New Pyrimidines Derived from Thymidine and 5-Fluorouracil and Some of their Biochemical Properties

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During continued studies of reduction products of pyrimidines and pyrimidine nucleosides [1], some new compounds with characteristic spectral properties have been detected. This report deals with products formed when thymidine and 5-fluorouracil, respectively, is treated with 3 % NaHg in 0.2 M aqueous acetic acid.

Our investigations strongly indicate that these compounds are 5-methyl-2-pyrimidone-2′-deoxyriboside and 5-fluoro-2-pyrimidone [2].

The 5-methyl-2-pyrimidone-2′-deoxyriboside was purified by chromatography on a Dowex 1 x 4 column in the borate form[3], followed by paper chromatography in the butanol:ethanol:ammonia(conc.):water (4:1:2:1) system. The substance was crystallized from absolute ethanol as white platelets. Its absorption maxima in 0.1 N NaOH, distilled water, and 0.1 N HCl are, respectively, 321, 314, and 325 mμ. The corresponding values for ε_{max} are 7.1×10^3, 6.1×10^3, and 8.2×10^3. Using the spectrophotometric method of Fox and Shugar [4], the p*K*a values were determined to be 2.2−2.4 and >12. The latter is probably due to dissociation in the sugar moiety. Contrary to thymidine, the glycoside bond is very labile under acid condition.

5-Fluoro-2-pyrimidone was purified by chromatography on a Dowex 1 x 8 column followed by paperchromatography in the butanol:ethanol:ammonia(conc.):water (4:1:2:1) system. The compound was recrystallized from ethyl acetate and obtained as white needles. The 5-fluoro-2-pyrimidone exhibits a shift in absorption maxima. In 0.1 N NaOH, distilled water and 0.1 N HCl the absorption maxima are respectively 311, 316, and 319 mμ. The spectrophotometrically determined dissociation constants are 1−2 and 7.2−7.3. The molecular extinction coefficient is 4.4×10^3 in 0.1 N HCl.

5-Methyl-2-pyrimidone-2′-deoxyriboside has been tested as a growth factor for the organism *Lactobacillus acidophilus* R 26 Orla Jensen, which requires a deoxyriboside for growth. By using the method described by Hoff-Jörgensen [5], the 5-methyl-2-pyrimidone-2′-deoxyriboside was determined to have the same activity as thymidine in promoting growth in this organism. The substance has no activity as substrate for the thymidine phosphorylase, isolated from horse liver [6].

In agreement with the finding that 5-methyl-2-pyrimidone-2′-deoxyriboside served as a growth factor for *Lactobacillus acidophilus*, the 5-fluoro-2-pyrimidone could be converted to the corresponding deoxyribose-compound by a transglycosidase prepared from the same organism according to MacNutt [7].

In contrast to 5-fluorouracil which inhibits the growth of *E. coli* K-12 strain at very low concentrations, 5-fluoro-2-pyrimidone has no effect on the growth even at relatively high concentrations.

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Effect of Cordycepin on DNA Synthesis and the Ribotide Pool of Ehrlich Ascites Tumor Cells *in vitro*

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The adenine nucleoside cordycepin [1] has been found not only to inhibit incorporation of $^{32}P_i$ into DNA of Ehrlich ascites tumor cells *in vitro* but also to give rise to accumulation of phosphorylated derivatives in the cells [2].

Investigation of the effect of increasing concentrations of cordycepin has revealed that the presence of cordycepin triphosphate (ACTP) in the cells has no great effect on either