Some Factors Affecting Inhaler Dosing

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Some factors affecting the dose from an inhalant dosage form have been studied. It was found that rate of dosing, but not pressure, influenced the amine dose from propylhexedrine inhalant N.F.

SOME ASPECTS of inhaler technology were discussed in this journal in 1962 by Kennon and Gulesich (1). From their work they concluded that the vapor pressure of the drug and additives in an inhalant dosage form was not the dose-determining factor. They contended that inhaler dosing is a process controlled by factors affecting the rates of volatilization, whereas, vapor pressure values represent an equilibrium situation. Recently, in answer to an inquiry from the National Aeronautics and Space Administration, the authors have substantiated the above findings and further studied the factors affecting the dose from an inhalant dosage form. The inquiry from NASA concerned the possible inclusion of propylhexedrine inhalant N.F. in the medical kit for the Apollo Space Program. Since the pressure inside the spacecraft is maintained at 5 lb./sq. in. absolute (p.s.i.a.), it was necessary to know the amount of propylhexedrine per inhalation which would emanate from the inhaler at this reduced pressure.

EXPERIMENTAL

A dosing chamber (Fig. 1) which could be operated at reduced pressures and varying flow rates was constructed. An oxygen source was attached to the inlet valve of the system and the outlet was attached to an aspirator. The chamber then was adjusted to maintain the desired pressure at a specific flow rate of oxygen. At the time of dosing, a valve which maintained an open system between the chamber and the dosing tube was closed. This caused the oxygen flow to pass through the inhaler unit carrying vapors down into the dosing tube which contained a standardized solution of sulfuric acid. The assay of the amine was done by making the solution alkaline and extracting with chloroform. The chloroform extract was titrated potentiometrically in an isopropanol–ethylene glycol solution with hydrochloric acid. Three inhalers were dosed and assayed at each condition.

RESULTS AND DISCUSSION

The results of the inhaler dosings are given in Table I.

The data indicate that reducing the pressure above the inhaler to 5 p.s.i.a. does not affect the dose delivered by the inhaler. However, the rate at which the oxygen is passed through the inhaler significantly affects the dose.

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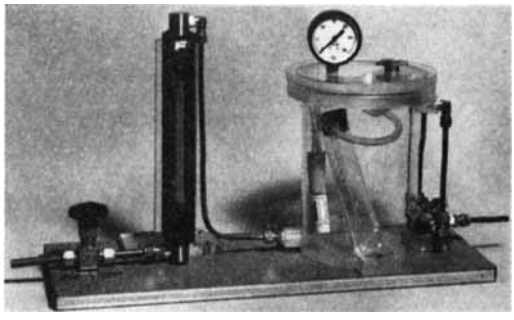

Fig. 1.—Dosing chamber for inhaler units. Chamber can be operated at varying pressures and flow rates.

TABLE I.—MILLIGRAMS OF PROPYLHEXEDRINE FROM INHALERS DOSED AT VARYING PRESSURES AND FLOW RATES

Flow Rate through Inhaler	Pressure	Propylhexedrine/L. of Oxygen passed through Inhaler, mg.
6 L./min.	5 p.s.i.a.[a]	0.39
6 L./min.	Atmospheric	0.45
1 L./min.	5 p.s.i.a.	0.71
1 L./min.	Atmospheric	0.75

[a] Pounds per square inch absolute.

The dosing of an inhaler may be considered analogous to a distillation process in that the active driving force of the system is the tendency for liquid and vapor to approach equilibrium. In the inhaler system this equilibrium is never attained. The fact that the vapor dose varied at different flow rates is direct evidence of this. If sufficient time were allowed for the passage of a constant volume of oxygen through the inhaler, the amount of drug evaporated would be independent of time since equilibration would occur. However, at a certain dosing rate of oxygen per unit time, the evaporation rate becomes dose determining. Thus, at a constant evaporation rate more drug is obtained per unit volume from a slow dosing rate than from a faster rate.

Since the change of pressure did not affect the dose, it may be assumed that the gases are behaving ideally at the pressures present in the system. Had the system been operated at higher pressures, collision with higher concentrations of molecules would have retarded the amount of amine vaporized and conceivably the dose would become pressure dependent.

REFERENCE

(1) Kennon, L., and Gulesich, J. J., *J. Pharm. Sci.*, **51**, 278(1962).