

CEPHALOSPORIN POWDERS STERILIZED BY γ -RAYS

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Increasing application of ionizing radiation to the sterilization of drugs has prompted this study into the effect of γ -irradiation on a number of the cephalosporins. The necessary practice of sterilizing powders for injections by costly and highly demanding aseptic techniques makes sterilization by γ -rays most desirable.

The cephalosporins tested were cephalixin, cephaloridine, cephalothin Na and cephalapirin Na. 5g samples were irradiated (Jacobs & Melumad 1976) in open vessels with 1, 2.5 and 5 Mrad doses from a ^{137}Cs γ -ray source. Following irradiation samples were subjected to pertinent chemical and microbiological tests. Results of m.pt. determinations, microbiological (Jacobs 1977) and B.P. chemical assays, UV absorbance of aqueous solutions and specific optical rotation measurements (SOR) are presented in Table 1. NMR determinations show no differences between irradiated (5 Mrads) and unirradiated cephalixin. With the other three antibiotics there does appear to be some change in intensity of the peaks assigned to the two β -lactam protons. No products of radiolysis have been detected by Tlc.

Table 1. Analysis data for irradiated cephalosporins

Cephalosporin	Dose (Mrads)	M.pt. ^a (°C)	Micro assay (%)	sd	Chemical assay ^a (%)	UV ^{ab}	SOR ^a (°)
Cephalixin	0	191	(100)		(100)	415	+123
	1	191	99.3	0.6	99.7	405	+123
	2.5	190	97.2	0.5	98.9	410	+122
	5	189	93.3	2.6	99.2	405	+120
Cephaloridine	0	184	(100)		(100)	710	+44
	1	184	95.6	6.1	102.6	710	+43
	2.5	184	99.4	4.8	102.1	700	+44
	5	182	92.4	4.1	103.1	715	+44
Cephalothin Na	0	210	(100)		(100)	653	+114
	1	206	93.2	2.3	101.3	645	+114
	2.5	205	90.6	3.0	100.0	630	+111
	5	202	89.8	1.6	97.8	635	+119
Cephalapirin Na	0	198	(100)		(100)	725	+129
	1	195	96.1	1.6	99.2	730	+129
	2.5	194	93.4	4.1	98.3	740	+128
	5	189	88.4	5.6	96.1	715	+123

a means of \pm 2 determinations within $\pm 1.5\%$; b UV absorbance ($\times 10^5$)

Sterility testing (Jacobs 1977) showed that both irradiated and unirradiated powders were free of microorganisms. Whilst bacterial growth did occur in unirradiated samples previously contaminated with 10^6 *B.pumilus* spores, no growth was apparent in similarly contaminated samples which received the minimal radiation dose.

Cephalixin displays reduced potency with increasing radiation dose as indicated by microbiological assay. None of the other tests seem to support this observation. Cephaloridine is unaffected by radiation doses of up to 5 Mrads. The tests employed indicate that γ -irradiation reduces the potencies of cephalothin Na and cephalapirin Na. However, radiolysis products are in too small a concentration to be detected by Tlc. It is noteworthy that both cephalothin and cephalapirin possess an acetoxymethyl substituent in the C-3 position of the dihydrothiazine ring.

The cephalosporins were kindly donated by Glaxo (U.K.) and Bristol (U.S.A.).

Jacobs, G.P., Melumad, D. (1976) *Pharm. Acta Helv.* 51: 313-314

Jacobs, G.P. (1977) *Ibid.* 52: 302-304