Hazardous Drug Locking Capacity of Activated Carbon-Based CSTD: 3 Approaches

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Objective

Closed system transfer devices (CSTDs) incorporate various hazardous drug (HD) vapor containment technologies. While containment capacity of balloon-based devices is limited to balloon volume, that of devices with activated carbon drug-binding mechanical barriers is independent of physical size (Figure 1). Studies have shown that such devices can contain at least 75 L of HD vapors[1] (> 25 µg) but have not determined upper limits of containment capacity.

The aim was to calculate and experimentally determine the maximum HD vapor adsorption capacity of an activated carbon matrix-based CSTD.

Figure 1 Containment capacity of balloon-based devices (A) is limited by balloon volume, while activated carbon in drug-binding mechanical barrier devices (B) contain microscopic pores that bind hazardous molecules inside, invisible to the human eye.

Methods

Maximum adsorption capacity was determined using three different approaches:

Method 1

Weight % adsorption capacity specifications using ethyl acetate uptake were obtained from the activated carbon manufacturer (Figure 2). Adsorption capacity per device was calculated using mean carbon mass per device (n = 10 on analytical balance).

Figure 2 Schematic representation of ethyl acetate adsorption capacity method. Dry activated carbon is maintained in a desiccator in the presence of ethyl acetate and weight increase is monitored.

Method 2

Vapors of propylene glycol methyl ether (PGME) surrogate were produced in a Dreschel-type device and pumped at constant concentration (5.9 mg/L) and flow (13 L/min) through a CSTD containing the carbon drug-binding matrix until release was detected by volatile organic compound detector (Figure 3).

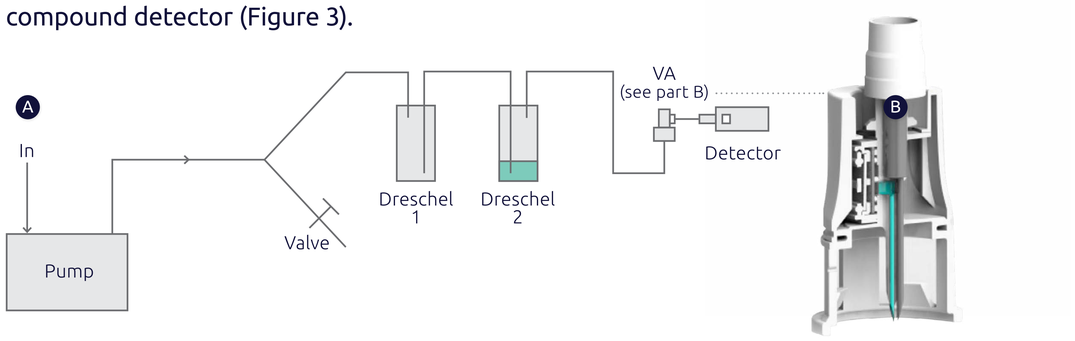

Figure 3 (A) Schematic representation of experimental set up for adsorption capacity determination by methods 2a and 2b. Air was supplied at constant flow through a container containing liquid PGME and PGME vapor. Vapor concentration above the liquid was 5.9 mg/L. VA = Vial Adaptor containing an activated carbon drug-binding mechanical barrier. Air flow was from the spike of the Vial Adaptor towards the activated carbon component. (B) Air path (in green) of Vial Adaptor through which the challenge vapor was flown.

Method 2a: Carbon matrices from 3 devices were weighed before and after the procedure. Using mass increase, maximum adsorption capacity was determined.

Method 2b: Using time until release, maximum adsorption capacity was determined, using the equation:

Time x Flow rate x Concentration = Adsorbed mass

Vapor concentrations of HDs at room temperature were calculated using published Henry's constants[2]. Theoretical and experimental surrogate adsorption capacities were used to determine the vapor volume of a worst-case real HD required to reach this capacity.

Results

5-Fluorouracil (5-FU) has the highest vapor concentration of HDs at room temperature: 339 ng/L.

Using ethyl acetate uptake (method 1), adsorption capacity was determined to be 17 mg per device For PGME.

Mean adsorption capacity was 4.2 mg by mass increase (method 2a) and 25.9 mg by time till release (method 2b).

Table 1 Calculated gas phase concentrations of most volatile hazardous drugs in closed containers at room temperature. 5-FU is the largest.

Drug	Gas phase conc. at 25°C (ng/l)
Thiotepa	1.16×10^{2}
Cyclophosphamide	2.78×10^{2}
Cisplatin	8.55×10^{-16}
Carboplatin	2.25×10^{-2}
Carmustine	6.42
Etoposide	1.43×10^{-18}
5-Fluorouracil	3.39×10^{2}

Mass increase by time until detection was calculated as follows:

Time x Flow rate x Concentration = Adsorbed mass

20.3 s x 13 L/min x 1 min/60 s x 5.9 mg/L = 25.9 mg

Table 2 Mass increase and time until detection for 3 samples of activated carbon matrices subjected to PGME vapor flow (methods 2a and 2b).

Sample	1	2	3
Mass increase (mg)	3.8	4.1	4.7
Mean mass increase (mg)		4.2	
Time until detection (s)	21	14	26
Mean time until detection (s)		20.3	

Volume of 5-FU vapors required to reach maximum adsorption capacity is equivalent to adsorption capacity divided by vapor concentration (Table 3):

$$\frac{\text{Adsorption capacity [mg]} \times 10^{6}\ \text{ng/mg}}{339\ \text{ng/L}} = \text{Vapor volume capacity}$$

Table 3 Calculated volumes of 5-FU vapors required to reach adsorption capacity, according to results of each method.

Method	Adsorption capacity (mg)	Vapor volume capacity (L)
1	17	50,000
2a	4.2	12,000
2b	25.9	76,000

Discussion & Conclusions

Three approaches estimated maximum adsorption capacity per activated carbon-based CSTD corresponding to 12,000-76,000 L of worst-case HD vapors, 160-1000 times higher than the volume used to challenge the device in previous studies (75 L). Volumes are expected to be higher for HDs other than 5-FU.

Considering that a CSTD typically will not have more than 100-200 ml of drug vapor forced through the activated carbon matrix, the CSTD tested provides a safety margin of 60,000-fold or more.

Sponsorship

Sponsored by Simplivia Healthcare Ltd, the manufacturer of Chemfort® CSTD.

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References [1] Levin G, Sessink PJM, *J. Oncol. Pharm. Pract.* 2021; doi: 10.1177/10781552211030682. Epub ahead of print.
[2] Wilkinson AS, Allwood MC, et al. *PLoS One.* 2018;13(10): e0205263.