

# Effects of Naturally Occurring Polyols and Urea on Mitochondrial $F_0F_1$ ATPase

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We show that urea inhibits the ATPase activity of MgATP submitochondrial particles (MgATP-SMP) with  $K_i = 0.7$  M, probably as a result of direct interaction with the structure of  $F_0F_1$ -ATPase. Counteracting compounds (sorbitol, mannitol or inositol), despite slightly (10-20%) inhibiting the ATPase activity, also protect the  $F_0F_1$ -ATPase against denaturation by urea. However, this protection was only observed at low urea concentrations (less than 1.5 M), and in the presence of three polyols, the  $K_i$  for urea shift from 0.7 M to 1.2 M. Urea also increases the initial activation rate of latent MgATP-SMP in a dose-dependent-manner. However, when the particles (0.5 mg/ml) were preincubated in the presence of 1 M, 2 M or 3 M urea, a decrease in the activation level occurred after 1 h, 30 and 10 min, respectively. At high MgATP-SMP concentration (3 mg/ml) a decrease in activation was observed after 2 h, 1 h and 20 min, respectively. These data indicate that the effect of urea on the activation of MgATP-SMP depends on time, urea and protein concentrations. It was also observed that polyols suppress the activation of latent MgATP-SMP in a dose-dependent manner, and protect the particles against urea denaturation during activation. We suppose that a decrease in membrane mobility promoted by interactions of polyols with phospholipids around the  $F_0F_1$ -ATPase may also increase the compaction of protein structure, explaining the inhibition of natural inhibitor protein of ATPase ( $IF_1$ ) release and the activation of the enzyme.