Effect of *p*-dimethylaminoazobenzene on the nucleic acids : potassium ratios of rat liver

It was observed recently in this laboratory[1] that the growth of the Crocker sarcoma S-180 in Swiss mice caused an increase of the DNA: K ratio in the liver, lung, and kidney of the host, but that the RNA: K ratio remained unchanged. ASIMOV *et al.*[2] reported that in human carcinoma there was no change in the DNA: K ratio of the tumor as compared with the tissue surrounding it. In the present experiments, we have studied the effects of *p*-dimethylaminoazobenzene (*p*-DAB), where a well defined tumor can be compared with the tissue from which it arises.

As shown in Table I, the hepatoma is characterized by a DNA: K ratio definitely much higher than that of normal liver. The ratio is also significantly higher for the liver of rats fed *p*-DAB, but which have not yet developed a hepatoma. The RNA: K ratio in the liver decreases significantly, but for the hepatoma the change is not significant at a level of $p = 0.05$.

TABLE I

PERCENTAGE CHANGE IN DNA:K AND RNA:K RATIOS IN THE LIVERS AND HEPATOMAS OF RATS FED *p*-DIMETHYLAMINOAZOBENZENE*

Group	*No. of rats*	*Change, %*	
		DNA : K	*RNA : K*
Liver, low riboflavin	14	+ 28	—18
Liver, high riboflavin	8	+ 16	— 9
Hepatoma	12	+ 186	— 4

* Ratios in the livers of the controls: DNK: K, 0.56 ± 0.03; RNA: K, 2.74 ± 0.08.

Riboflavin has long been recognized as a protective factor in animals fed *p*-DAB. In the present study, it has been observed that when the vitamin is fed at a high level, it causes less marked changes in both ratios in the liver tissue of the experimental rats, but no change whatsoever for the hepatoma.

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1 N. M. RODRIGUEZ, H. T. HOCHSTRASSER, J. O. MALBICA AND L. R. CERECEDO, *J. Biol. Chem.*, 211 (1954) 483.
2 I. ASIMOV, H. M. LEMON, R. M. REGUERA, M. M. DAVISON AND B. S. WALKER, *J. Cell. Comp. Physiol.*, 37 (1951) 355.

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A relation between cystine content and ultraviolet sensitivity of proteins

The action of ultraviolet light on proteins has been extensively studied[1,2], but the mechanism by which proteins are denatured by light is not understood. An excellent review of possible theories may be found in a recent article by DOTY AND GEIDUSCHEK[3]. MCLAREN[4] has shown that the quantum yield for the inactivation of proteins decreases as the molecular weight increases. The correlation between the quantum yield and molecular weight, however, is not a particularly good one.

The purpose of this note is to indicate that the quantum yield for the inactivation of enzymes by light of wavelength 2,537 A is very closely related to the cystine content of the molecule. Table I shows the quantum yield and the per cent cystine composition for all proteins for which data are available. The per cent abundance of the aromatic amino acids is indicated simply to show that no correlation exists between these quantities and the quantum yield. The calculated value of the quantum yield depends upon the value chosen for the molecular weight. The agreement between quantum yield and cystine content is quite remarkable, especially when we consider the many different circumstances upon which the quantum yield may depend.

TABLE I

THE QUANTUM YIELD FOR ENZYME INACTIVATION BY 2,537 A LIGHT AND THE PERCENT ABUNDANCE OF SEVERAL AMINO ACIDS

Molecule	*Molecular weight*	*Quantum* yield*	*Percent abundance of*			*Tryptophan*	*References*
			cystine	*phenylalanine*	*tyrosine*		
Insulin	12,000	$4.5 \cdot 10^{-2}$	11.6	5.8	7.8	0.0	1, 5
Ribonuclease	15,000	$2.6 \cdot 10^{-2}$	6.6	2.5	5.7	0.0	1, 5
Lysozyme	14,700	$2.4 \cdot 10^{-2}$	4.2	1.7	2.5	5.1	6, 7
Chymotrypsinogen	24,000	$1.1 \cdot 10^{-2}$	3.2	2.3	1.6	3.2	8, 5
Chymotrypsin	20,000	$6.5 \cdot 10^{-3}$ **	3.2	2.3	3.5	3.2	1, 5
Gramicidin trios phosphate	8,700	$3.4 \cdot 10^{-3}$	0.0	0.0	0.0	22.5	9, 10
Dehydrogenase	50,000	$3 \cdot 10^{-3}$	1.0	3.8	2.8	1.1	11, 5
Pepsin	34,400	$2.4 \cdot 10^{-3}$	1.3	4.2	5.2	1.3	1, 5
Aldolase	140,000	$1.9 \cdot 10^{-3}$	1.0	2.0	3.2	1.2	12, 5
Catalase	225,000	$1 \cdot 10^{-3}$	0.8	—	3.8	—	8, 13
Trypsin	20,000	$1.8 \cdot 10^{-2}$ ***	—	—	5	3	14

* In some cases the quantum yields have been recalculated from the original data so as to agree with the indicated molecular weight.
** In the dry state the quantum yield is $2 \cdot 10^{-2}$ (Ref. 17).
*** In the dry state the quantum yield is $2.1 \cdot 10^{-2}$ (Ref. 8).

The emphasis placed on the role of cystine in the inactivation of proteins by 2,537 A radiation does not mean that the aromatic amino acids are not also important. For very low concentrations of cystine, the quantum yield would depend on other factors, such as molecular weight. As is seen in Table I, however, large changes in molecular weight produce only small changes in quantum yield. At 2,500 A cystine absorption represents a larger fraction of the total absorption coefficient than at any other wavelength[16]. If, as the data of Table I indicate, a quantum absorbed in a cystine residue has a larger chance of inactivating a protein molecule than one absorbed in an aromatic amino acid, the quantum yield for the inactivation of proteins should show a maximum in the region of 2,500 A. This maximum is found for trypsin[1,9], chymotrypsin[17] and ribonuclease[9].

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1 A. D. MCLAREN, *Advances in Enzymol.*, 9 (1949) 75.
2 M. ERRERA, *Progress in Biophys.*, 3 (1953) 80.
3 P. DOTY AND E. P. GEIDUSCHEK, *The Proteins*, H. NEURATH AND K. BAILEY, Editors, Academic Press, New York, 1953, Ia.
4 A. D. MCLAREN, *Science*, 113 (1951) 716.
5 G. R. TRISTRAM, *The Proteins*, H. NEURATH AND K. BAILEY, Editors, Academic Press, New York, 1953, Ia.
6 D. SHUGAR, *Biochim. Biophys. Acta*, 8 (1952) 302.
7 C. FROMAGEOT AND M. PRIVAT DE GARILHE, *Biochim. Biophys. Acta*, 4 (1950) 509.
8 R. SETLOW AND B. DOYLE, *Biochim. Biophys. Acta*, 12 (1953) 508.
9 R. SETLOW AND B. DOYLE, to be published.
10 S. MOORE AND W. H. STEIN, cited by E. BRICAS AND C. FROMAGEOT, *Advances Protein Chem.*, 8 (1953) 1.
11 D. SHUGAR, *Biochim. Biophys. Acta*, 6 (1951) 548.
12 F. LABEYRIE AND D. SHUGAR, *J. Chim. Phys.*, 48 (1951) 447.
13 R. K. BONNICHSEN, *Arch. Biochem.*, 12 (1947) 83.
14 H. GOLDENBERG AND A. D. MCLAREN, *J. Am. Chem. Soc.*, 73 (1951) 1131.
15 J. H. NORTHROP, M. KUNITZ AND R. M. HERRIOTT, *Crystalline Enzymes*, 2nd Ed., Columbia Univ. Press, New York, 1948.
16 G. H. BEAVEN AND E. R. HOLIDAY, *Advances in Protein Chem.*, 7 (1952) 319.
17 R. SETLOW AND B. DOYLE, *Arch. Biochem. Biophys.*, 46 (1953) 39.

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