

EFFECT OF THYMINE HYDROPEROXIDE ON DNA BASES

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Since the discovery by Müller¹⁾ that X-ray causes mutagenic effects, the radiation chemistry of nucleic acids has received considerable attention.²⁾ It has been shown³⁾ that radiolysis of aerated aqueous solution of nucleic acids, pyrimidine nucleotides, uracil or thymine results in the formation of the hydroxyhydroperoxides. Among them thymine hydroperoxide (6-TOOH; cis-5-hydroxy-6-hydroperoxy-5,6-dihydrothymine) was reported to be mutagenic on transforming DNA of *Haemophilus influenzae*.⁴⁾ Moreover, transition metal ions were found to enhance the mutation frequency; Cu⁺⁺ was much more effective than other ions.

The studies presented here were undertaken to evaluate the effect of Cu⁺⁺ on the reaction between 6-TOOH and cytosine, and to demonstrate the effect of 6-TOOH on neighbouring DNA bases. For instance, a reaction of 6-TOOH with cytosine in the presence of copper sulfate at 35 °C in H₂O produced cis-5,6-dihydroxy-5,6-dihydrothymine (cis-Thy glycol), 5-hydroxy-5-methylhydantoin, and cytosine-N(3)-oxide. On the other hand, in the absence of copper sulfate, the above reaction afforded cis-Thy glycol (53.9%), 5-hydroxy-5-methylbarbituric acid (27.7%), 5-hydroxy-5-methylhydantoin (10.1%), and an unidentified compound (8.3%). As it was presumed that the 6-TOOH might form a complex with Cu⁺⁺, we recrystallized the 6-TOOH from copper sulfate solution to give prisms. However, the X-ray diffraction analysis indicated that the 6-TOOH crystallized as a dihydrate in the cis configuration, and that the 6-TOOH was not coordinated to copper in the crystal.

References:

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