer-mass spectrometer (LC/MS/MS) method. Specifically, a Waters Acquity Ultra Performance Liquid Chromatograph (UPLC) with a Waters Xevo TQ-XS mass spectrometer and Phenomenex Prodigy ODS-3, 3 μm, 100 A, 100 × 2 mm column operating at 40 °C was used for analysis. Calibration curves covering 1 – 1,000 ng/mL were established. A concentration change of 100 ng/mL in the collection reservoir between consecutive 30 min sample aliquots corresponds to a breakthrough permeation rate of 0.01 μg/cm^2/min—the calibration curve covered a range of concentrations one log higher and two logs lower than that associated with this permeation rate. The permeation rate is the rate at which the chemical passes through the glove material at the molecular level; the higher the result, the more chemical passing through (Grainger 2019). Breakthrough is defined as the elapsed time between initial contact of the chemical on one side of the glove material and the analytical detection of the chemical on the other side of the glove material. If breakthrough does not occur, permeation is not measured and reported as the lowest calibration standard (Grainger 2019). Any LC/MS/MS response below the lowest calibration standard were reported as “<1 ng/mL”. Approximately every tenth LC/MS/MS sample was a calibration standard (either 10 or 100 ng/mL) throughout the analysis of the unknown samples. Batches of up to 100 samples were analyzed in one analytical run.

Permeation rate calculation

The permeation rate ($\bar{P}$) was calculated in accordance with ASTM F739–12, Section 12.4.1 (Equation 1) and reported for each sample analyzed if there was a consistent increase in fentanyl concentration in the collection reservoir. To meet the ASTM D6978 and F739–12 minimum performance requirements, a glove specimen must not have a permeation rate above 0.01 μg/cm^2/min within the 240 min test. The breakthrough detection time—the time measured from the start of the test to the sampling time that immediately precedes the sampling time at which the permeation rate reached 0.01 μg/cm^2/min—was determined as specified in ASTM D6978–19, Section 3.1.2 and reported for each replicate. The average (avg.) and standard deviation (SD) breakthrough detection times for each glove replicates were calculated. The minimum permeation rate calculated and reported was 0.001 μg/cm^2/min, corresponding to the minimum of the calibration range (i.e., 10 ng/mL) or a difference in concentration of 10 ng/mL between consecutive 30 min samples. When the measured fentanyl or carfentanil concentration in the collection water increased by <10 ng/mL in 30-min sample increments, the permeation rate was reported as <0.001 μg/cm^2/min. Similarly, the maximum permeation rate reported was 0.1 μg/cm^2/min, corresponding to the maximum of the calibration range of 1000 ng/mL. The permeation rate as a function of time was plotted per ASTM F739–12, Section 12.5: Equation 1.

Permeation Rate Calculation

$$\bar{P} = \frac{(C_i - C_{i-1}) \times V}{(t_i - t_{i-1}) \times A}.$$

where

$\bar{P}$ = permeation rate (μg/cm^2/min)

C_i (μg/mL) = collection cell fentanyl or carfentanil concentration for the ith sample

C_{i-1} (μg/mL) = collection cell fentanyl or carfentanil concentration for the i − 1 sample

t (min) = time of collection of ith

i the sample

t_{i-1} (min) = time of collection of the i − 1 sample

A (cm^2) = Area of glove material exposed to challenge solution

V (mL) = Volume of collecting solvent (i.e., deionized water)

Results

The average glove thicknesses for each glove model are shown in Figure 2, in which 4 gloves were measured per manufacturing lot for a total of 12 glove replicates per model. The thickest glove palm (latex, G2) was 17. ± 0.5 mil (i.e., 0.43 mm ± 0.01), and the thinnest glove palm (nitrile, G9) was 2.5 ± 0.1 mil (0.06 mm ± 0.00). The average nitrile glove palm thickness was 4.3 ± 1.4 mil (0.11 mm ± 0.04).

Fentanyl permeation

Permeation rates for each glove replicate were calculated in accordance with Equation 1; the maximum permeation rates and breakthrough detection times are shown in Table 2. The breakthrough detection time was based on a permeation rate threshold of 0.01 μg/cm^2/min, which is consistent with and as calculated in accordance with ASTM D6978–19. The gray colors in the table indicate those replicates or lots that showed permeation rates above the permeation rate threshold. Additionally, where a manufacturer claims their product provides fentanyl protection, the table includes whether the data collected supported the manufacturer's claim; N/A refers to those products where no fentanyl protection claim was made.

No nitrile glove models (G4–G12) showed measurable fentanyl permeation above 0.001 μg/cm^2/min within the 240 min testing time, including the thinnest glove model included in this study (G9; 2.5 ± 0.1 mil). All glove models that claimed fentanyl protection were nitrile, thus all glove models with manufacturer claims for protection against fentanyl met their claims based on the study criteria.

Fentanyl permeation rates that exceeded the study defined permeation rate threshold of 0.01 μg/cm^2/min were observed for non-nitrile glove models when tested against fentanyl: all three G1 lots (thinner latex) exceeded this threshold, one of three G2 lots (thicker latex)

exceeded this threshold, and all three G3 lots (vinyl) exceeded this threshold. All three G1 and G13 lots had at least one replicate with a fentanyl collection reservoir concentration exceeding 1,000 ng/mL. Figure 3 shows the aggregated permeation rates of nine G1 gloves, in which the average breakthrough detection time was 80 min. Permeation rate is plotted as a function of the elapsed time from the beginning of the chemical contact to the mid-point of a sampling interval, which is consistent with ASTM 739. All nine G3 replicates had a fentanyl permeation rate >0.01 μg/cm^2/min before the end of the 240 min test in which Lot 1 exceeded this threshold within 30 min, while the average breakthrough detection time for G3 aggregated for all three lots was 30 min. (Figure 4). A negative relationship of maximum fentanyl permeation concentration as a function of glove thickness was observed for the vinyl glove model (G11, r = −0.48, p = 0.043).

All nine G2 (thick latex) replicates showed fentanyl permeation (i.e., had a maximum permeation rate >0.001 μg/cm^2/min), in which all 3 replicates for G2 Lot 2 exceeded the 0.01 μg/cm^2/min threshold. Averaging the maximum fentanyl permeation rates for G2 Lots 1–3 allowed the overall G2 model to narrowly fall below the 0.01 μg/cm^2/min threshold, with a maximum collection reservoir concentration of 270 ± 73 ng/mL at 240 min (Figure 5(a), showing concentration as a function of the sampling times) and an average maximum permeation rate of 0.0088 μg/cm^2/min (Figure 5(b)). G2 (thicker latex) showed an average fentanyl permeation concentration 10x less than G1 (thinner latex) at 240 min (130 ng/mL compared to 1300 ng/mL); the average G1 maximum permeation rate across the three lots was 0.039 μg/cm^2/min (overall exceeding the threshold for the model), while the average G2 maximum permeation rate across the three lots was 0.0088 μg/cm^2/min (overall not exceeding the threshold for the model). A negative relationship between maximum fentanyl permeation as a function of glove thickness was observed for the aggregated G1 and G2 latex glove models (r = −0.87, p < 0.001), i.e., less fentanyl permeation was observed as the thickness increased. G2 (thicker latex model) showed statistically significant inter-lot variability (F = 14.2, p = 0.005): G2 Lot 2 exceeded the threshold when challenged with fentanyl while the other two lots did not; no G2 lots exceeded the threshold when challenged with carfentanil. The average thickness for G2 Lot 2 was 17 ± 0.2 (n = 4) with the lowest SD of all three lots. No other glove models showed significant inter-lot variability.

Carfentanil permeation

Permeation rates for each glove replicate were calculated in accordance with Equation 1; the maximum carfentanil permeation rates and breakthrough detection times (as defined in ASTM D6978) are shown in Table 3. The gray colors in the table indicate those replicates or lots that showed permeation rates above the permeation rate threshold. The maximum permeation rate for G2 Replicate 2 was not calculated due to apparent contamination of the test cell.

No nitrile glove replicates for G4, G5, G56, G10, and G11 had a permeation rate exceeding 0.001 μg/cm^2/min. All 9 G3 replicates had a maximum permeation rate exceeding 0.01 μg/cm^2/min. The aggregated average collection reservoir concentration data across all three G3 lots is shown in Figure 6(a). The average permeation rate across the three G11 lots

is shown in Figure 6(b), which shows an average permeation rate exceeding the 0.01 μg/cm^2/min threshold at the sampling point between 135 and 165 min.

Four of the 9 G2 (thick latex) replicates had a permeation rate ≥0.001 μg/cm^2/min; however, overall the average G2 maximum permeation rate did not exceed the 0.01 μg/cm^2/min threshold. The three G2 lots showed an average carfentanil concentration of 10.7 ± 7.7 ng/mL by the end of the 240-min test (n = 9), with trends indicating the onset of permeation.

Using an analysis of variance (ANOVA), there was no difference ($\alpha = 0.05$) when comparing the maximum fentanyl and carfentanil permeation concentrations between the nitrile glove models ($F = 0.36$, $p = 0.55$), in which the mean maximum permeation concentrations for carfentanil and fentanyl were 1.4 ng/mL and 2.5 ng/mL, respectively. Compound-specific effects were observed: for both G2 (latex) and G3 (vinyl), higher permeation rates and higher maximum concentrations were observed for fentanyl compared to carfentanil. Using an ANOVA, there was a difference ($p < 0.05$) for G2 when tested against fentanyl or carfentanil, in which the mean maximum permeation concentrations for carfentanil and fentanyl were 16 ng/mL and 130 ng/mL, respectively. Fentanyl was also observed to permeate quicker than carfentanil for G3. The aggregated average G3 fentanyl permeation rate data across the three lots showed failure beginning at approximately 30 min, while that for carfentanil showed failure beginning at approximately 145 min. An average maximum fentanyl permeation rate was 0.043 μg/cm^2/min, while carfentanil showed an average maximum permeation rate of 0.029 μg/cm^2/min. There was a statistically significant difference ($p < 0.05$) for G3 when comparing the effect of testing fentanyl or carfentanil.

In summary, Figure 7 shows a comparison of the average maximum fentanyl and carfentanil permeation rates across all three lots for fentanyl permeation testing (G1–G12) and carfentanil permeation testing (G2, G3, G4, G5, G10, and G11). The red dashed line represents the study-defined permeation rate threshold of 0.01 μg/cm^2/min. The asterisks show the models where all three lots within a given model failed.

Discussion

Adaptation of ASTM D6978–19 for synthetic opioids

While first responders may be more likely to be exposed to powdered opioids and thus an inhalation hazard, opioids may also be encountered in a liquid matrix, such as when illicitly used in nasal sprays and eye droppers (Lexipol 2018; Department of Justice 2018b). The fentanyl and carfentanil solution concentrations used in this study (1,000 μg/mL) were within the recommended concentration ranges in ASTM D6978–19 for chemotherapy drugs. For medical gloves cleared by the Food and Drug Administration for fentanyl protection, a concentration of 50 μg/mL fentanyl citrate has been reported by manufacturer-submitted test data using ASTM D6978–19, which may simulate concentrations used for patient fentanyl pain management. The concentrations used in this study were 20 times higher. The scope of this research and adaptation of the test method is to simulate potential first responder exposure to fentanyl and carfentanil. This adapted method for use with liquid synthetic opioids was able to discern permeation performance differences between material types and thicknesses and the results were aligned with generalizations of glove performance. For

example, nitrile gloves and thicker gloves have greater chemical resistance and vinyl gloves, generally, have poorer performance compared to most other disposable glove materials (Wallemacq et al. 2006; Oriyama et al. 2017).

Summary of findings

The observed permeation trends for both material and thickness are consistent with glove permeation of chemotherapy drugs for nitrile, latex, and vinyl gloves (Wallemacq et al. 2006; Oriyama et al. 2017). Nitrile gloves provided the best protection for fentanyl and carfentanil under the described test conditions. It is important to note that thicknesses vary across the glove (e.g., the fingertips are generally thicker than the palm), and manufacturers typically report the fingertip and/or the palm thickness. Glove palms were tested to provide "worst-case scenario" compared to the thicker fingertips.

The difference in permeation rates between fentanyl and carfentanil for some glove models may be due to the differences in molecular size and lipophilicity between the two compounds. Fentanyl has a lower molecular weight of 336.5 grams per mol (g/mol), while carfentanil has a molecular weight of 394.5 g/ mol; carfentanil contains a carbomethoxy group, which increases its lipophilicity (National Center for Biotechnology Information 2020a, 2020b).

The test results are limited to fentanyl HCl and carfentanil HCl in deionized water and cannot be extrapolated to other fentanyl analogs, salts, or solutions. Further, this testing does not account for the possible effects of decontamination solutions that may be used in conjunction with first responder tasks involving opioid exposures. Unlike the chemotherapy drugs required in ASTM D6978–19, the concentration of synthetic opioids encountered in the field by first responders is currently unknown and may be highly variable in part due to varying levels of purity and concentrations in mixtures (Department of Justice 2018b) making it difficult to choose a challenge concentration during the glove testing. Moreover, synthetic opioids such as fentanyl and carfentanil are often found in mixtures with other drugs that are used illicitly (e.g., cocaine, heroin) (Drug Enforcement Administration 2018; Department of Justice 2018b) which may affect glove permeation and should be explored. The effect of glove field storage conditions should be evaluated to assess the effect of storage temperature and storage time on fentanyl/carfentanil permeation performance. Additional assessments should be undertaken to evaluate the impact of representative field conditions—e.g., additional fentanyl and carfentanil challenge concentrations, and the application of decontamination solutions on contaminated gloves.

Based on our results, we propose that a new ASTM test method could be established to evaluate glove and other types of PPE permeation resistance to synthetic opioids as a standard test method to provide consistency across the industry. Because carfentanil is more potent than fentanyl, consideration should be given to assigning separate breakthrough detection threshold criteria. This can provide a basis for manufacturers to validate product claims and allow first responders and other end users to have consistent information in proper selection of PPE.

Conclusion

A test method following ASTM D6978–19 “Standard Practice for Assessment of Resistance of Medical Gloves to Permeation by Chemotherapy Drugs” was successfully adapted to measure the permeation of fentanyl and carfentanil against 12 commercially available glove models, including those models where the manufacturer claims fentanyl protection.

Nitrile gloves provided the best fentanyl and carfentanil protection under the described test conditions, which supports NIOSH’s first responder glove recommendations for protection against illicit drugs, including fentanyl and its analogs (NIOSH 2020). Although nitrile gloves showed effective protection against fentanyl and carfentanil, it is still recommended for end users to acquire available manufacturer’s test data when fentanyl claims are made. Vinyl and latex gloves exhibited breakthrough for both fentanyl and carfentanil solutions within the 240-min test. Unless a manufacturer can provide permeation test data to show otherwise, vinyl and latex glove materials should be avoided when handling these drugs. These data support NIOSH’s opioid glove recommendations for use of nitrile gloves when potentially handling fentanyl and carfentanil. A thicker glove may offer more protection, but consideration should be given to dexterity and hand function.

Acknowledgments

The authors would like to acknowledge CDC’s Center for Preparedness and Response (formerly the Office of Public Health Preparedness and Response) for funding this project, Patrick Keyes from Battelle Memorial Institute for the method implementation, testing, and data reduction, and Patrick Yorio (NIOSH NPPTL) for assistance with the statistical analyses. The authors would like to thank Jennifer Hornsby-Myers, Lee Portnoff, and Jeffrey Stull for their technical review of this manuscript.

References

Ansell. 2020. Microflex midknight XTRA 93–862. https://www.ansell.com/us/en/products/microflex-midknight-xtra-93-862.

ASTM International. 2012. ASTM F739–12 standard test method for permeation of liquids and gases through protective clothing materials under conditions of continous contact. https://www.astm.org/Standards/F739.htm.

ASTM International. 2019. ASTM D6978–19 standard practice for assessment of resistance of medical gloves to permeation by chemotherapy drugs. https://www.astm.org/Standards/D6978.htm.

Centers for Disease Control and Prevention. 2018. Understanding the epidemic. 19 December. https://www.cdc.gov/drugoverdose/epidemic/index.html.

Department of Justice. 2018a. A briefing guide for first responders. https://www.nvfc.org/wp-content/uploads/2018/03/Fentanyl-Briefing-Guide-for-First-Responders.pdf.

Department of Justice. 2018b. Fentanyl and related threats. https://www.justice.gov/usao/page/file/1083791/download.

Drug Enforcement Administration. 2018. 2018 national drug threat assessment. U.S. Department of Justice. https://www.dea.gov/documents/2018/10/02/2018-national-drug-threat-assessment-ndta.

Grainger. 2019. Choosing chemical resistant gloves. January. https://www.grainger.com/content/qt-166-chemical-resistance-gloves.

Hedegaard H, Minino AM, Warner M. 2020. Drug overdose deaths in the United States, 1999–2018. Centers for Disease Control and Prevention, January. https://www.cdc.gov/nchs/products/databriefs/db356.htm.

Howard J, Hornsby-Myers J. 2018. Fentanyls and the safety of first responders: science and recommendations. Am J Ind Med. 61(8):633–639. doi:10.1002/ajim.22874

Lexipol. 2018. First responder fentanyl exposure: what you need to know. https://www.lexipol.com/resources/blog/first-responder-fentanyl-exposure-what-you-need-to-know/.

Moss MJ, Warrick BJ, Nelson LS, McKay CA, Dube PA, Gosselin S, Palmer RB, Stolbach AI. 2018. ACMT and AACT position statement: preventing occupational fentanyl and fentanyl analog exposure to emergency responders. Clin Toxicol (Phila). 56(4):297–300. doi:10.1080/15563650.2017.1373782 [PubMed: 28872357]

National Center for Biotechnology Information. 2020a. PubChem Database. Fentanyl, CID = 3345. https://pubchem.ncbi.nlm.nih.gov/compound/Fentanyl.

National Center for Biotechnology Information. 2020b. PubChem Database. Carfentanil, CID = 62156. https://pubchem.ncbi.nlm.nih.gov/compound/Carfentanil.

NIOSH. 2015. Hierarchy of controls. 13 January. https://www.cdc.gov/niosh/topics/hierarchy/default.html.

NIOSH. 2020. Preventing emergency responders' exposures to illicit drugs. 11 February. Available: https://www.cdc.gov/niosh/topics/fentanyl/risk.html.

Oriyama T, Yamamoto T, Yanagihara Y, Nara K, Abe T, Nakajima K, Aoyama T, Suzuki H. 2017. Evaluation of the permeation of antineoplastic agents through medical gloves of varying materials and thickness and with varying surface treatments. J Pharm Health Care Sci. 3(13):13. doi:10.1186/s40780-017-0082-y [PubMed: 28469932]

Park JN, Weir BW, Allen ST, Chaulk P, Sherman SG. 2018. Fentanyl-contaminated drugs and non-fatal overdose among people who inject drugs in Baltimore, MD. Harm Reduct J. 15(1):34. doi:10.1186/s12954-018-0240-z [PubMed: 29976195]

RAND Corporation. 2019. The future of fentanyl and other synthetic opioids. Santa Monica: RAND Corporation.

Suzuki J, El-Haddad S. 2017. A review: fentanyl and non-pharmaceutical fentanyls. Drug Alcohol Depend. 171: 107–116. doi:10.1016/j.drugalcdep.2016.11.033 [PubMed: 28068563]

Wallemacq PE, Capron A, Vanbinst R, Boeckmans E, Gillard J, Favier B. 2006. Permeability of 13 different gloves to 13 cytotoxic agents under controlled dynamic conditions. Am J Health Syst Pharm. 63(6):547–556. doi:10.2146/ajhp050197 [PubMed: 16522891]

Wilson N, Kariisa M, Seth P, Smith H, Davis NL. 2020. Drug and opioid-involved overdose deaths: United States, 2017–2018. MMWR Morb Mortal Wkly Rep. 69(11): 290–297. doi:10.15585/mmwr.mm6911a4 [PubMed: 32191688]

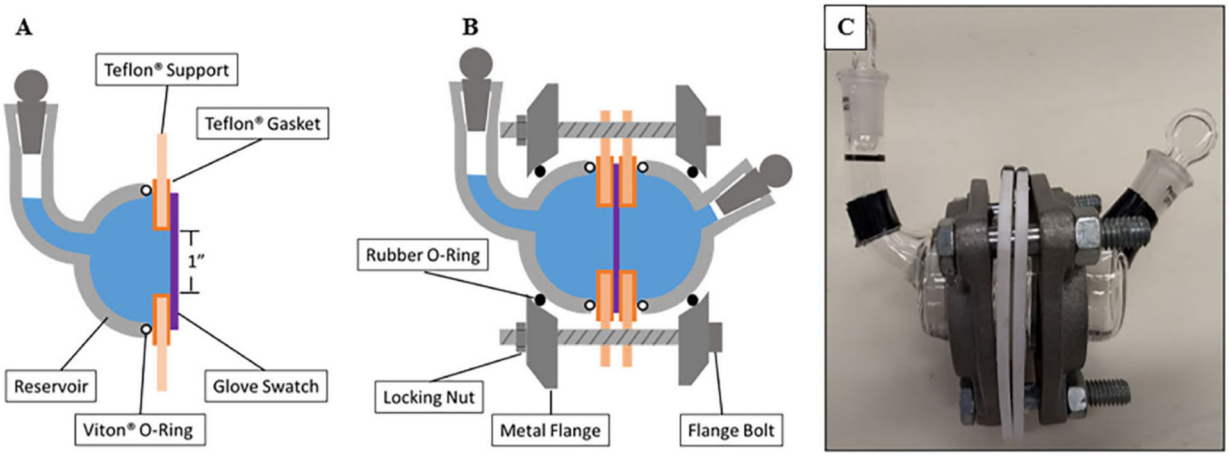

Figure 1.

Schematic representation of the permeation cell depicting the main components, partial assembly (A) and full assembly (B); side view of one loosely assembled permeation cell without a glove swatch (C).

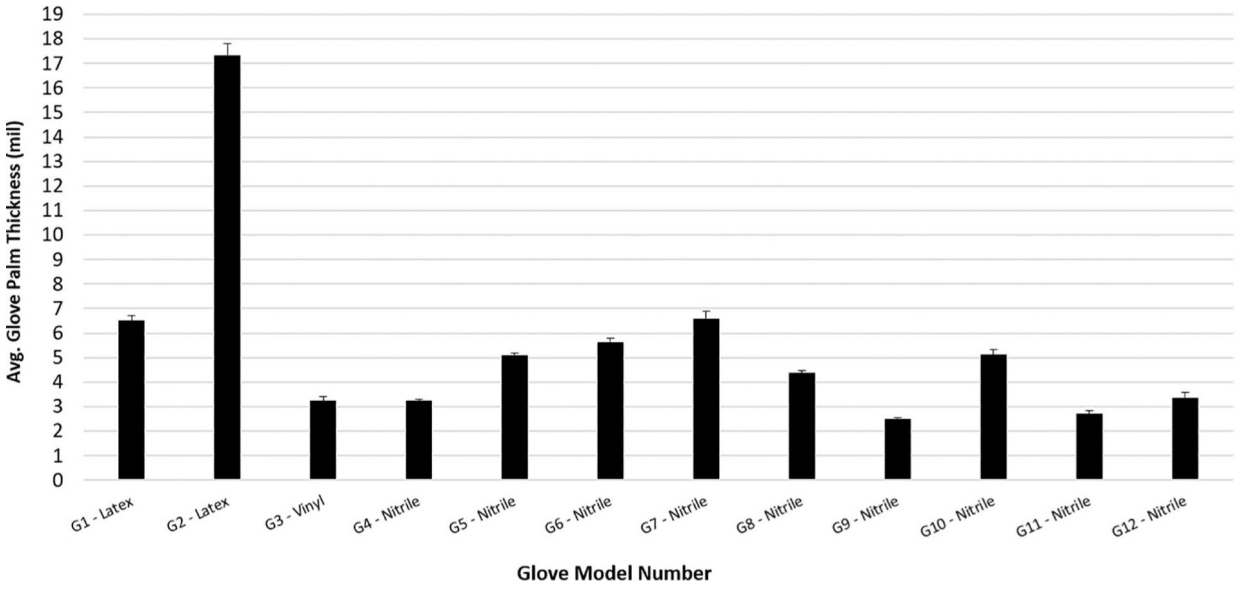

Figure 2.

Average glove model thicknesses across all three lots with four replicates per model lot (n = 12). Error bars shown as standard deviation.

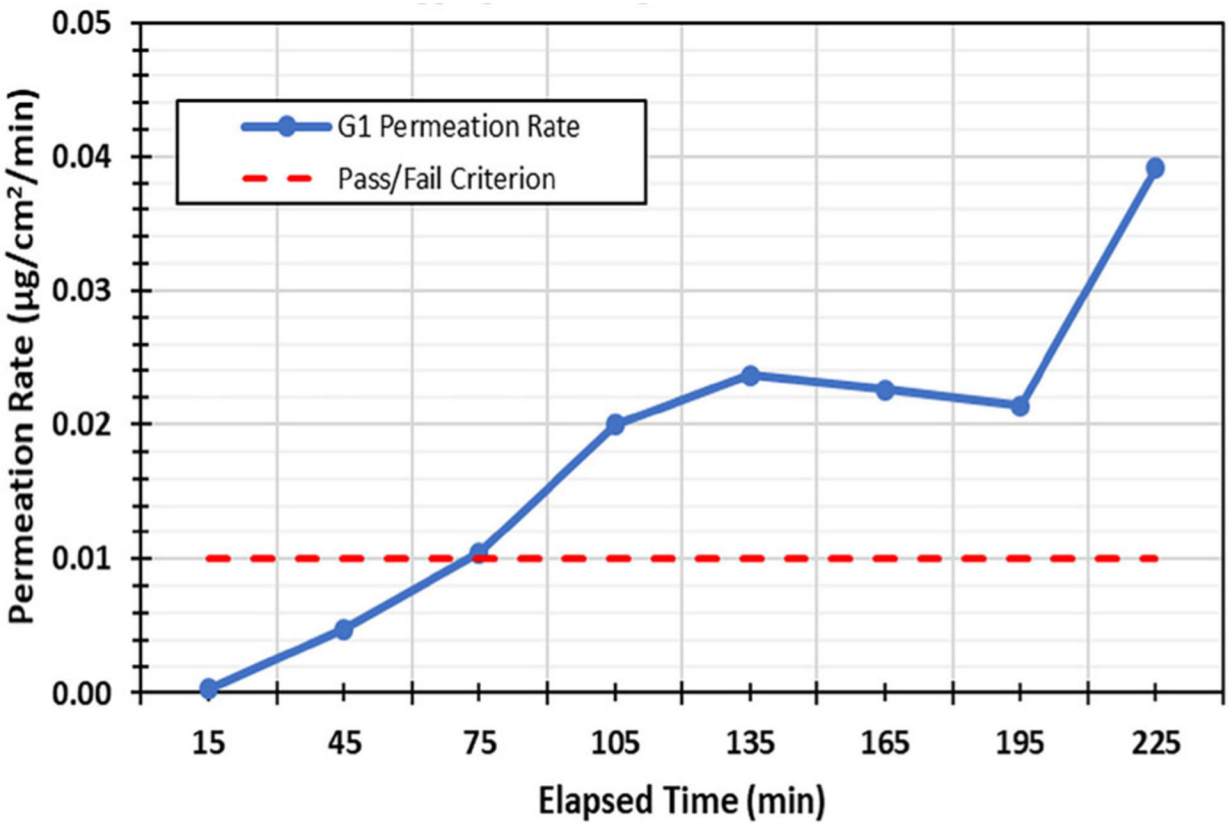

Figure 3.
G1 aggregated permeation rate for Lots 1–3 as a function of elapsed exposure duration (n = 9 per time point).

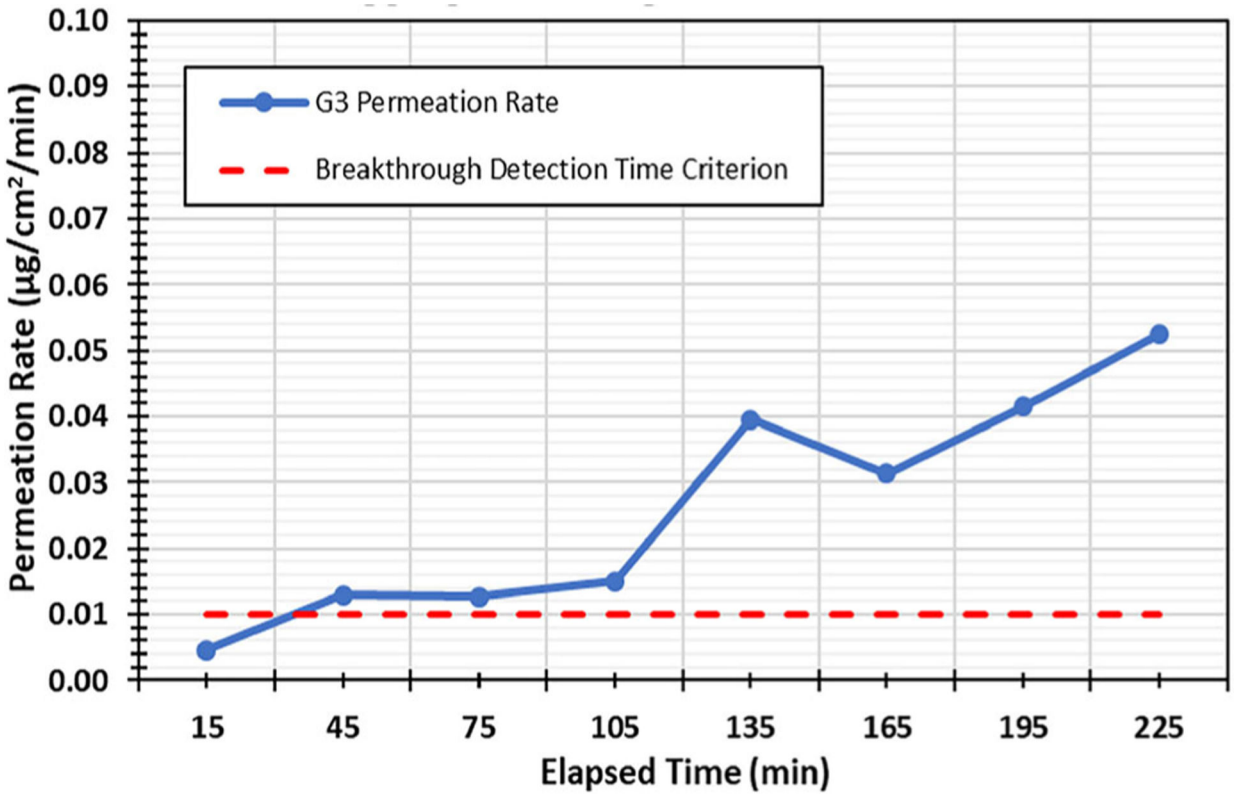

Figure 4.

G3 aggregated permeation rate data for Lots 1–3 as a function of elapsed exposure duration (n = 9 per time point).

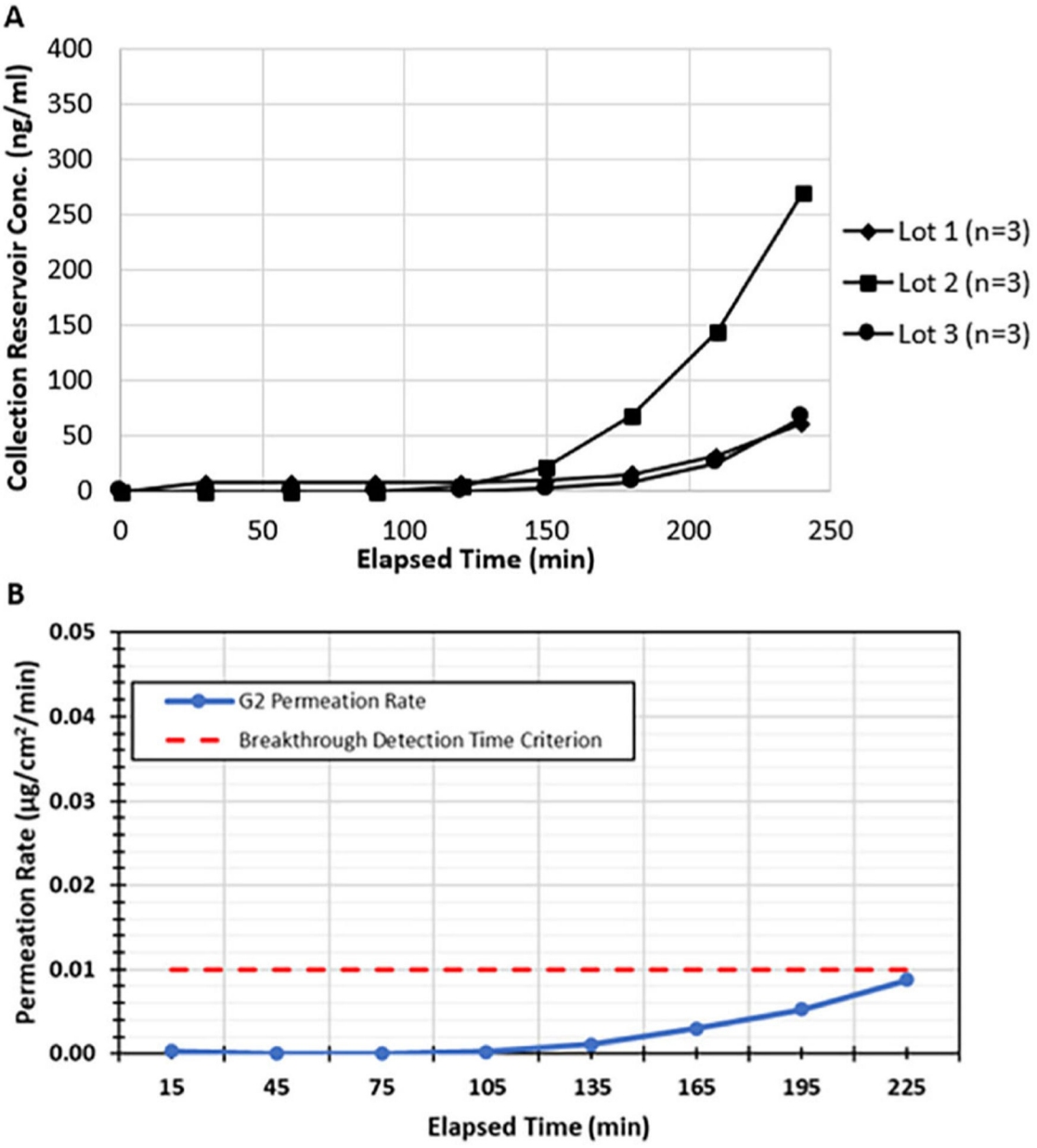

Figure 5.

(A) G2 fentanyl challenge concentration as a function of time for Lots 1 – 3 (n = 3 per time point). (B) G2 aggregated permeation rate for Lots 1–3 as a function of elapsed exposure duration (n = 9 per time point).

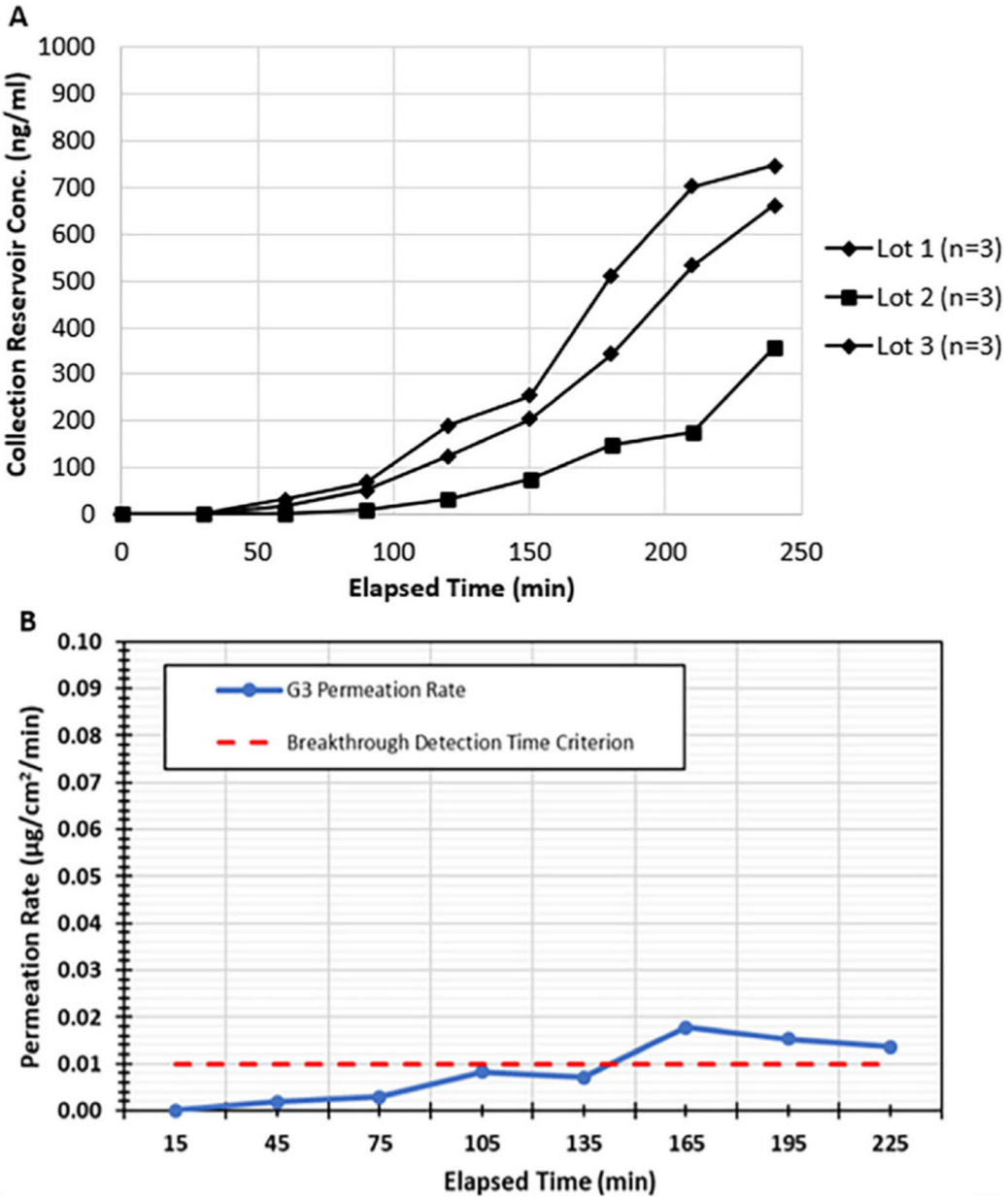

Figure 6.

(A) G3 carfentanil challenge concentration as a function of time for Lots 1–3 (n = 3 per time point). (B) G3 aggregated permeation rate data (n = 9 per time point).

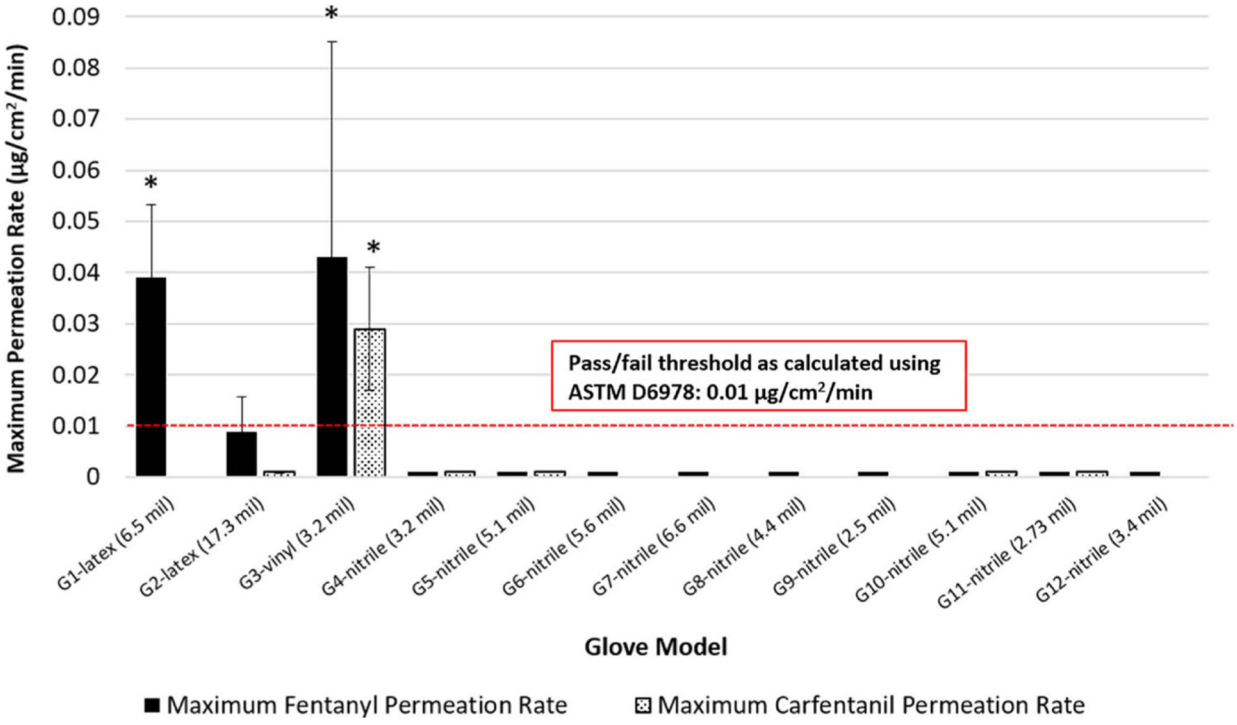

Figure 7.

Comparison of the average maximum fentanyl (black bar) and carfentanil (dotted bar) permeation rates (n = 9 per glove model). Asterisks (*) denote where all three lots in a given model had permeation rates above 0.01 µg/cm^2/min and were considered failures (in accordance with ASTM D6978–05 and as represented by the red dashed line). Error bars are represented as standard deviation.

Table 1.

Summary of the selected glove models for fentanyl and carfentanil permeation testing. The "F" superscript identifies those models that were tested against fentanyl only, where the "FC" superscript identifies those models that were tested against both fentanyl and carfentanil solutions.

Glove Model	Material	Mfr. Date; Exp. Date	Mfr.-Reported Thickness (mil)	Claim Fentanyl Protection?	Chemotherapy-Rated?
G1[F]	Latex	Lot 1: Mfr. 01/2018; N/A Lot 2: Mfr. 02/2018; N/A Lot 3: Mfr. 07/2018; N/A	Fingertip: 7.1 Palm: 5.9		
G2[FC]	Latex	Lot 1: N/A; N/A Lot 2: N/A; N/A Lot 3: N/A; N/A	Fingertip: 18 Palm: N/A		✓
G3[FC]	Vinyl	Lot 1: Mfr. 05/2018; N/A Lot 2: Mfr. 04/2018; N/A Lot 3: Mfr. 08/2018; N/A	Fingertip: 4.3 mil Palm: N/A		
G4[FC]	Nitrile	Lot 1: Mfr. 08/2018; 07/2020 Lot 2: Mfr. 06/2018; 05/2021 Lot 3: Mfr. 07/2018; 06/2021	Fingertip: 5.5 Palm: 3.9	✓	
G5[FC]	Nitrile	Lot 1: Mfr. 04/2018; N/A Lot 2: Mfr. 06/2018; N/A Lot 3: Mfr. 10/2017; N/A	Fingertip: 5.9 Palm: 4	✓	
G6[F]	Nitrile	Lot 1: Mfr. 11/2016; N/A Lot 2: Mfr. 12/2016; N/A Lot 3: Mfr. 07/2016; 06/2021	Fingertip: 8 Palm: 5.5	✓	
G7[F]	Nitrile	Lot 1: N/A; N/A Lot 2: N/A; N/A	Fingertip: 6 mil Palm: N/A	✓	
G8[F]	Nitrile	Lot 1: Mfr. 04/2017; 03/2022 Lot 2: Mfr. 04/2018; 03/2023 Lot 3: Mfr. 07/2018; 06/2023	Fingertip: 5.9 Palm: 4.7		✓
G9[F]	Nitrile	Lot 1: Mfr. 11/2017; N/A Lot 2: Mfr. 06/2018; N/A Lot 3: Mfr. 11/2017; N/A	Fingertip: 10 Palm: N/A		✓
G10[FC]	Nitrile	Lot 1: Mfr. 09/2017; 08/2022	Fingertip: 6.1 mil	✓	

Glove Model	Material	Mfr. Date; Exp. Date	Mfr.-Reported Thickness (mil)	Claim Fentanyl Protection?	Chemotherapy-Rated?
		Lot 2: Mfr. 10/2017; 09/2022	Palm: 5.2		
		Lot 3: N/A; N/A			
G11[FC]	Nitrile	Lot 1: Mfr. 09/2017; N/A	Fingertip: 2.8		✓
		Lot 2: Mfr. 02/2016; N/A	Palm: 2.0		
		Lot 3: Mfr. 12/2016; N/A			
G12[F]	Nitrile	Lot 1: Mfr. 03/2018; N/A	Fingertip: 3.9 mil		✓
		Lot 2: Mfr. 03/2018; N/A	Palm: N/A		
		Lot 3: Mfr. 12/2016; N/A			

Table 2.

Maximum fentanyl permeation rate for 12 glove models.

		Fentanyl: Maximum Permeation Rate (μg/cm^2/min)						
Glove Model (Material)	**Lot**	**Replicate 1**	**Replicate 2**	**Replicate 3**	**Lot Avg. (n = 3)**	**Model Avg. (n = 9)**	**Breakthrough Detection Time (min)**	**Data Supports Mfr. Claim for Fentanyl Protection?**
G1 (Latex)	1	0.043	0.043	0.025	0.031	0.039	60	N/A
	2	0.065	0.024	0.053	0.045		90	
	3	0.041	0.021	0.02	0.024		90	
G2 (Latex)	1	0.007	0.002	0.002	0.003	0.0088	>240	N/A
	2	0.021	0.014	0.018	0.016		180	
	3	0.003	0.003	0.007	0.005		>240	
G3 (Vinyl)	1	0.095	0.17	0.071	0.081	0.043	30	N/A
	2	0.027	0.029	0.028	0.029		90	
	3	0.062	0.045	0.047	0.026		90	
G4, G5, G6, G7, G8, G9, G10, G11, & G12 (All Nitrile)	1	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	>240	G5, G6, G7, G10, and G11: Yes
	2							(G4, G8, G9, G12: N/A)
	3							

Table 3.

Maximum carfentanil permeation rate for six glove models.

Glove Model (Material)	Lot	Carfentanil: Maximum Permeation Rate (μg/cm^2/min)					Breakthrough Detection Time (min)
		Replicate 1	Replicate 2	Replicate 3	Lot Avg. (n = 3)	Model Avg. (n = 9)	
G2 (Latex)	1	<0.001	N/A	<0.001	<0.001	<0.001	>240
	2	0.002	<0.001	0.001	0.001		>240
	3	0.001	<0.001	<0.001	<0.001		>240
G3 (Vinyl)	1	0.025	0.027	0.061	0.038	0.029	90
	2	0.029	0.021	0.012	0.021		210
	3	0.029	0.024	0.028	0.027		150
G4, G5, G6, & G7 (All Nitrile)	1, 2, & 3	<0.001	<0.001	<0.001	<0.001	<0.001	>240