



Cardiotoxicity of 5-fluorouracil: a question of formulation

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Mots-clés	Animals [6], Chemistry, Pharmaceutical [7], Drug Stability [8], Fluorouracil [9], Heart Diseases [10], Rabbits [11], Risk Factors [12], solubility [13] The cardiotoxicity of 5-fluorouracil (FU) was attributed to degradation compounds present in the injected vials, fluoroacetaldehyde (Facet) and fluoromalonaldehydic acid (FMald). These compounds are formed with time in the basic medium necessary to solubilize FU. FU-NaOH vials were much less cardiotoxic than FU-Tris vials on the isolated perfused rabbit heart model since, in FU-Tris vials, Facet and FMald are stored in stable "depot" forms, which are adducts with Tris, whereas, in FU-NaOH vials, they are extensively chemically transformed. Cardiotoxic fluoroacetate (FAC), arising from Facet metabolism, was found in urine of patients, with a ratio FAC/FU catabolites 10-30 fold lower in patients treated with FU-NaOH than in those treated with FU-Tris.
Résumé en anglais	The cardiotoxicity of 5-fluorouracil (FU) was attributed to degradation compounds present in the injected vials, fluoroacetaldehyde (Facet) and fluoromalonaldehydic acid (FMald). These compounds are formed with time in the basic medium necessary to solubilize FU. FU-NaOH vials were much less cardiotoxic than FU-Tris vials on the isolated perfused rabbit heart model since, in FU-Tris vials, Facet and FMald are stored in stable "depot" forms, which are adducts with Tris, whereas, in FU-NaOH vials, they are extensively chemically transformed. Cardiotoxic fluoroacetate (FAC), arising from Facet metabolism, was found in urine of patients, with a ratio FAC/FU catabolites 10-30 fold lower in patients treated with FU-NaOH than in those treated with FU-Tris.
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