Evaporation behavior of antineoplastic drugs: relevance of gaseous & airborne particle inhalation

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Introduction and Aims

Handling of antineoplastic drugs (ADs) has possible side adverse effects such as mutagenicity, teratogenicity or cancerogenicity[1]. Health-care personnel handling such agents may be exposed via several pathways including dermal contact, inhalation (aerosols or vapours) or unintentional ingestion.

Previous studies have shown frequent contamination of working areas by ADs including contamination of various surfaces (floor, tables, vials, telephones etc.). However, air contamination by ADs has been documented sporadically and dermal uptake is considered the main route of exposure.

On the other hand, presence of ADs in the ambient air has not been studied in detail, although vapor pressures (VP) of selected ADs (such as carmustin, cisplatin, cyclophosphamide, dacarbazine, doxorubicine, etoposide, fluorouracil and paclitaxel) has been measured and reach up to 22.5mPa at 20 degrees Celsius (**Table 1**). For small particles (d = 1 micrometer), these values are high enough to expect evaporation time in the range of several seconds to minutes[2].

Based on the previous measurements of VPs, here we present experimental studies of evaporation of selected antineoplastic agents under controlled laboratory conditions (ventilated BSC cabinet).

Results

Only minor non-significant evaporation of four of the studied compounds (cisplatin, cyclophosphamide, fluorouracil and paclitaxel) was observed (Fig. 1).

About 40% of doxorubicin (loaded at 60 ng/cm^2) evaporated within 12 hours (Fig. 2).

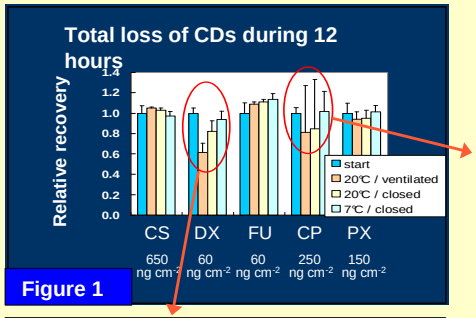


Figure 1

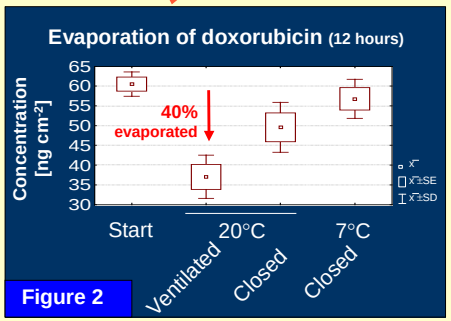


Figure 2

Specific interaction was found between cyclophosphamide and PVC that absorbed about 30 % of loaded cyclophosphamide under the laboratory temperature (Fig. 3A).

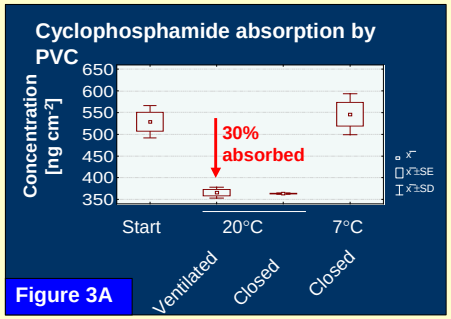


Figure 3A

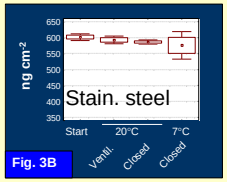


Fig. 3B

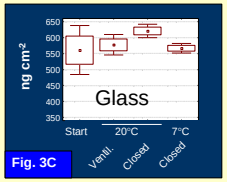


Fig. 3C

Discussion and conclusions

Previous studies focused on evaluation of VP of ADs have shown that evaporation/sublimation of these agents can be expected (see comparison in **Table 1**).

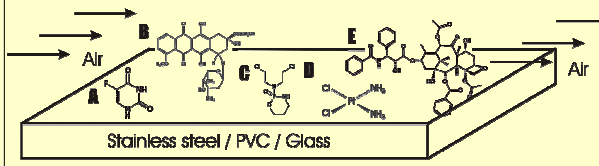
Table 1: VP of CDs in comparison with some well-known substances

Substance	Vapour pressure at 20℃ [Pa]
Antineoplastic drugs	$1\text{-}23*10^{-3}$
Diethyl phthalate	$99*10^{-3}$
Mercury	$16*10^{-2}$
Water	$23*10^{-2}$

This experimental study confirms that at least some commonly used ADs (such as doxorubicin) can evaporate under laboratory temperatures and conditions. Interestingly, our results do not fully correspond to the measured vapour pressure values: doxorubicin (VP = 1 mPa) was expected to evaporate less than for example paclitaxel (VP = 23 mPa; no evaporation for paclitaxel observed).

Significant absorption of cyclophosphamide by PVC corresponds to relatively easy permeation of this compound through vinyl material (e.g. gloves and gowns)[3]. We propose that PVC and related materials (e.g. linoleum) should be avoided in oncology wards and pharmacies. These materials may retain ADs and interfere with efficient decontamination.

Further indoor fate of ADs and their possible health impacts on occupationally exposed health-care personnel should be studied, and appropriate preventive and protective measures should carefully be applied.



Materials and methods

Trace amounts of five ADs (fluorouracil (A), doxorubicin (B), cyclophosphamide (C), cisplatin (D), and paclitaxel (E)) were experimentally dosed on the surfaces of three diferent materials (stainless steel, PVC, glass) and placed into the biological safety cabinet for 12 hours. After this period the surfaces were sampled, analyzed by HPLC or AAS and compared with appropriate controls (closed vials kept at room temperature 20°C and/or in refrigerator). Significant differences were analyzed by non-parametric statistics (Mann-Whitney test, $p < 0.05$).

References

[1] IARC. Monographs on the evaluation of cancinogenic risk of chemicals to humans: Pharmaceutical drugs. Lyon, France. **[2]** Kiffmeyer T, Kube C, Opiolka S, Schmidt KG, Schoppe G, Sessink PJM. *The Pharmaceutical Journal.* 2002; 268: 331-337. **[3]** Wallemacq PE, Capron A, Vanbinst R, Boeckmans E, Gillard J, Favier B. *American Journal of Health-System Pharmacy.* 2006; 63(6): 547-556.

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