10P

EFFECT OF VAPOUR PRESSURE ON THE DEPOSITION PATTERN FROM SOLUTION PHASE METERED DOSE INHALERS

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The introduction of highly lipophilic drugs such as tulobuterol, used in the treatment of asthma, have resulted in formulations in which the drug is dissolved rather than suspended in propellant. Previous work carried out in our laboratory (Ashworth et al in press) has shown that the behaviour of such drugs can be modelled using technetium-99m labelled hexamethyl propylene amine oxime (Tc-99m HMPAO) dissolved in chlorofluorocarbon (CFC) propellant mixtures. Deposition studies in man indicate that greater than 40% of drug can be delivered to the lungs, compared to 10% deposition for suspended particles (Newman et al 1981). In the present study, we have extended our investigations to examine the deposition from two CFC preparations with vapour pressures of 255KPa (Low Vapour Pressure Aerosol, LVPA containing Propellants 11,12 & 114 in the ratio 5:60:35) and 448KPa (High Vapour Pressure Aerosol, HVPA in which the ratio was 5:90:5) respectively. Sorbitan trioleate (0.067g) and Tc-99m HMPAO (approx 300 MBq) were added before crimping and sealing.

The aerosols fitted with a 50µl metering valve were administered to 11 volunteers as 5 sequential inhalations with ten-second breath holds (3MBq Tc-99m), following krypton-81m gas scans to delineate lung margins. Gamma scintigraphy was then used to assess deposition in central and peripheral airways. The study followed a crossover design and approval to administer the radioactive aerosols granted by the University Ethical Committee and the D.o.H.

Total lung deposition (mean ± s.d.) was 65 ± 10.4% for HVPA and 50.9 ± 17.0% for LVPA, which were significantly different ($P<0.05$, paired t test). Deposition was then determined for central and peripheral lung regions, oesophagus and stomach. The ratio of peripheral to inner zone activity from right and left lungs was used to calculate the 'Penetration Index' (Agnew et al 1981). The results are shown Table 1.

Table 1. Regional distribution of radiopharmaceuticals following pulmonary administration of aerosols or gas. Significant differences between LVPA & HVPA were tested using paired t test (*$P<0.05$)

	LVPA	HVPA	Kr-81m
	(mean ± s.d., n=11 in each group)		
Right lung centre	10.4±4.7%	13.4±3.2%	19.1±2.0%
Right lung periphery	15.8±5.4%	21.8±3.2% *	31.6±2.3%
Stomach	33.4±18.0%	18.5±7.4 %*	0.7±0.7%
Oesophagus	15.7±5.0%	16.4±6.1%	4.4±0.8%
Mean Penetration Index	1.6 ± 0.7	1.8 ± 0.4	

The data showed that a lower proportion of the dose was swallowed for HVPA compared with LVPA. Within the lung the proportion of the dose reaching the peripheral airways as determined by the penetration index was the same for both aerosols, although a greater pulmonary deposition of the dose was observed with HVPA. Additionally, the results obtained confirm previous observations that greater than 40% of the marker achieves pulmonary deposition when dissolved in the propellant phase.

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