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Effect of gamma radiation and ethylene oxide on neomycin sulphate

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Summary

Neomycin is affected by ethylene oxide but not by gamma radiation (2.75 Mrad). Differential refractometer is more advantageous in quantitating neomycin A, B and C than is the ninhydrin method.

Neomycin sulphate (I) was sterilized by ethylene oxide (EO) by the conventional procedure (British Pharmaceutical Codex, 1980), and by gamma radiation at a dose of 2.75 Mrad. The neomycin A, B and C of I were isolated by column chromatography on Biorad Ag 1×2 (British Pharmacopoeia, 1980). The eluate was passed through the analytical channel of a differential refractometer (RI) detector (DuPont Model 845) and collected in a fraction collector (Microcal TDC 80, Gilson Medical Electronics, U.S.A.). The reference channel of the RI detector contained water. The RI detector was connected to a 10 mV recorder to trace the histogram. The duration for collecting 160 fractions of 0.3 ml each was about 30 h.

Prior to the experiment, aqueous solutions of I at different concentrations (0.1, 0.2, 0.3, 0.4 and 0.5% w/v) were passed through the analytical channel of the RI detector, maintaining water in the reference channel. The response curve of RI was observed to be linear throughout the concentration range studied and up to 8×10^{-4} RI units, and passed through the origin.

The determination of the neomycins A, C and B (which is the order of elution) was carried out by: (i) reacting the eluate fractions with ninhydrin (British Pharmacopoeia, 1980); and (ii) planimetric measurement of the areas of the neomycin peaks in the histogram. The percentage of neomycins A and C with respect to that of

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TABLE I

Physical appearance	Control			2.75 Mrad			EO		
	Off white; free flowing			Off white; free flowing			Brown hard mass		
	U	A	C	U	A	C	U	A	C
Colorimetry	NR	6	10	NR	6	11	NR	4	11
RI method	2	5	13	1	3	8	1	3	11

U = unknown species; A = neomycin A; C = neomycin C; All values are expressed as % of B. NR = no reaction.

B as determined by both methods is given in Table I along with the physical appearance of the samples.

The disadvantages of the colorimetric method are: (i) it is affected by CO_2, NH_3 and impurities in ethanol and the ion exchange resin; and (ii) the analysis of the fractions takes 16 h. The advantages of the RI detector is: (i) its sensitivity to temperature variation (10^{-6} RI units/h at room temperature) can be easily controlled by thermostatting the detector; (ii) the planimetry of the peak areas is easy and can be carried out in 2 h; and (iii) it can reveal an unknown species which could not be detected by colorimetry and which exists in all of the 3 samples and emerges from the column before neomycin A. The RI method can therefore be a reliable alternative to colorimetry.

Gamma radiation does not induce any perceptible change in the physical appearance of I. As the loss in the microbiological activity, even at a 5 Mrad dose, is reported to be negligible (Fleurette et al., 1975) gamma radiation would be preferable to sterilize I. As I may have low or susceptible bioburdens, I can be sterilized effectively at lower doses than 2.5 Mrad (USP XX-NF XV).

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