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Reaction Rates of a Muscle Model with Nucleotides

We have previously reported (*1*) that UTP (uridine triphosphate) might replace ATP (adenosine triphosphate), mole for mole, in eliciting the contractile response that is characteristic of the glycerol-extracted muscle fiber model. The present report (*2*) is an extension of this work to include an analysis of the rates of response of the model to ATP, UTP, and CTP (cytidine triphosphate). In addition, some indirect evidence is exhibited to support the hypothesis that the reaction of these nucleotides with the contractile protein may be a direct one that need not be mediated by a high-energy phosphate group transfer system such as the nucleoside diphosphokinase system identified by Krebs and Hems (*3*) and recently purified by Berg and Joklik (*4*).

The methods were essentially the same as those used in earlier experiments (*5*). Dog or rabbit psoas muscle fiber bundles were extracted at rest length in 2.9*M* glycerol at −15°C. A fiber bundle of about 0.1-mm² cross-sectional area was isolated and divided to provide a pair of shorter duplicate preparations, one of which was induced to contract with ATP, and the other of which was contracted in the presence of either CTP or UTP (*6*). The medium in which contraction was induced was phosphate-buffered $5 \times 10^{-2}M$ KCl containing $5 \times 10^{-3}M$ $MgCl_2$, at *p*H 7.8 and ionic strength 0.11 at 25°C. Nucleotides, as sodium salts, were added to the system to make their concentrations 4, 6, or $8 \times 10^{-4}M$. The latter value approximates the minimum amount of nucleotide necessary to induce maximal contraction (*5*). The tension developed by the model in the first minute following nucleotide addition was used as the criterion of the rate of the contractile response.

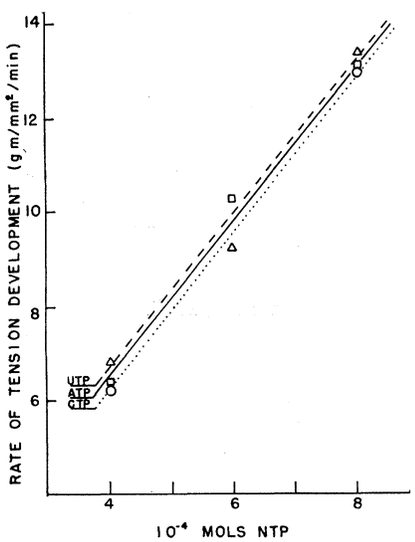

Fig. 1. Rate of tension development of the muscle model system when either ATP, CTP, or UTP was used as the stimulating nucleotide. Each point is the mean response of three or more fiber preparations. ATP, △——△; CTP, ○·····○; UTP, □ - - - - - □. The abbreviation NTP stands for any one of the three nucleotides tested.

The rates of tension development in a rabbit psoas model system are shown in Fig. 1. As nucleotide concentrations were increased toward the value necessary for maximal contraction, the rate of contraction increased linearly. It would appear that there was no significant difference in the model responses to either ATP, CTP, or UTP. Through accident the data for CTP at $6 \times 10^{-4}M$ were useless. Limited amounts of this material prevented complete repetition of the experiment, but a second comparison at this concentration alone showed no significant difference in the rates of tension development when either ATP, CTP, or UTP was used to stimulate contraction of the model system.

It is of interest that preliminary experiments employing guanosine triphosphate or adenosine tetraphosphate (*7*) as the nucleotide in this model system showed greatly reduced rates of tension development when they were compared with ATP-stimulated responses. Confirmation of these observations would indicate that a certain degree of specificity exists in the nucleotide-actomyosin reaction that might be related to nucleotide structure.

In order to elucidate further the similarities of the reaction of these nucleotides with the contractile proteins, the rates of tension development were diminished by employing several nonspecific inhibitors of the contractile response. Table 1 shows the similarity in degree of inhibition of the ATP or UTP response achieved by (i) aging the fibers 21 days at −15°C; (ii) partial sulfhydryl-group blockade with *p*-chloromercuribenzoate; and (iii) two intensities of trypsin digestion. These data have been interpreted as indicating that even when some essential sulfhydryl groups were blocked or when partial denaturation was achieved either by aging or by digestion, no significant differentiation in the model response to these two nucleotides was effected.

In certain energy-transfer systems (*4*), only one of the purine or pyrimidine nucleotides reacts directly with its acceptor substance. We must conclude from the present evidence, however, that for the muscle model system utilized in this investigation, three constituents of the "nucleotide pool," ATP, CTP, and UTP, may be equally available for direct and independent reaction with actomyosin to effect the molecular rearrangement that is the essence of muscular contraction.

Table 1. Nonspecific inhibition of the model response to ATP or UTP addition. (Dog psoas fibers extracted for 7 days were treated with each inhibitor and the rates of contraction of duplicate fibers were measured when either $10^{-3}M$ ATP or $10^{-3}M$ UTP was used to stimulate tension development)

Treatment	Percentage inhibition	
	ATP	UTP
Fibers aged 21 days at −15°C	58	62
p-Chloromercuribenzoate ($10^{-4}M$)	46	59
Tryptic digestion (trypsin concentrate, 2μg/ml, 5 min at 25°C)	34	50
Tryptic digestion (trypsin concentrate, 2μg/ml, 10 min at 25°C)	73	72

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References and Notes

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6. Cytidine triphosphate was generously provided by the Pabst Laboratories, Milwaukee, Wis., through the kindness of S. H. Lipton. Adenosine and uridine triphosphates were purchased from the same concern.
7. These nucleotides were obtained from Sigma Chemical Co., St. Louis, Mo.

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North-South Asymmetry of the Pleistocene Ice Sheet

Geologists have long considered the great continental ice sheets of Pleistocene time to have been more or less symmetrical. An examination of the meteorology involved, however, does not lead to such a conclusion.

The cold winds that sweep across the Northern Hemisphere land masses may be described as polar air moving south-