FLAVIN CATALYSTS BEARING SULFUR FUNCTIONAL GROUPS

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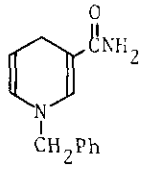
Flavins catalyze a variety of biologically important chemical transformations in a living body. A few flavoenzymes, i.e., lipoamide dehydrogenase, glutathione reductase and thioredoxin reductase, have been known to promote reduction of physiological disulfides with dihydronicotinamide adenine dinucleotide phosphate (NADPH) to the corresponding thiols (reaction 1). Active sites of these enzymes

$$RS\text{-}SR + NADPH \xrightarrow{\text{flavoenzyme}} 2\ RSH + NADP^{+} \qquad (1)$$

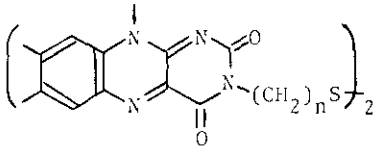
commonly possess neighboring flavin adenine dinucleotide (FAD) and disulfide group due to cystine residue. Investigation of the catalytic function of flavines bearing sulfur functional groups, enzyme model systems, revealed that the thiol group in proximity to the flavin plays essential role in the reduction of aliphatic disulfides such as phisiologcally important disulfides with dihydropyridine derivatives to the corresponding thiols.

1) 1-Benzyl-1,4-dihydronicotinamide (BNAH), a model of NADPH, was found to reduce aromatic disulfides to the arenethiols without any catalyst upon heating at 80° or irradiation with visible light via free radical chain processes. However, under the same conditions, aliphatic disulfides could not be reduced.

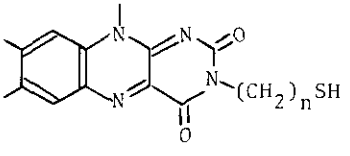
2) An addition of catalytic amount of 3-methyllumiflavin into the above reaction system accelerated the reduction of aromatic disulfides, however, still aliphatic disulfides could not be reduced by this system. Thus, ω-mercaptoalkyl group was introduced in the flavin catalyst. In the presence of catalytic amount of $(3\text{-FlS})_2$ the reduction of aliphatic disulfides with BNAH appeared to proceed successfully affording the thiols. The function and mechanism of flavins which bear sulfur functional groups will be discussed.



BNAH



$(3\text{-FlS})_2$



3-FlSH