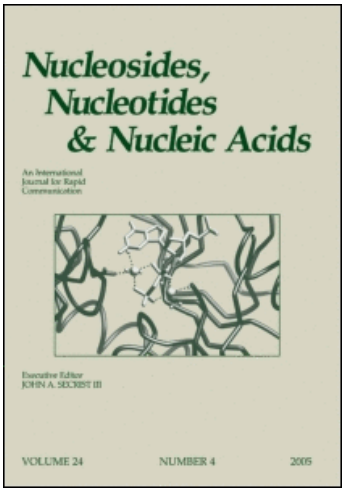


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# Acetaldehyde Adducts of DNA

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# ACETALDEHYDE ADDUCTS OF DNA?

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**Abstract:** In this paper we report that acetaldehyde, the major metabolite of ethanol oxidation, is bound to DNA in dose-dependent manner under conditions comparable to physiological.



Acetaldehyde (AA) is the first metabolite of ethanol oxidation. The association between heavy alcohol consumption and the carcinogenic potential of ethanol seems well established. The biochemical characterization of AA adducts in this laboratory as well as by others (see ref. 1 and references therein) has mainly been limited to proteins; AA binds covalently to amino groups of proteins by a two-step addition-elimination mechanism, resulting in labile imine, enamine or hydroxyalkyl structures, and in more stabile reduced structures of imines and enamines. However, very little is known as to the possible interactions of DNA and AA. 2',3'-O-isopropyllidine-adenosine, -cytidine, and guanosine have been described as reacting with formaldehyde in ethanol solution, giving N-etoxymethyl derivatives (2) and it has also been reported that acetaldehyde forms nucleoside adducts in in vitro circumstances by cooperative reaction of 1-50% acetaldehyde and alcohols (3).

To clarify the possible AA adduct formation in nucleic acids we incubated calf thymus DNA (2 mg/ml) with 0 to 500 $\mu$M concentrations of [1,2-$^{14}$C]-AA in phosphate-buffered saline (pH 7.4) without any reducing agents. After incubation, DNA

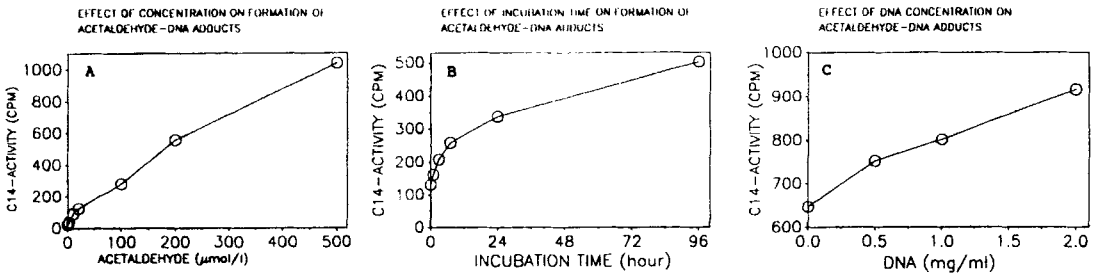


FIGURE 1. Binding of [1,2-$^{14}$C]-AA to DNA in phosphate-buffered saline (pH 7.4) at 37°C. After incubation, DNA was precipitated with perchloric acid together with 200 μg of carrier DNA. a) Dose-curve with different AA concentrations. Incubation time was 96 hours. The DNA concentration was 2 mg/ml. b) Time-curve with 400 μmol/l AA, 2 mg/l of DNA and 120 μg of carrier DNA. c) Dose-curve with 400 μmol/l AA and different concentrations of DNA.



was precipitated with perchloric acid and the amount of AA-derived radioactivity, co-precipitated with DNA, was measured (Fig 1a). Appearance of AA-derived radioactivity increased rapidly during the first hours (Fig 1b). Thereafter a slower increase of the binding was recorded. Fifty percent of the maximum binding was reached at 24 hours' incubation. The amount of AA-derived radioactivity increased linearly with AA concentration; even low AA concentrations from 3 to 20 μM caused detectable binding of radioactivity to DNA. A considerable amount of AA was bound immediately to carrier DNA (Fig 1c). However, a dose-dependent increase in the AA-binding was noted with higher DNA concentrations.

The results of the present investigation indicate that AA forms DNA adducts under conditions comparable to physiological. A more detailed characterization of these DNA-AA adducts is in progress in our laboratory.

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