Activation of Calcium Transport in Skeletal Muscle Sarcoplasmic Reticulum by Monovalent Cations*

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The rates of calcium transport and Ca⁺⁺-dependent ATP hydrolysis by rabbit skeletal muscle sarcoplasmic reticulum were stimulated by monovalent cations. The rate of decomposition of phosphoprotein intermediate of the Ca⁺⁺-dependent ATPase of sarcoplasmic reticulum was also increased by these ions to an extent that is sufficient to account for the stimulation of calcium transport and Ca⁺⁺-dependent ATPase activity. The order of effectiveness of monovalent cations tested at saturating concentrations in increasing the rate of phosphoprotein decomposition is: K⁺, Na⁺ > Rb⁺, NH₄⁺ > Cs⁺ > Li⁺, choline⁺, Tris⁺.

Sarcoplasmic reticulum membranes isolated from skeletal muscle accumulate calcium against a concentration gradient in the presence of ATP and Mg⁺⁺ (2–7). This calcium accumulation is coupled stoichiometrically to the activity of a membrane-bound Ca⁺⁺- and Mg⁺⁺-dependent ATPase (3–7). The hydrolysis of ATP by this enzyme involves a phosphoprotein intermediate that has characteristics of an acyl phosphate (8–11). A simplified reaction scheme may be written as follows (7–11):

\[ \text{ATP} + E \rightarrow \text{Mg}^{2+}, \text{Ca}^{2+} \rightarrow \text{P} + \text{ADP} \]

\[ E \rightarrow \text{P} + \text{Mg}^{2+} \]

The formation of the phosphoprotein intermediate (E → P) requires Ca⁺⁺ and Mg⁺⁺ in the external medium, and its decomposition is activated by Mg⁺⁺ and inhibited by Ca⁺⁺, probably at the interior of the membrane (7–16). Removal of phospholipid from sarcoplasmic reticulum membranes by phospholipase C digestion inhibits decomposition of the phosphoprotein intermediate (7, 17).

It was reported previously that monovalent cations such as K⁺ and Na⁺ inhibit calcium uptake and concomitant ATP hydrolysis by the isolated skeletal and cardiac sarcoplasmic reticulum membranes (18–22). De Meis and De Mello (22, 23) reported that K⁺ or Na⁺ inhibit formation of the phosphoprotein intermediate as the result of competition of these ions with Ca⁺⁺ for the active site, whereas these ions have no effect on decomposition of the phosphoprotein intermediate. In contrast, several investigators had reported previously that both K⁺ and Na⁺ have a stimulatory effect on calcium uptake and ATP hydrolysis by the sarcoplasmic reticulum membranes (24–27).

In the present study we reinvestigated the effects of monovalent cations on the calcium pump of skeletal muscle sarcoplasmic reticulum in view of the previous conflicting reports. Our data indicate that (a) monovalent cations stimulate calcium uptake and Ca⁺⁺-dependent ATP hydrolysis by skeletal muscle sarcoplasmic reticulum and (b) the increased rate of ATP hydrolysis in the presence of these ions is probably due to the increased rate of decomposition of the phosphorylated intermediate of Ca⁺⁺-dependent ATPase.

EXPERIMENTAL PROCEDURE

Preparation of Skeletal Muscle Microsomes—Microsomes were prepared from rabbit hind leg white muscle by the method described previously (28, 29). Microsomes were suspended in 50 mM KCl and 20 mM Tris/HCl buffer (pH 6.8), stored on ice, and used within 4 days after preparation.

Treatment of Microsomes with Diethyl Ether—Microsomes were treated with diethyl ether according to the method of Inesi et al. (30). Diethyl ether (1.4 ml) was added to a 10-ml reaction mixture which contained 1.4 mg/ml of microsomes, 50 mM KCl, and 10 mM Tris/maleic buffer (pH 6.8). The mixture was stirred at room temperature for 20 min after which time microsomes were recovered by centrifugation at 15,000 × g for 60 min at 3°C and resuspended in 50 mM KCl and 30 mM Tris/HCl buffer (pH 6.8). In agreement with the experiments reported by Inesi et al. (30), microsomes treated with diethyl ether no longer accumulated Ca⁺⁺ while ATPase activity remained unpimpaired.

Removal of Monovalent Cations from Microsome Preparations—To remove contaminating salt, microsomes were passed through a Sephadex G-50 column (2 × 10 cm), which had been equilibrated with 10 mM histidine/HCl buffer (pH 6.8), immediately before use. The sodium and potassium content of desalted microsomes, analyzed by flame photometry, was less than 0.1 mM and 0.03 mM, respectively. Since microsomes were diluted 20-fold in the final reaction mixture, the sodium and potassium introduced with microsomes into the final reaction mixture was considerably less than these values. Desalted microsomes were kept on ice in 0.25 to 0.30 M sucrose and 10 mM histidine/HCl buffer (pH 6.8) and used within 60 min.

Assay of ATPase Activity and Phosphoprotein Level—ATPase activity and phosphoprotein levels were measured at 0–25°C in 30 to 80
Stimulation of Calcium Pump by Monovalent Cations

µg of protein/ml. 50 mM Tris/maleate buffer (pH 6.8), 0 to 100 mM sucrose, 0.5 to 2.0 mM MgCl₂, 0.01 to 1.0 mM [γ-32P]ATP, 0 to 4.0 mM Tris/oxalate, and 0.20 mM EGTA or a calcium/EGTA buffer containing 0.15 to 0.40 mM CaCl₂ and various concentrations of EGTA. Microsomes were preincubated at 0°C with various concentrations of monovalent cations for at least 10 min after which the reaction was started by addition of [γ-32P]ATP to give a final volume of 1.0 ml. Reactions were stopped by addition of 10% trichloroacetic acid solution which contained 0.12 mM Pi and 1.0 mM ATP as carriers. After centrifugation at 16,000 g for 10 min at 3°C, aliquots were taken from the supernatant and 32P, was extracted by the method of Martin and Doty (31). The pellets in each tube were suspended in 4.0 ml of ice cold 4% perchloric acid containing 20 mM P, and 1.0 to 2.0 mM ATP. Dovine serum albumin (2 mg) was then added to each tube as a carrier protein. The denatured protein was collected by centrifugation and washed four times with 4.0 ml of ice cold 4% perchloric acid containing 20 mM P. The washed pellets were solubilized in 0.4 ml of solution containing 0.05% sodium dodecyl sulfate and 0.25 mM NaOH and then heated in boiling water for 10 min. The content of each tube was then transferred to vials and assayed for radioactivity in Bray’s solution by liquid scintillation spectrometry. Ca⁺⁺-dependent ATPase activity and Ca⁺⁺-dependent 3P incorporation into microsomes were estimated by subtracting the ATPase activity and the amount of 32P incorporated into microsomes in the presence of 0.2 mM EGTA from those at each ionized Ca⁺⁺ concentration.

Assay of Calcium Uptake—Calcium uptake was measured as described previously (29) under experimental conditions similar to those used for the ATPase assay except that 50 µM "CaCl₂ and various concentrations of EGTA were added to the reaction medium to attain specific ionized Ca⁺⁺ concentrations. The calcium uptake reaction was started by addition of ATP after microsomes were preincubated with various concentrations of monovalent cations for at least 10 min.

Determination of Ionized Ca⁺⁺ Concentration—The ionized Ca⁺⁺ concentration for a given mixture of CaCl₂ and EGTA at pH 6.8 was calculated with an association constant of 4.4 x 10⁻⁵ for the calcium-EGTA complex (32).

Protein Concentration Determination—Protein concentration was determined by the method of Lowry et al. (33) with bovine serum albumin as a standard.

Materials—Tris, ATP, and EGTA were obtained from Sigma Chemical Co., St. Louis, Mo. Na₂ATP solution was passed through a Dowex 50W-X8 (H⁺) column and then adjusted to pH 6.8 with Tris. [γ-32P]ATP tetra(triethylammonium) salt (25 to 30 mCi/mmol) and "CaCl₂ (30 mCi/mg of calcium) were purchased from ICN Pharmaceuticals, Inc., Irvine, Cal. Monovalent cations used were all pharmaceuticals, Inc., Irvine, Cal. Monovalent cations used were all chlorides. All reagents were analytical grade. Distilled water was deionized and redistilled in glass prior to use.

RESULTS

Effects of Monovalent Cations on Calcium Uptake and Ca⁺⁺-dependent ATPase Activity—The rates of both calcium uptake and ATP hydrolysis by skeletal muscle microsomes were stimulated in the same order of effectiveness by salts of various monovalent cations (Table I). In 10.5 µM ionized Ca⁺⁺ and at 25°C, 100 mM KCl, NaCl, RbCl, and NH₄Cl each increased the rates of calcium uptake and ATP hydrolysis 2- to 5-fold. The same concentrations of LiCl, choline/Cl, or Tris/Cl had little effect. The order of effectiveness of these salts (100 mM) in increasing these activities is: KClNaCl, RbCl, NH₄Cl > CsCl > LiCl, choline/Cl, Tris/Cl (Table I). Sucrose up to 200 mM had no effect on calcium uptake and ATP hydrolysis.

Ca⁺⁺-dependence of ATPase Activity and Phosphoprotein Level in Presence and Absence of K⁺ and Na⁺—The Ca⁺⁺-dependent ATPase activity and the steady state level of phosphoprotein measured at 10 s in the presence and absence of 75 mM KCl are shown as a function of ionized Ca⁺⁺ concentration in Fig. 1. In the absence of added KCl, the rate of ATP hydrolysis increased only slightly with increasing ionized Ca⁺⁺ concentration, whereas in the presence of KCl, it showed marked activation by Ca⁺⁺. Similar results were obtained when the Ca⁺⁺-dependence of the rate of calcium uptake was measured. The steady state level of phosphoprotein increased with increasing ionized Ca⁺⁺ concentrations in both the presence and absence of added KCl, reaching almost the same maximum at high ionized Ca⁺⁺ concentrations (Fig. 1). At low ionized Ca⁺⁺ concentrations (>0.1 to 1.0 mM), phosphoprotein levels were significantly lower in the presence of added KCl than in its absence. The ionized Ca⁺⁺ concentration required for the phosphoprotein level to reach its apparent half-maximal values (Kca) in the presence of 75 mM KCl was about 2 times higher than that in the absence of added KCl (Fig. 1). At 0°C, the values of Kca were similar both in the presence and absence of 75 mM KCl (Fig. 2). However, in the presence of 75 mM NaCl, the value of Kca was increased about 2-fold (Fig. 2).

Effect of Monovalent Cation Concentration on Ca⁺⁺-dependent ATPase Activity and Phosphoprotein Level—The rate of

Table I  Effects of monovalent cations on calcium transport and Ca⁺⁺-dependent ATPase activity of skeletal muscle microsomes

<table>
<thead>
<tr>
<th>Addition</th>
<th>µmol mg⁻¹ min⁻¹</th>
<th>% of control</th>
<th>µmol mg⁻¹ min⁻¹</th>
<th>% of control</th>
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</thead>
<tbody>
<tr>
<td>None</td>
<td>433 ± 7</td>
<td>100</td>
<td>310 ± 13</td>
<td>100</td>
</tr>
<tr>
<td>Na⁺</td>
<td>1107 ± 7</td>
<td>256</td>
<td>1125 ± 15</td>
<td>363</td>
</tr>
<tr>
<td>K⁺</td>
<td>1279 ± 10</td>
<td>295</td>
<td>1447 ± 28</td>
<td>467</td>
</tr>
<tr>
<td>NH₄⁺</td>
<td>957 ± 25</td>
<td>221</td>
<td>1199 ± 85</td>
<td>387</td>
</tr>
<tr>
<td>Rb⁺</td>
<td>1166 ± 10</td>
<td>289</td>
<td>1160 ± 9</td>
<td>371</td>
</tr>
<tr>
<td>Cs⁺</td>
<td>716 ± 6</td>
<td>105</td>
<td>401 ± 20</td>
<td>129</td>
</tr>
<tr>
<td>Li⁺</td>
<td>382 ± 4</td>
<td>88</td>
<td>286 ± 23</td>
<td>92</td>
</tr>
<tr>
<td>Sucrose</td>
<td>565 ± 6</td>
<td>117</td>
<td>288 ± 51</td>
<td>95</td>
</tr>
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</table>

Fig. 1. Effect of K⁺ on Ca⁺⁺-dependence of ATPase activity and phosphoprotein level at 10 s. Reactions were carried out for 20 s in the presence (circles) and absence (squares) of 75 mM KCl with 40 µmol/ml of microsomes, 50 µM [γ-32P]ATP, 50 mM Tris/maleate buffer (pH 6.8), 1 mM MgCl₂, 2.5 mM Tris/oxalate, 0.15 mM CaCl₂, and various concentrations of EGTA. In this and all subsequent figures, the Ca⁺⁺-dependent portions of the ATPase activity and phosphoprotein level are plotted and each point represents an average of duplicate determinations.
ATP hydrolysis and the steady state level of phosphoprotein measured at 10° and at saturating ionized Ca2+ concentrations are shown as a function of KCl and NaCl concentrations (Fig. 3). In these studies, the microsomes were pretreated with diethyl ether as described under "Experimental Procedure" so as to assure that the cation concentration inside the sarcoplasmic reticulum membranes was the same as that in the reaction medium. Under these conditions, the rate of ATP hydrolysis was enhanced approximately 3-fold at high concentrations of KCl or NaCl whereas the phosphoprotein level was inhibited slightly. The ratio, \( V/[E - P] \), which represents the ratio between the rate of ATP hydrolysis and the phosphoprotein level and is a measure of the rate of phosphoprotein decomposition, was plotted against either KCl or NaCl concentration (Fig. 4). The values of \( V/[E - P] \) were found to increase with increasing salt concentration and reached almost the same maximum at approximately 20 mM KCl and 100 mM NaCl. The concentration of KCl that produced apparent half-maximal increase of \( V/[E - P] \) was significantly lower than that of NaCl (Fig. 4 and Table II).

The experiments depicted in Fig. 3 were repeated with RbCl, NH4Cl, CsCl, and LiCl. The values of \( V/[E - P] \) increased with increasing concentrations of RbCl, NH4Cl, and CsCl, and showed saturation at high concentrations of these salts. The observed maximum values of \( V/[E - P] \) and the concentra-

![Fig. 2. Effects of K+ and Na+ on the Ca2+-dependence of the phosphoprotein level at 0°. Assay conditions were the same as those described in the legend to Fig. 1 except that reactions were carried out at 0° in 25 \( \mu \)M \([\gamma^3P]ATP\) in the presence of 75 mM KCl (○), 75 mM NaCl (△), or their absence (□).](https://example.com/fig2.png)

![Fig. 3. K+ and Na+ concentration dependence of the ATPase activity and phosphoprotein level in diethyl ether-treated microsomes. Reactions were carried out at 10° for 15 s with 70 \( \mu \)g/ml of diethyl ether-treated microsomes, 50 \( \mu \)M \([\gamma^3P]ATP\), 50 mM Tris/maleate buffer (pH 6.8), 2 mM MgCl2, 2.5 mM Tris/oxalate, 0.4 mM CaCl2, 0.42 mM EGTA, and various concentrations of KCl (circles) or NaCl (triangles).](https://example.com/fig3.png)

![Fig. 4. K+ and Na+ concentration dependence of the ratio of the rate of ATP hydrolysis to the phosphoprotein level, \( V/[E - P] \), in diethyl ether-treated microsomes. \( V/[E - P] \) was calculated from the experiment shown in Fig. 3. K+, ○; Na+, △.](https://example.com/fig4.png)

**Table II**

<table>
<thead>
<tr>
<th>Addition</th>
<th>( K_{in} ) (mM)</th>
<th>Maximal value of ( V/[E - P] ) (relative)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td></td>
<td>1.0</td>
</tr>
<tr>
<td>Na+</td>
<td>21.3, 20.0</td>
<td>3.9, 4.2</td>
</tr>
<tr>
<td>K+</td>
<td>5.1 ± 0.4 (5)*</td>
<td>4.2 ± 0.2 (5)*</td>
</tr>
<tr>
<td>NH4+</td>
<td>5.6</td>
<td>2.9</td>
</tr>
<tr>
<td>Rb+</td>
<td>8.4, 13.3</td>
<td>3.2, 3.1</td>
</tr>
<tr>
<td>Cs+</td>
<td>29.0, 28.0</td>
<td>2.9, 2.4</td>
</tr>
</tbody>
</table>

*The values represent the average ± S.E. of the number of preparations indicated in parentheses.
TABLE III
Effects of LiCl and sucrose on ATPase activity and phosphoprotein level

<table>
<thead>
<tr>
<th>Concentration</th>
<th>ATPase activity (V)</th>
<th>E-P</th>
<th>V([E - P])</th>
<th>ATPase activity (V)</th>
<th>E-P</th>
<th>V([E - P])</th>
</tr>
</thead>
<tbody>
<tr>
<td>mM</td>
<td>nmol mg⁻¹ min⁻¹</td>
<td></td>
<td>min⁻¹</td>
<td>nmol mg⁻¹ min⁻¹</td>
<td></td>
<td>min⁻¹</td>
</tr>
<tr>
<td>0</td>
<td>32.8</td>
<td>1.79</td>
<td>18.3</td>
<td>28.3</td>
<td>1.44</td>
<td>19.7</td>
</tr>
<tr>
<td>50</td>
<td>34.0</td>
<td>1.70</td>
<td>20.0</td>
<td>29.1</td>
<td>1.41</td>
<td>20.6</td>
</tr>
<tr>
<td>100</td>
<td>34.7</td>
<td>1.74</td>
<td>19.9</td>
<td>28.9</td>
<td>1.39</td>
<td>20.8</td>
</tr>
<tr>
<td>150</td>
<td>35.9</td>
<td>1.68</td>
<td>21.4</td>
<td>29.6</td>
<td>1.35</td>
<td>21.9</td>
</tr>
</tbody>
</table>

Fig. 5. K⁺ and Na⁺ concentration dependence of the ATPase activity and the phosphoprotein level in the presence of 1.0 μM ionized Ca²⁺. Reactions were carried out at 0°C for 30 s in 76 μg/ml of microsomes (not treated with diethyl ether), 50 μM [γ-³²P]ATP, 50 mM Tris/maleate buffer (pH 6.8), 0.5 mM MgCl₂, 4 mM Tris/oxalate, 0.15 mM CaCl₂, 0.49 mM EGTA, and various concentrations of KC (circles) or NaCl (triangles).

Fig. 6. Effects of K⁺ and Na⁺ on the rate of phosphoprotein decomposition. Microsomes (54 μg/ml) were phosphorylated for 15 s at 0°C in 20 μM CaCl₂, 10 μM [γ-³²P]ATP in the presence of no added salt (squares) or 75 mM KC (circles) or 75 mM NaCl (triangles) under standard conditions. At 15 s (I), further phosphorylation was inhibited by chelation of Ca²⁺ with 1.92 mM EGTA. Phosphoprotein decomposition and accompanying Pᵢ liberation were measured by denaturing the microsomes with trichloroacetic acid at various time intervals.

Fig. 7. Time course of phosphoprotein decomposition. Data shown in Fig. 6 was replotted semilogarithmically. Time of EGTA addition (I) in Fig. 6 is the zero time on this graph. No added salt, ○; 75 mM KCl, ●; 75 mM NaCl, △.
almost stoichiometric amount of P, was liberated after Ca**
chelation, indicating that the phosphoprotein decomposed to yield P. The initial phase of phosphoprotein decomposition followed first order kinetics, and the rates of phosphoprotein decomposition estimated from the slope in the initial phase were 2.4 min \(^{-1}\) in the absence of added salt and 7.6 min \(^{-1}\) in the presence of 75 mM KCl or NaCl (Fig. 7). In three additional experiments, a similar 3.1- to 4.2-fold stimulation of the rate of phosphoprotein decomposition was observed in the presence of 75 mM KCl at 0°.

**DISCUSSION**

The present findings demonstrate that monovalent cations stimulate calcium transport and concomitant Ca**
+ dependent ATP hydrolysis by skeletal muscle sarcoplasmic reticulum (Table I). The stimulation of ATP hydrolysis and thus presumably of calcium transport by these cations can be attributed to an increased decomposition rate of the phosphoprotein intermediate of Ca**
+ dependent ATPase (Figs. 3, 4, and 7, and Table II).

Among the monovalent cations tested, K+ was found most effective. The finding that the concentration of K+ that produces apparent half-maximal stimulation of the rate of phosphoprotein decomposition is relatively low, namely 5.1 mM (Table II), probably explains why the stimulatory effects of monovalent cations were not observed in some previous studies (18, 21). In such studies, effects of salts were examined in systems that already contained significant amounts of K+.

The finding that several other cations (viz. Na+, NH4+, Rb+, and Cs+) were stimulatory suggests that the hydrolysis of the phosphoprotein intermediate of Ca**
+ dependent ATPase of skeletal muscle sarcoplasmic reticulum does not have a strict ion specificity. It is interesting to note that the order of effectiveness of the cations tested in saturating concentrations is not reflected in the affinities of these cations for the enzyme site(s) (Table II). Na+ in saturating concentrations was found as effective as K+ and more stimulatory than NH4+, whereas the concentration of Na+ that produced apparent half-maximal stimulation was much higher than that for either K+ or NH4+. The order of decreasing affinities of the cations for the enzyme site(s) was found to be K+, NH4+ > Rb+ > Na+, Cs+ (Table II), which suggests that the binding site for these cations is probably of a size which matches the potassium radius (34).

It has been reported previously that the decomposition of phosphoprotein intermediate of Ca**
+ dependent ATPase of sarcoplasmic reticulum is activated by Mg**
+ and inhibited by high Ca**
+ concentration, probably in the membrane interior (7–16). The results reported in the present study indicate that monovalent cations are also involved in phosphoprotein decomposition. Carvalho and Leroi (35), who studied the cation binding capacity of sarcoplasmic reticulum membranes, showed that the total amount of bound Ca**
+ + Mg**
+ + K+ remained approximately constant and that ATP-dependent calcium uptake is accompanied by the loss of an amount of Mg**
+ and K+ equivalent to the amount of Ca**
+ bound. These observations and the present observation of the stimulatory action of monovalent cations on the rate of phosphoprotein decomposition suggest that not only Mg**
+ but also cations such as K+ or Na+ may be transported as a counter ion to Ca**
+.

Under certain conditions, the monovalent cations were found to decrease the steady state level of phosphoprotein (Figs. 1, 2, and 5). At 10° and in 1.0 μM ionized Ca**
+ , K+, and Na+ at high concentrations reduced phosphoprotein levels to a greater extent (Fig. 5) than was found at saturating ionized Ca**
+ concentrations (Fig. 3). At 0°, however, 75 mM K+ did not significantly decrease the phosphoprotein level even at low ionized Ca**
+ concentrations (Fig. 2), suggesting that this K+ concentration is not inhibitory to phosphoprotein formation under these conditions. These findings thus suggest that the decrease in phosphoprotein level by K+ observed at 10° and at low ionized Ca**
+ concentrations (1 mM) (Fig. 5) is probably due to (a) stimulation of the rate of phosphoprotein decomposition by K+ and (b) the limited rate of phosphoprotein formation which results from the lesser availability of Ca**
+ at low ionized Ca**
+ concentrations. In contrast, 75 mM Na+ at low ionized Ca**
+ concentrations decreased the steady state phosphoprotein level to a greater extent than K+ at 0° (Fig. 2) as well as at 10° (Fig. 5). At 10° and in 1.0 μM ionized Ca**
+ , Na+ at high concentrations enhanced the rate of ATP hydrolysis to a lesser extent than K+ at the same concentrations (Fig. 5). Since Na+ is equally or less stimulatory than K+ to phosphoprotein decomposition under these conditions (see text and Fig. 4 and Table II), these observations suggest that the decrease in phosphoprotein level by Na+ observed at both 10° (Fig. 5) and 0° (Fig. 2) can be attributed not only to (a) and (b) mentioned above, but also to the inhibition of phosphoprotein formation by Na+ probably as a result of competition with Ca**
+ for the calcium binding site as suggested by De Meis (22).

In the absence of added monovalent cations, a low Ca**
+ dependent ATPase activity was observed (Table I, Figs. 1 and 3). This ATPase activity was accompanied by a low rate of calcium uptake (Table I) and a slow turnover of the Ca**
+ dependent phosphoprotein (Figs. 6 and 7). As the concentration of either K+ or Na+ contaminating the microsomal preparations used in the present study are well below the effective concentrations of these cations (see "Experimental Procedure" and Table II), this residual ATPase activity probably represents a component of the Ca**
+ dependent ATPase activity that does not require the presence of monovalent cations. However, it cannot be shown conclusively that the residual ATPase activity is not due to the presence of a small amount of membrane-bound cations. These and other problems, such as the numbers of monovalent cations involved and interrelation among monovalent cations, Ca**
+ and Mg**
+ in the process of phosphoprotein decomposition, are currently being studied using preparations of purified Ca**
+ dependent ATPase of skeletal muscle sarcoplasmic reticulum.

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**REFERENCES**

Stimulation of Calcium Pump by Monovalent Cations

22. de Meis, L. (1972) Biochemistry 11, 2460-2565
34. Williams, R. J. P. (1970) Q. Rev. 24, 331-365
35. Carvalho, A. P., and Leo, B. (1967) J. Gen. Physiol. 50, 1327-1352
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