Compatibility of QimoHarpoon Device with Cytotoxic Drugs

RESEARCH WITH PLYMOUTH UNIVERSITY

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INTRODUCTION

The QimoHarpoon system is a new closed–system drug transfer device (CSTD) for cytotoxic compounding. It uses a silicon balloon to expand and contract to equalise air pressure and prevent aerosols.

This study evaluated the physical/chemical compatibility of the device with cytotoxic drug solutions to ensure drug safety and efficacy were maintained.

Six drugs were selected; cisplatin, docetaxel, epirubicin, etoposide, 5-fluorouracil and paclitaxel. These represented hydrophilic and lipophilic molecules, high- and low – pH formulations, and the presence of various solubilisers and co-solvents to provide a comprehensive challenge to the device.

A separate study challenged the permeability of the balloon to the drugs to simulate inadvertent contamination with solution.

METHODS

QimoHarpoon CSTD's were connected to original manufactures vials of each of the 6 test drugs; cisplatin, docetaxel, epirubicin, etoposide, 5-fluorouracil and paclitaxel at concentrations of 1, 20, 2, 20, 25, and 6mg/mL, respectively.

Triplicate "test" vials of each drug, with the solution in contact with the device fluid-path, were stored at 5 and 25°C for 7 days, together with triplicates of Control vials with no device attached.

Samples of each solution were taken at 0, 1, 3, 4 and 7days and were subjected to drug assay (validated stability-indicating HPLC), pH, visual and sub-visual particle counts, and assay for Cr and Fe metals by ICP-MS.

In a separate experiment, device balloons were filled with 50mL of each drug solution and then immersed in recipient solution (water except for cisplatin where 0.9% NaCl was used) at 25° for 24 hr, followed by analysis of recipient solution for drug permeation.

RESULTS AND DISCUSSION

Compatibility study: There was no difference between test (with device) and control (no device) vials in visual appearance, sub-visual particulate counts and pH at any of the sample points. The drug assay remained between 95-105% of initial concentration in all test and control vials at all time-points. In some cases there was an increase in Fe and Cr concentrations in the test vials compared to controls (Table 1, below). However, these were all significantly below the calculated levels permitted in EMEA guidelines[1] .

Table 1: Levels of Fe and Cr in test and control vials

Drug solution	Temp °C	[Fe] day 7 (ppb) Control	Test	[Cr] day 7 (ppb) Control	Test	Fe limit (ppb)*	Cr limit (ppb)*
Cisplatin	2-8	28	45	4	5	6500	150
	25	8	47	2	7		
Docetaxel	2-8	9	14	6	6	130,000	3,000
	25	9	22	6	7		
Epirubicin	2-8	24	135	7	23	9600	220
	25	42	188	9	30		
Etoposide	2-8	55	96	20	28	108,000	2,500
	25	74	87	18	27		
5-FU	2-8	4	5	1	1	32,500	750
	25	4	5	1	1		
Paclitaxel	2-8	9	14	6	6	22,300	520
	25	9	22	6	7		

Balloon Permeability study: No drug was detected in any of the recipient solutions (power to detect <0.00009% permeation) so the expansion balloon of the QimoHarpoon device was impermeable to the test drugs even under an extreme contamination challenge that would not be encountered in practice.

CONCLUSIONS

1. The QimoHarpoon device was physically and chemically compatible with the 6 test drug solutions after extended contact at 5 and 25°C. The device did not affect the quality of the representative selection of drugs tested.
2. Drug permeation of the expansion balloon did not occur
3. The QimoHarpoon device can be introduced into practice

Reference: 1. Guidelines on the Specification Limits for Residues of Metal Catalysts. Committee for Human Medicinal Products, European Medicines Agency, January 2007, London

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