# Differential effect of canagliflozin, a sodium-glucose cotransporter 2 (SGLT2) inhibitor, on slow and fast skeletal muscles from nondiabetic mice

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There has been a concern that sodium-glucose cotransporter 2 (SGLT2) inhibitors could reduce skeletal muscle mass and function. Here, we examine the effect of canagliflozin (CANA), an SGLT2 inhibitor, on slow and fast muscles from nondiabetic C57BL/6J mice. During SGLT2 inhibition, fast muscle function is increased, as accompanied by increased food intake, whereas slow muscle function is unaffected, although slow and fast muscle mass is maintained. When the amount of food in CANA-treated mice is adjusted to that in vehicle-treated mice, fast muscle mass and function are reduced, but slow muscle was unaffected during SGLT2 inhibition. In metabolome analysis, glycolytic metabolites and ATP are increased in fast muscle, whereas glycolytic metabolites are reduced but ATP is maintained in slow muscle during SGLT2 inhibition. Amino acids and free fatty acids are increased in slow muscle, but unchanged in fast muscle during SGLT2 inhibition. The metabolic effects on slow and fast muscles are exaggerated when food intake is restricted. This study demonstrates the differential effects of an SGLT2 inhibitor on slow and fast muscles independent of impaired glucose metabolism, thereby providing new insights into how they should be used in patients with diabetes, who are at a high risk of sarcopenia.