

Uracil, a Precursor of Polynucleotide Pyrimidines in the Mouse

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While it has been shown that uracil can satisfy the growth requirements of pyrimidine deficient bacteria, the experiments of Plentl and Schoenheimer¹ have demonstrated that N¹⁵-uracil was not utilized by the rat for pyrimidine synthesis. Isotopic uridine² and uridylic acid³, however, were incorporated into polynucleotide pyrimidines by this animal. The rat seems to be the only mammal, where a more systematic investigation of pyrimidine utilization has been carried out, and the only free pyrimidine — with the possible exception of thymine⁴ — that could be used as orotic acid⁴.

We have for some time been interested in the pyrimidine biosynthesis in the Ehrlich ascites tumor in the mouse. During this work we found that the tumor cells *in vitro* could utilize both N¹⁵-orotic acid and N¹⁵-uracil for the synthesis of polynucleotide pyrimidines. Further experiments showed that N¹⁵-uracil was also incorporated *in vivo* into normal tissues.

The results of our experiments are summarized in Table 1.

It is clear that the utilization of uracil is of the same order of magnitude in all the tissues studied as that of orotic acid. As in no case occurred any incorporation of isotope into the purines, we consider it highly likely that the incorporation into pyrimidines did not depend on a more extensive degradation of the precursors. The species difference found is somewhat reminiscent of the demonstrated difference in the utilization of guanine by the rat and the mouse⁵.

A detailed account of the experimental procedures will be given together with a forthcoming publication of our work with the Ehrlich ascites tumor cells.

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Table 1. Incorporation of N¹⁵-orotic acid (16 % excess N¹⁵) and N¹⁵-uracil (9 % excess N¹⁵) into polynucleotide pyrimidines.

Organ	Atom % excess N ¹⁵ calculated on basis of 100 % N ¹⁵ in the precursor			
	Pentose nucleic acid		Desoxypentose nucleic acid	
	Uridine	Cytidylic acid	Thymine	Cytosine
Orotic acid:				
Ascites cells <i>in vitro</i>	2.18	0.36	0.16	0.07
» » <i>in vivo</i>	1.48	0.28	0.16	0.11
Mixed internal organs	0.89	0.28		
Uracil:				
Ascites cells <i>in vitro</i>	3.20	0.59	0.88	0.24
Liver <i>in vivo</i>	0.47	0.21		
Intestine <i>in vivo</i>	1.08	0.47		

In vitro: 0.1 mmoles of pyrimidine was incubated with 20 ml of ascites fluid during 3 hours. *In vivo*: 0.02 mmoles of pyrimidine / mouse was injected into ten mice and the animals were killed after 2 hours.