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Permeability of 13 different gloves to 13 cytotoxic agents under controlled dynamic conditions

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Purpose. The permeability of 13 different gloves to 13 cytotoxic agents under controlled dynamic conditions is described.

Methods. Thirteen cytotoxic agents were prepared at the highest concentrations normally encountered by pharmacy personnel. Four glove types—neoprene, natural rubber latex, nitrile, and vinyl—were exposed to the cytotoxic agents for 15, 30, and 60 minutes. Tests were conducted using the middle finger of each glove. Linearity, reproducibility, and sensitivity were evaluated for each drug tested. Assays were run using liquid chromatographic tandem mass spectrometry (LC/MS/MS) and high-performance liquid chromatography with ultraviolet light (HPLC-UV). Permeability testing was conducted using an original system designed to evaluate dynamic constraints, such as rubbing, stretching, and tension.

Results. Linearity by LC/MS/MS and HPLC-UV was confirmed at concentrations up to 1000 ng/mL for all drugs. Most glove materials were permeable at rates below ASTM recommendations over the one-hour testing period. Vinyl was the most permeable material. Carmustine permeated the widest variety of materials. Due to the high sensitivity of the analytic methods, all materials displayed low but significant permeability for at least one drug after one hour. Higher resistance to permeation was recorded for all neoprene, some natural rubber latex, and one nitrile glove.

Conclusion. Neoprene, natural rubber latex, and nitrile gloves displayed the highest resistance to permeation of the 13 cytotoxic agents studied. Additional factors, such as duration of exposure, glove thickness, and drug liposolubility and molecular weight, also affected permeability.

Index terms: Antineoplastic agents; Carmustine; Concentration; Gloves; Latex; Molecular weight; Neoprene; Nitrile rubber; Permeability; Permeation; Polymers; Polyvinyl chloride; Solubility; Thickness

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Occupational exposure to cytotoxic agents has been clearly identified by the detection of trace concentrations of these drugs in the urine of health care personnel.[1-5] Exposure to cytotoxic drugs mainly occurs through skin contact and inhalation.[6-8] Adverse effects related to occupational exposure to cytotoxic agents include acute toxicity,[9] nausea, headache, dizziness, hair loss,[10] liver damage,[11] spontaneous abortions,[12] and chromosomal damage.[13] Most cytotoxic agents are considered carcinogenic to humans according to the classification system of the International Agency for Research on Cancer.[14] Because gloves offer the first line of protection when handling cytotoxic drugs, material should be tested for resistance to the permeation of these drugs. Two methods of such evaluation include (1) the mutagenicity test[15-19] and (2) the quantification of cytotoxic drugs based on standards for permeation testing,[20,21] such as European Standard EN 374-3[22] and ASTM International standards F739-99a[23] and D6978-05.[24]

The mutagenicity test uses *Salmonella typhimurium* strains with a known sensitivity to mutation. In this test, the fingertip of a glove is

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turned inside out, and a known quantity of cytotoxic solution is poured into the glove, ensuring contact with the outer surface. The internal fingertip is pressed against a filter-paper disk, which is later transferred to agar plates seeded with a layer of bacteria. Any drug that permeates the glove material and is absorbed by the filter diffuses into the agar plate and mutates the bacteria, producing a ring of colonies directly related to the concentration of the drug.

Quantification of cytotoxic drugs is based on the application of a known concentration of a cytotoxic drug in the donor solution to the outer surface of the glove and the detection of the drug in the acceptor solution (usually water) in contact with the inner surface of the glove.[22] Drug quantity is measured at multiple intervals.

Studies have found that permeation of cytotoxic agents into gloves could be related to glove material and thickness.[15-21] These methods, however, involve static experimental models, which may not reflect the dynamic conditions to which gloves are exposed by health care personnel (e.g., stretching, rubbing). Moreover, most analytic techniques used in these studies lacked some degree of sensitivity and allowed only the detection of massive permeation flux. According to European Standard EN 374-3, gloves should not allow the permeation of chemicals or microorganisms at a rate of 1000 ng/(cm^2 · min) or greater.[22] A similar American standard is slightly more restrictive, requiring gloves to limit permeation to chemicals and microorganisms to rates of 100 ng/(cm^2 · min) or lower.[23] The recent updated standard ASTM D6978-05 is even more restrictive, with a limit of <10 ng/(cm^2 · min).[24]

The objectives of this study were to develop a dynamic permeation method that more closely reflects the real-use conditions of medical gloves and to optimize the analytic sensitivity of this method by using liquid chromatographic tandem mass spectrometry (LC/MS/MS) and high-performance liquid chromatography with ultraviolet light (HPLC-UV) to identify low permeation rates. This study describes the permeation of 13 cytotoxic drugs through 13 different gloves.

Methods

Materials. Thirteen types of gloves were tested, consisting of four different materials: neoprene, natural rubber latex (NRL), nitrile, and vinyl (Table 1). Mean thickness was determined by the manufacturer with a dial micrometer in accordance with ASTM International standards D3577-01a[25] and D3578-01a.[26] Tests were conducted using the middle finger of the gloves (size medium for examination gloves and size 7½ for surgical gloves).

The permeability of 13 cytotoxic drugs was investigated: fluorouracil, carmustine, cisplatin, cyclophosphamide, ifosfamide, cytarabine, docetaxel, doxorubicin, etoposide, irinotecan, methotrexate, thiotepa, and vinorelbine. The permeability of vinyl gloves, known for their poor protective properties and unlikely use when handling cytotoxic drugs, was only tested with 6 drugs (cyclophosphamide, thiotepa, irinotecan, ifosfamide, carmustine, and etoposide). All drugs were tested at the highest stock concentration for the formulation (range, 1–100 mg/mL). If delivered in a solid form, the substances were dissolved in distilled water or in the diluent supplied by the manufacturer. Acetonitrile was HPLC grade, and ammonium acetate and triethylammonium phosphate were analytic reagent grade (Merck, Darmstadt, Germany). Deionized water was obtained from a Milli-Q water purification system (Millipore, Milford, MA).

Testing equipment. In the absence of commercially available equipment meeting our objectives for dynamic testing, an original system, shown in Figures 1 and 2, was conceived, designed, and built by engineers at the medical school of the Catholic University of Louvain in Brussels. The purpose of the device was to expose glove material to standardized dynamic constraints, such as rubbing, stretching, and tension.

The device was equipped with a motor-driven plate, with 20 drilled holes adjusted to receive brass shafts. These shafts were animated by a regular up-and-down movement (18 cycles/min, adjustable) into inner polyethylene tubes (outer diameter, 12.0 mm), coated by a glove's middle finger containing 200 µL of the cytotoxic solution. The finger was inverted to allow the drug to come into contact with the outer surface of the glove. The inner tube coated with the glove finger was pushed into a second larger collecting tube (inner diameter, 14.0 mm), containing 1.5 mL of water, and firmly fastened to the fix plate by Teflon screws. The glove finger was fastened on the outer tube by an O-ring (Figure 2). The middle finger was exposed to 350 g of tension via the brass shaft. Cutting of the glove middle finger was standardized at about 8.5 cm from the top of the finger, and the mean ± S.D. area of material exposed to the drug according to the procedure described above was 22.3 ± 1.2 cm^2 (n = 13). The amount of cytotoxic drug passing through the glove was measured in the collecting solution at four time intervals (immediately after preparation and at 15, 30, and 60 minutes). To avoid any change in the volume and drug concentration of the collecting medium, each time interval corresponded to a separate experiment. All tests were conducted in triplicate, yielding 2028 results. Twenty samples were tested simultaneously on this equipment. All manipulations were performed by the same person in accordance with our hospital's safety regulations and using a vertical-laminar-airflow cabinet.

All tests were conducted at a constant temperature of 25 °C, and all

samples were protected from direct exposure to light. To minimize degradation of the drugs, collected samples and calibrators were kept frozen (–20 °C) until analysis.

Permeation rates were calculated using the following equation:

$$P = (C \times V)/(t \times S)$$

where P = permeation rate (ng/[min · cm^2]), C = drug concentration (ng/mL) in the collecting solution, V = volume of the collecting solution (1.5 mL), t = duration of exposure (minutes), and S = surface area of the glove exposed to the drug (22.3 cm^2).

Analytic methods. A Quattro micro tandem mass spectrometer[a] fitted with a Z-Spray ion source was used for LC/MS/MS analyses. The instrument was operated in electrospray positive ionization mode and was attached to a high-throughput HPLC system[b] with an integrated autosampler. All aspects of system operation and data acquisition were controlled with MassLynx NT, version 3.5, software with automated data processing using the QuanLynx application manager, as described elsewhere.[27] Rapid separation was obtained using a C_{18} column.[c]

HPLC-UV analyses were performed using an analytical column[d] and a system equipped with a diode array detector.[e]

The LC/MS/MS analytic conditions were identical for nine cytotoxic drugs (cyclophospharmide, ifosfamide, cytarabine, docetaxel, doxorubicin, irinotecan, methotrexate, thiotepa, and vinorelbine). Since analyses were performed with aqueous solutions, the procedure did not require any extraction phase. Ten microliters of each solution was injected into the system. Briefly, the mobile phase consisted of 25% acetonitrile (v/v) and 75% of a buffer (pH 3.5) of ammonium acetate 2 mM. The flow rate was 0.4 mL/min. The oven temperature was set at 53 °C. The run time under these conditions was 4 minutes. Specific product ions resulting from the fragmentation of the drug's precursor ions were detected using multiple-reaction-monitoring (MRM) detection mode (Figure 3). High-purity argon was used as the collision gas. Ionization was achieved in the positive ion mode with the following settings: capillary voltage, 3.5 kV; cone voltage, 15–60 V; source block temperature, 140 °C; desolvation temperature, 200 °C at a nitrogen flow of approximately 63 L/hr. The four remaining drugs (carmustine, cisplatin, etoposide, and fluorouracil) did not properly respond to the mass spectrometric conditions described above. Therefore, an HPLC–UV de-

Table 1.
Characteristics of Gloves Tested for Permeability

Product[a]	Material	Thickness (mm)	Lots
AccuTech Gammex 91-225	NRL[b]	0.24	030952004
DermaClean	NRL	0.19	0311363228
DermaPrene Ultra	Neoprene	0.19	0307481704
EP Surgical Style	NRL	0.24	0312553604
Gammex PF	NRL	0.22	0312549104
Micro-Touch DermaPrene	Neoprene	0.17	03092001EQ
Micro-Touch PF[2]	NRL	0.24	0310053721
Micro-Touch Plus	NRL	0.18	0305047677
Nitra-Tex	Nitrile	0.16	03097013ES
Perry Encore 85	NRL	0.23	0307011705
Perry Encore Orthopaedic	NRL	0.33	0309000605
Synsation PF	Vinyl	0.12	0308487104
Touch N Tuff	Nitrile	0.14	04010107AU

[a]All products manufactured by Ansell Healthcare.
[b]NRL = natural rubber latex, PF = powder free.

Figure 1. Device used to test permeation of cytotoxic agents through glove material under dynamic conditions.

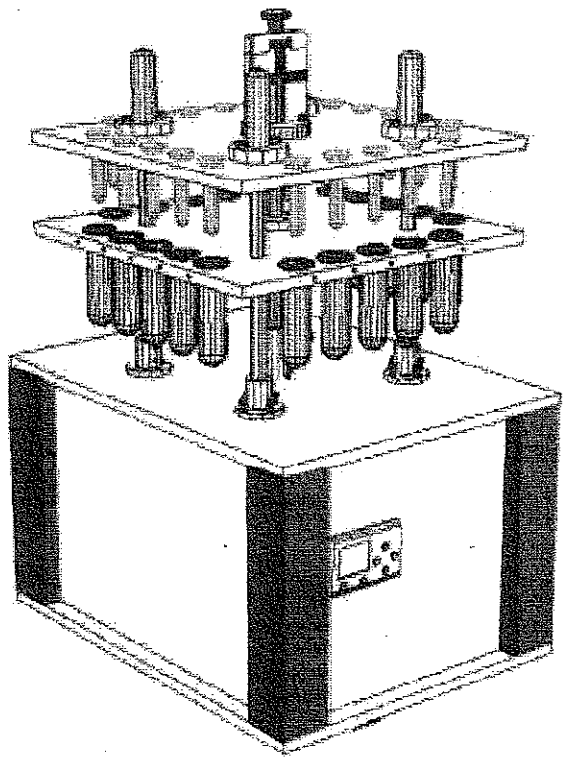
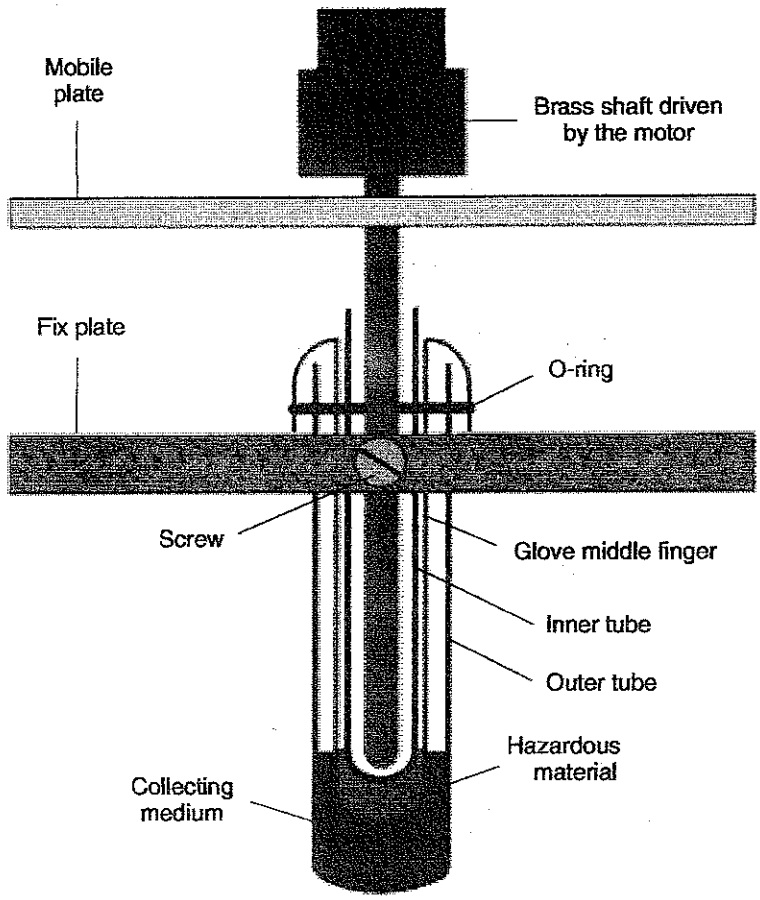


Figure 2. Detailed diagram of the permeation testing unit.



tection method was developed for these drugs. The mobile phase consisted of 5–15% acetonitrile (v/v) and 95–85% of a buffer (pH 3) of triethylammonium phosphate 25 mM. The composition, flow rate (0.5–1.5 mL/min), wavelength (214–280 nm), and run time (2–12 minutes) varied according to the drug analyzed. The oven temperature was set at 40 °C, and a 20-µL sample of each solution was injected into the column. Aqueous phases were filtered through Durapore membrane filters[f], and mobile phases further passed through the degassing chamber of the analyzer. Tables 2 and 3 summarize the analytic conditions of the LC/MS/MS and HPLC-UV methods, respectively.

Validation of the analytic methods. Calibrations were obtained in aqueous solution spiked with different drug concentrations ranging from 1 to 10,000 ng/mL and 50 to 10,000 ng/mL for the LC/MS/MS and HPLC–UV methods, respectively. Appropriate dilutions were performed for all results above the upper analytic range. All calibration lines passed through the origin.

Linearity, reproducibility, and sensitivity were evaluated for each drug tested. Within-assay agreement was evaluated with a minimum of five concentrations of each cytotoxic agent, ranging from the limit of quantification (LOQ) to 10,000 ng/mL by LC/MS/MS (LOQ, 100, 500, 1,000, and 10,000 ng/mL) and HPLC–UV (LOQ, 250, 500, 1,000, and 10,000 ng/mL), injected in triplicate. Linearity and between-assay agreement were determined by testing the above drug concentrations in triplicate during five consecutive days. The limit of detection (LOD) and LOQ were determined for each drug. Carryover and stability of the standard solutions were further investigated by consecutively injecting a sample of 1,000 ng/mL of cytotoxic agent followed by a blank sample, a three-cycle freeze–thaw protocol, and storage for seven days at –20 or 4 °C. Two concentrations (50 and 500 ng/mL for drugs measured by LC/MS/MS and 200 and 1,000 ng/mL for drugs analyzed by HPLC-UV) were then tested at days 0 and 7 in triplicate. Statistical analyses were performed using JMP, version 4.0.2, software (SAS Institute, Cary, NC). Student's t test was used to determine significance ($p < 0.05$).

Results

Linearity by LC/MS/MS and HPLC-UV was confirmed at concentrations up to 10,000 ng/mL for all drugs. The calibration curves displayed correlation coefficients ranging from 0.997 to 0.999. Briefly, between- and within-assay coefficients of variation (CV) were maintained (<15% within the analytical range and <20% at the LOQ). Between-assay CV ranged from 0.6% to 18.3%. Depending on the drug analyzed, the LOD ranged from 0.97–35.2 ng/mL (LC/MS/MS) and 37.4–63 ng/mL (HPLC-UV), or 0.001–0.039 ng/(cm^2 · min) (LC/MS/MS) and 0.041–0.070 ng/(cm^2 · min) (HPLC-UV) after 60 minutes. The analytic values of both methods are listed in Table 4 and appear far more sensitive than the limit proposed by the recent ASTM standard D6978-05.[24]

No carryover was observed. The freeze–thaw testing yielded no changes during the three-cycle protocol. At –20 °C, no significant changes were observed in drug concentrations. At 4 °C, only docetaxel and carmustine displayed statistically significant degradation after seven days. Docetaxel concentrations de-

Figure 3. Mass spectra of parent (A) and product ions (B) of cyclosphosphamide 1000 ng/mL by multiple-reaction-monitoring detection mode.

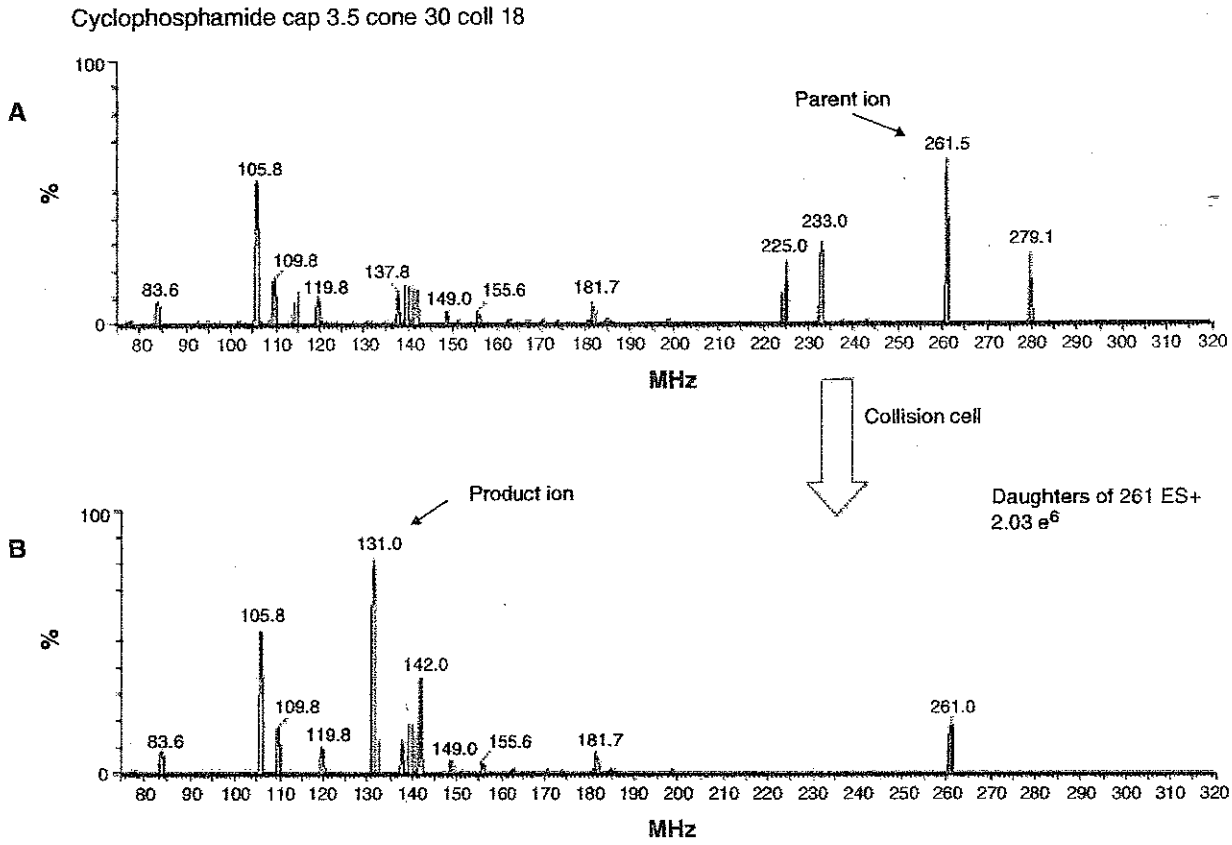


Table 2.
Cytotoxic Formulations Tested by LC/MS/MS[a]

Drug	Manufacturer	Conc. (mg/mL)	Log P	Parent/Product Ions (m/z)	Cone Voltage (V)	Collision Energy (eV)
Cyclophosphamide	Asta Medica	20	0.6	261.5/131	30	18
Methotrexate	Lederle	100	−1.8	455.2/308	40	18
Thiotepa	Wyeth-Lederle	10	0.5	190.0/146.9	20	14
Cytarabine	Pharmacia & Upjohn	100	−2.5	243.2/111.8	15	10
Irinotecan	Aventis-Pharma	20	NA	587.1/123.9	60	30
Docetaxel	Aventis-Pharma	10	NA	808/182	40	12
Vinorelbine	Pierre-Fabre	10	NA	779/323	30	25
Ifosfamide	Asta Medica	100	NA	261/139.8	30	20
Doxorubicin	Pharmacia	2	1.3	545.5/398	30	13

[a]LC/MS/MS = liquid chromatographic tandem mass spectrometry, NA = not available.

Table 3.
Cytotoxic Formulations Tested by HPLC-UV[a]

Drug	Manufacturer	Conc. (mg/mL)	Log P	Flow Rate (mL/min)	Wavelength (nm)	Ratio of Mobile Phase (v/v)[b]
Carmustine	Almirrall-Prodesfarma	3	1.53	1	230	85:15
Cisplatin	Bristol-Myers Squibb	1	−2.19	1.5	214	95:5
Etoposide	Bristol-Myers Squibb	20	0.6	1	280	95:5
Fluorouracil	Pharmacia & Upjohn	50	−1	0.5	265	85:15

[a]HPLC-UV = high-performance liquid chromatography with ultraviolet light.
[b]Triethylammonium phosphate buffer 25 mM, pH 3:acetonitrile.

creased significantly from mean values of 45.9 and 503 ng/mL to 20.5 and 322 ng/mL ($p < 0.001$), and carmustine concentrations decreased from 195.7 and 979.5 ng/mL to <59 and 291 ng/mL, losing about 40–70% of their initial concentrations after seven days at 4 °C ($p < 0.001$).

The results of the permeability testing of the various glove types after 15, 30, and 60 minutes are summarized in Tables 5, 6, and 7, respectively. Most materials were permeable at rates below the recommendations of ASTM D6978-05 (10 ng/[cm² · min]) over the one-hour testing period.[24] As expected, vinyl was the most permeable material. After 15 minutes, four of the six drugs tested already had permeation rates exceeding 10 ng/(cm² · min). After 30 minutes, five drugs exceeded this rate, suggesting a rapid and massive permeation of drugs through vinyl.

Carmustine permeated the widest variety of materials. After 15 minutes, four types of gloves (two NRL, one nitrile, and one vinyl) did exhibit unacceptable permeability (>10 ng/[cm² · min]). Two additional NRL gloves exposed to carmustine exhibited unacceptable permeability after 60 minutes. Among the other drugs studied and excluding vinyl gloves, only three drugs (fluorouracil, etoposide, and cisplatin) had permeation rates exceeding 10 ng/(cm² · min) after 60 minutes, involving three gloves (two NRL and one nitrile). Due to the high sensitivity of the analytic methods, all materials displayed low but significant permeability (>1 ng/[cm² · min]) for at least one drug after 60 minutes. Higher resistance, even to carmustine, was recorded for all neoprene (DermaPrene Ultra and Micro-Touch DermaPrene), some NRL (Gammex PF, EP Surgical Style, Micro-Touch PF, and Perry Encore Orthopedic), and one nitrile (Nitra-Tex) glove. These gloves should be recommended for use when handling cytotoxic drugs.

Table 4.
Analytic Values of Cytotoxic Agents Determined by LC/MS/MS and HPLC-UV[a]

Drug	Retention Time (min)	Initial LOD (ng/mL)[b]	LOD after 60 min (ng/cm² · min)[b]	Initial LOQ (ng/mL)[b]	LOQ after 60 min (ng/cm² · min)[b]	Initial Analytic Range (ng/mL)	Analytic Range after 60 min (ng/cm² · min)	Within-Assay CV (%)[c]	Between-Assay CV (%)[c]
LC/MS/MS									
Cyclophosphamide	1.38	1.95 ± 0.2	0.002 ± 0.0002	31.6 ± 3	0.034 ± 0.003	31.6–10,000	0.034–11.2	14.5–1.7	16.4–5.9
Cytarabine	0.55	0.97 ± 0.08	0.001 ± 0.0001	4.9 ± 0.5	0.005 ± 0.0007	4.9–10,000	0.005–11.2	11.7–1.5	14.4–6.5
Docetaxel	2.57	3.11 ± 0.25	0.003 ± 0.001	17.3 ± 2.1	0.019 ± 0.007	17.3–10,000	0.019–11.2	13.4–1.9	14.6–5.2
Doxorubicin	1.10	35.2 ± 1.1	0.039 ± 0.008	55.1 ± 4.9	0.061 ± 0.005	55.1–10,000	0.061–11.2	12.1–0.2	17.4–4.3
Ifosfamide	1.28	4.1 ± 0.35	0.004 ± 0.001	45.1 ± 4.0	0.050 ± 0.004	45.1–10,000	0.050–11.2	14.6–0.7	13.7–5.2
Irinotecan	0.92	16.3 ± 1.4	0.018 ± 0.003	30.7 ± 3.1	0.033 ± 0.004	30.7–10,000	0.033–11.2	13.6–0.6	11–0.6
Methotrexate	0.73	1.41 ± 0.11	0.002 ± 0.0001	12.8 ± 1.1	0.013 ± 0.002	12.8–10,000	0.013–11.2	18.4–0.7	18.3–1.4
Thiotepa	1.1	3.06 ± 0.25	0.003 ± 0.0003	17.4 ± 1.2	0.019 ± 0.003	17.4–10,000	0.019–11.2	12.1–0.7	9.3–1.8
Vinorelbine	2.20	6.48 ± 0.51	0.007 ± 0.0005	43.7 ± 3.9	0.048 ± 0.003	43.7–10,000	0.048–11.2	11.5–1.2	15.3–4.5
HPLC-UV									
Carmustine	10.5	59 ± 3.1	0.066 ± 0.01	196.7 ± 35.1	0.219 ± 0.06	196.7–10,000	0.219–11.2	5.8–0.4	3.4–2.9
Cisplatin	1.6	49.7 ± 4.1	0.055 ± 0.006	165.6 ± 42	0.184 ± 0.07	165.6–10,000	0.184–11.2	15.1–1.6	10.2–3.7
Etoposide	8.4	63 ± 7.8	0.070 ± 0.02	210.1 ± 50	0.235 ± 0.09	210.1–10,000	0.235–11.2	8.7–1.7	6.7–2.2
Fluorouracil	3.1	37.4 ± 3.5	0.041 ± 0.004	124.9 ± 21	0.139 ± 0.03	124.9–10,000	0.139–11.2	6.2–0.7	3.7–1

[a] LC/MS/MS = liquid chromatographic tandem mass spectrometry, HPLC-UV = high-performance liquid chromatography with ultraviolet light, LOD = limit of detection, LOQ = limit of quantification, CV = coefficient of variation.
[b] Mean ± S.D., $n = 15$.
[c] CV for concentrations ranging from LOQ to 10,000 ng/mL, $n = 15$.

Discussion

Apart from glove material, other factors contributed to glove permeability, such as the duration of exposure, the thickness of the material, and the liposolubility or the molecular weight of the drug. Permeation was clearly related to the duration of exposure. All glove materials displayed a general trend toward greater permeation over time, increasing by a mean 5-fold factor between 15 and 60 minutes (the steepest increase being observed during the first 15 minutes). Cyclophosphamide, ifosfamide, and docetaxel displayed a 10-fold factor between 15 and 60 minutes. Such observation is consistent with the general recommendation to change gloves every 30 minutes. The highest resistance to permeation was generally observed in NRL gloves with a thickness of at least 0.24 mm and for nitrile gloves at least 0.16 mm thick. Thickness of neoprene gloves offered a high level of resistance to permeation. The thinnest gloves (Synsation vinyl, 0.12-mm thickness) were the most permeable and the thickest (Perry Encore Orthopaedic, 0.33-mm thickness) were the least permeable.

Regarding the liposolubility of the drugs, analysis of their partition coefficient between octanol and water (log P) suggests a trend toward higher permeation rates for drugs with a log P of >0.5 (carmustine, cyclophosphamide, and thiotepa), whereas drugs characterized by the lowest log P values generally have the lowest mean permeation rates (methotrexate, cytarabine, cisplatin). Interestingly, two drugs with similar log P values—carmustine (log P, 1.5) and doxorubicin (log P, 1.3)—have significantly different permeation rates. A possible explanation could be their different molecular weights (214 for carmustine and 543.5 for doxorubicin).

One should be aware of the possible involvement of inactive ingredients of the drug formulation and the glove-manufacturing process, both of which could influence permeation rates. Two different NRL, powder-free, 22-mm thick gloves (Gammex PF and Perry Encore 85) were permeated by carmustine at different rates after 60 minutes (<0.06 and 203.6 ng/[cm^2 · min], respectively). Such results make it difficult to predict the permeation rate of a particular drug through a specific type of glove.

In actual practice, additional factors must be considered when determining permeability, including temperature, humidity, skin pH, and concentration of the pharmaceutical solution. As described above, the temperature in this study was set at 25 °C. However, gloves in contact with the skin have an external temperature of about 30 °C. Since permeation is proportional to temperature, the permeation rates in this study may be underestimated. On the other hand, the extreme dynamic conditions used during our protocol, including persistent friction and exposure to drug solutions, are rarely observed in real-life situations, negating any possible underestimation.

Appropriate protection is crucial when handling cytotoxic agents. The recent permeation limit proposed by ASTM standard D6978-05 appears more appropriate than the previous ASTM standard F739-99a and the European Standard EN 374-3.[22-24] Some permeation was found in all types of gloves studied. Major factors determining permeation include glove material and thickness, duration of exposure, stretching and rubbing, physicochemical properties of drugs, temperature, and perspiration. Permeation must be assessed for each glove type, as permeation rates can be influenced by both inactive ingredients in the drug formulation and the glove-manufacturing process.

During the reconstitution phase, gloves should be changed at least every 30 minutes, preferably every 15–20 minutes. Gloves should be changed immediately if torn or punctured. Special caution is advised when working with lipophilic and low-molecular-weight cytotoxic agents.

Conclusion

Neoprene, NRL, and nitrile gloves displayed the highest resistance to permeation of the 13 cytotoxic agents studied. Additional factors, such as duration of exposure, glove thickness, and drug liposolubility and molecular weight, also affected permeability.

[a]Micromass UK Ltd., Manchester, United Kingdom.
[b]Waters 2795 Alliance, Waters Corporation, Milford, MA.
[c]Xterra 50 × 2.1 mm inner diameter, 3.5-µm particle size, Waters.
[d]LiChroCART 125-4 Superspher 100 RP-18, 4 × 125 mm inner diameter, 5-µm particle size, Hewlett-Packard, Palo Alto, CA.
[e]Agilent, Palo Alto.
[f]0.45-µm HV, Millipore, Cork, Ireland.

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Table 5.
Permeation of Cytotoxic Agents through Gloves after 15 Minutes

Drug	Permeation Rate (ng/[cm² · min])[a]					
	Touch N Tuff	Nitra-Tex	Micro-Touch Plus	DermaClean	Gammex PF	Perry Encore 85
Carmustine	63.68 ± 6.7	4.28 ± 0.11	ND	94.6 ± 9.4	ND	11.17 ± 0.7
Cisplatin	1.22 ± 0.05	ND	ND	ND	ND	8.52 ± 1.8
Cyclophosphamide	0.62 ± 0.1	ND	ND	ND	ND	ND
Cytarabine	0.01 ± 0.00	0.01 ± 0.00	ND	0.28 ± 0.04	ND	ND
Docetaxel	ND	ND	ND	ND	ND	ND
Doxorubicin	ND	ND	0.27 ± 0.03	0.74 ± 0.08	ND	ND
Etoposide	ND	ND	ND	0.79 ± 0.00	ND	4.93 ± 0.36
Fluorouracil	8.07 ± 1.36	ND	ND	ND	ND	ND
Ifosfamide	0.57 ± 0.1	0.32 ± 0.00	ND	ND	ND	0.32 ± 0.01
Irinotecan	0.37 ± 0.05	ND	ND	ND	0.34 ± 0.06	ND
Methotrexate	0.17 ± 0.00	ND	ND	ND	ND	ND
Thiotepa	0.08 ± 0.00	ND	0.07 ± 0.01	0.32 ± 0.03	ND	0.26 ± 0.02
Vinorelbine	ND	0.22 ± 0.03	ND	0.18 ± 0.02	ND	ND

[a]Mean ± S.D. of three replicates. ND = not detected (less than the limit of detection), NA = not available. Permeation limits acceptable by ASTM standards D6978-05 and F739-99a and European Standard EN 374-3 are 10, 100, and 1000 ng/cm² · min, respectively.

Table 6.
Permeation of Cytotoxic Agents through Gloves after 30 Minutes

Drug	Permeation Rate (ng/[cm² · min])[a]					
	Touch N Tuff	Nitra-Tex	Micro-Touch Plus	DermaClean	Gammex PF	Perry Encore 85
Carmustine	102.2 ± 8.5	3.3 ± 0.05	68.6 ± 0.04	204.9 ± 17	ND	30.5 ± 4
Cisplatin	3.1 ± 0.4	ND	ND	ND	ND	30.5 ± 5.41
Cyclophosphamide	0.4 ± 0.0	0.14 ± 0.01	0.05 ± 0.0	0.05 ± 0.01	0.09 ± 0.00	ND
Cytarabine	0.01 ± 0.00	0.02 ± 0.00	ND	0.72 ± 0.01	0.06 ± 0.01	ND
Docetaxel	0.04 ± 0.01	0.03 ± 0.00	0.07 ± 0.01	0.03 ± 0.00	0.05 ± 0.01	0.03 ± 0.00
Doxorubicin	0.25 ± 0.03	ND	0.26 ± 0.04	0.83 ± 0.1	ND	ND
Etoposide	60.5 ± 8.5	ND	ND	7.6 ± 1.3	ND	15.2 ± 1.8
Fluorouracil	20.2 ± 3.6	ND	ND	ND	ND	1.4 ± 0.2
Ifosfamide	0.81 ± 0.05	0.3 ± 0.01	0.58 ± 0.14	1.2 ± 0.07	0.13 ± 0.02	0.65 ± 0.08
Irinotecan	0.71 ± 0.03	0.05 ± 0.05	ND	0.07 ± 0.01	0.36 ± 0.06	ND
Methotrexate	0.14 ± 0.01	0.02 ± 0.00	0.03 ± 0.00	0.01 ± 0.00	ND	0.01 ± 0.0
Thiotepa	0.07 ± 0.01	ND	0.07 ± 0.00	0.31 ± 0.05	0.06 ± 0.00	0.23 ± 0.01
Vinorelbine	ND	0.23 ± 0.00	ND	0.43 ± 0.2	ND	ND

[a]Mean ± S.D. of three replicates. ND = not detected (less than the limit of detection), NA = not available. Permeation limits acceptable by ASTM standards D6978-05 and F739-99a and European Standard EN 374-3 are 10, 100, and 1000 ng/cm² · min, respectively.

Table 7.
Permeation of Cytotoxic Agents through Gloves after 60 Minutes

Drug	Permeation Rate (ng/[cm² · min])[a]					
	Touch N Tuff	Nitra-Tex	Micro-Touch Plus	DermaClean	Gammex PF	Perry Encore 85
Carmustine	203.1 ± 25	4.24 ± 0.01	77.1 ± 0.08	376.6 ± 6.3	ND	203.6 ± 34
Cisplatin	7.6 ± 1.3	ND	3.9 ± 0.4	ND	ND	67.7 ± 7.6
Cyclophosphamide	0.81 ± 0.07	1.43 ± 0.1	0.07 ± 0.0	0.21 ± 0.02	0.10 ± 0.01	0.067 ± 0.0
Cytarabine	0.02 ± 0.00	0.05 ± 0.00	ND	1.46 ± 0.07	0.16 ± 0.01	0.40 ± 0.00
Docetaxel	0.15 ± 0.01	0.04 ± 0.00	0.19 ± 0.01	0.36 ± 0.01	0.60 ± 0.02	0.03 ± 0.00
Doxorubicin	0.28 ± 0.04	ND	0.32 ± 0.02	0.97 ± 0.17	0.05 ± 0.00	ND
Etoposide	129.1 ± 8.9	ND	ND	55.1 ± 5.8	5.3 ± 0.8	43.4 ± 7.6
Fluorouracil	56.9 ± 5.8	ND	ND	ND	ND	6.7 ± 1.3
Ifosfamide	0.77 ± 0.02	0.30 ± 0.01	0.57 ± 0.01	1.32 ± 0.03	0.15 ± 0.01	1.22 ± 0.07
Irinotecan	0.16 ± 0.1	0.02 ± 0.00	0.03 ± 0.00	0.01 ± 0.00	0.01 ± 0.04	0.01 ± 0.00
Methotrexate	0.16 ± 0.01	0.02 ± 0.00	0.03 ± 0.00	0.01 ± 0.00	0.01 ± 0.00	0.01 ± 0.00
Thiotepa	0.17 ± 0.00	0.07 ± 0.00	0.15 ± 0.00	1.14 ± 0.07	0.13 ± 0.01	0.41 ± 0.03
Vinorelbine	0.09 ± 0.00	0.26 ± 0.02	ND	0.24 ± 0.01	0.1 ± 0.01	0.07 ± 0.00

[a]Mean ± S.D. of three replicates. ND = not detected (less than the limit of detection), NA = not available. Permeation limits acceptable by ASTM standards D6978-05 and F739-99a and European Standard EN 374-3 are 10, 100, and 1000 ng/cm² · min, respectively.

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