

THE EFFECT OF RADIATION STERILISATION ON DISULFIRAM IN SOLID STATE

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Disulfiram (Antabuse, Esperal, bisdiethylthiocarbamoyl disulphide) is a well-known drug administered in treatment of chronic alcohol disease as a substance producing many unpleasant side effects such as headaches, memory lapses, cardiac and circular system problems, alimentary system problems, allergies and others in response to alcohol consumption. These symptoms appear because disulfiram inhibits alcohol oxidation at the stage of acetate aldehyde, binds alcohol forming strongly toxic ammonium complexes and blocks synthesis of norepinefrine.

Disulfiram is applied in the form of tablets or hypodermal implants. According to the pharmacopoeia recommendations the latter as well as many other forms of drugs (injections, infusions or eye drops) should be sterile. In the 1980s and 1990s the first attempts were made at application of radiation sterilisation. According to literature [1] small doses of radiation < 1 kGy can be used without any risk of degradation of disulfiram. Results of our recent study performed for the standard doses (10-25 kGy) recommended for radiation sterilisation by European Union Standards (EN 552) do not confirm the earlier reports. As a result of radiation sterilisation disulfiram emits specific unpleasant smell and changes its colour from white to grey-green. To recognise fully the character of these changes a thorough study of disulfiram sterilised *in substantia* has been performed in an extended range of radiation doses from 10 to 100kGy. Sterilisation was carried out in solid state, at room temperature, and at normal air humidity with the electron beam of 9.96 MeV from an accelerator. The irradiation caused changes in the substance were analysed 2 days after the irradiation. All measurements were made simultaneous for the irradiated and non-irradiated substance.

The analyses were performed by a number of instrumental methods including: spectrophotometric (UV, IR, NMR, MS), chromatographic (TLC, HPLC), thermal (TG, DSC), X-ray diffraction (XRD) and other (SEM, EPR).

The results obtained were discussed against a background of literature data and the final conclusion was that disulfiram in solid state is characterised by a too low radiochemical stability to ensure no risk of its degradation on its radiation sterilisation with an electron beam.

[1] Phillips M., Agarwal R.P., Brodeur R.J., Garagusi V.F., Mossan K.L.: Stability of an injectable disulfiram formulation sterilized by gamma radiation. Am. J. of Hosp. Pharm.42, 343-345, 1985.