

THE RETENTION OF CINEOLE IN FREEZE DRYING

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As more volatile therapeutically active substances and flavourings are discovered, it becomes important to find ways of ensuring that preparations containing them are stable. Many substances are more stable in the dry state than when they are present in an aqueous formulation. Freeze drying is one important method of drying preparations without loss of potency. However, when an aqueous liquid containing volatile material is freeze dried, some of the volatile component will vapourise.

Little work has been carried out on pharmaceutical preparations to improve the retention of volatile substances in freeze drying. The purpose of this communication is to show that, when aqueous dispersions of cineole are slowly frozen in the presence of certain protective substances and then freeze dried, the amount of cineole retained can be increased.

Dispersions of 1 ml cineole in 20 ml 4% methylcellulose 450 were (A) rapidly frozen in liquid nitrogen or (B) slowly frozen over a 48 hr period in glass vessels enclosed in cardboard boxes insulated with 2 cm polyurethane foam in a freezer at $-12 \pm 2^\circ\text{C}$. The frozen samples were freeze dried to 0.2 torr. They were then reconstituted with 20 ml purified water and an accurately weighed quantity of 1-pentanol, as internal standard, was added to the reconstituted material, which was extracted with 20 ml ether and analysed by gas liquid chromatography, using a 15% Carbowax-20M on Chromosorb W column at 150°C , nitrogen carrier gas at 30 ml min^{-1} and an injection temperature of 200°C . 5.8% of the original sample was retained in method A samples, whereas 9.6% was retained in method B samples. It is assumed that the growth of large crystals of pure ice in method B resulted in the formation of microregions in which the cineole was trapped in the methylcellulose (Flink 1975). When the material is rapidly frozen only small crystals of ice are formed (Loncin & Merson 1979) and the protective action of the methylcellulose is less effective.

1 ml quantities of cineole were dispersed in 20 ml quantities of the aqueous vehicles given in the table below and freeze dried by method B. The order of protection afforded on freeze drying is Sucrose < Methyl Cellulose < Gelatin.

	Sucrose %				Methylcellulose %				Gelatin %				
	10	15	20	25	30	1	2	4	6	1	2	4	6
% cineol retained*	3.3	3.65	4.0	5.5	4.75	3.0	4.8	9.6	15.5	16.1	46.7	50.5	65.2
Standard deviation(%)	0.89	0.83	1.08	1.85	0.16	0.62	1.7	1.5	5.1	8.1	13.2	5.9	10.1

* Means of 6 samples.

Preliminary work with 1% and 10% sucrose enhanced the protective action of 4% methylcellulose 450, but aqueous concentrations of 0.05% and 0.25 % sodium chloride and 5% sodium glutamate in the same vehicle decreased percentages of cineole retained when they were freeze dried by method B.

Flink, J. (1975) in *Freeze Drying and Advanced Food Technology*. Ed. Goldblith, S.A., Rey, L. and Rothmayr, W.W. pp.351-412. Academic Press - London.

Loncin, M. and Merson, R.L. (1979) *Food Engineering Principles and Selected Applications*. pp.160-9. Academic Press - London.