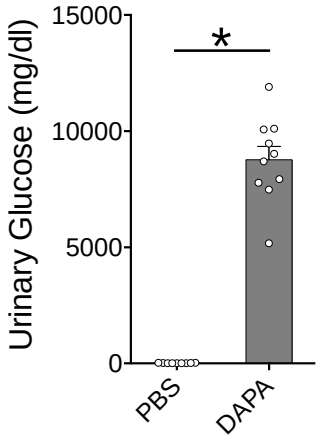
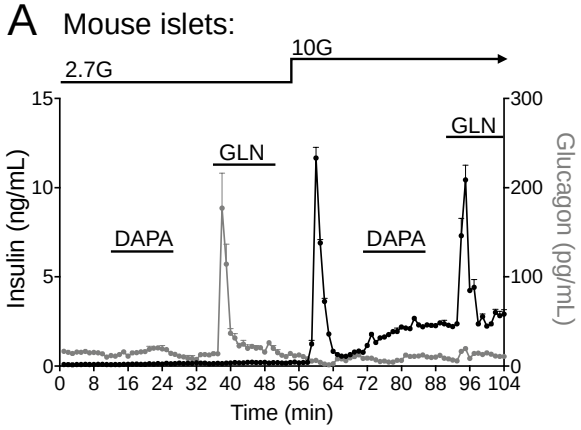
SUPPLEMENTARY DATA

Supplementary Figure 1. Dapagliflozin increases urinary glucose excretion. Urine collected from WT mice treated with dapagliflozin contained substantially more glucose that PBS-control conditions. * - $p<0.05$ vs. PBS control, values are mean ± SEM.

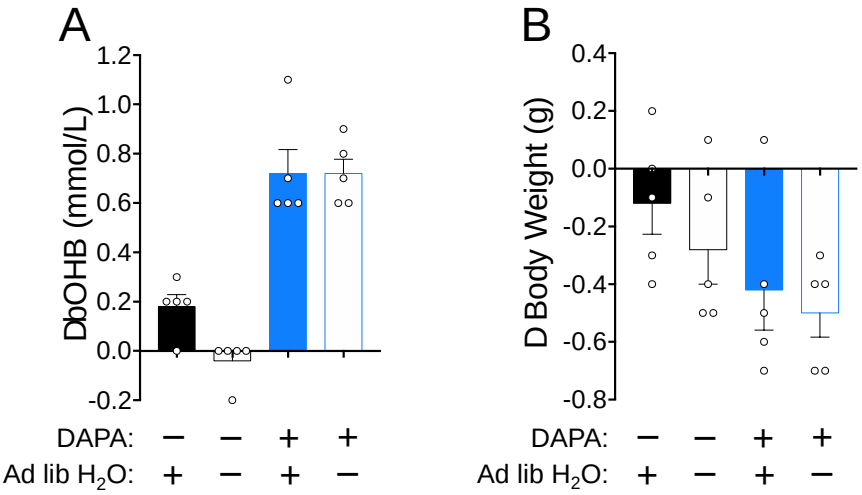


Supplementary Figure 2. Dapagliflozin does not stimulate glucagon or insulin secretion in mouse islets. Dapagliflozin did not stimulate glucagon or insulin at 2.7mM glucose (2.7G) or 10mM glucose (10G). Glutamine served as a positive control and stimulated glucagon at both low- and high-glucose and insulin secretion at high-glucose.

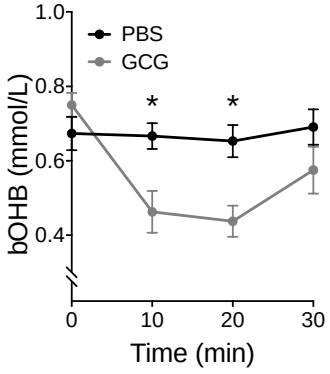


SUPPLEMENTARY DATA

Supplementary Figure 3. Dapagliflozin stimulates ketosis independent of hydration. A) Dapagliflozin stimulated ketogenesis to the same extent in mice with free access to water versus no water access for 3 hrs of treatment. B) Body weight loss over the fasting and dapagliflozin treatment were similar across groups. Data are presented as mean ± SEM.

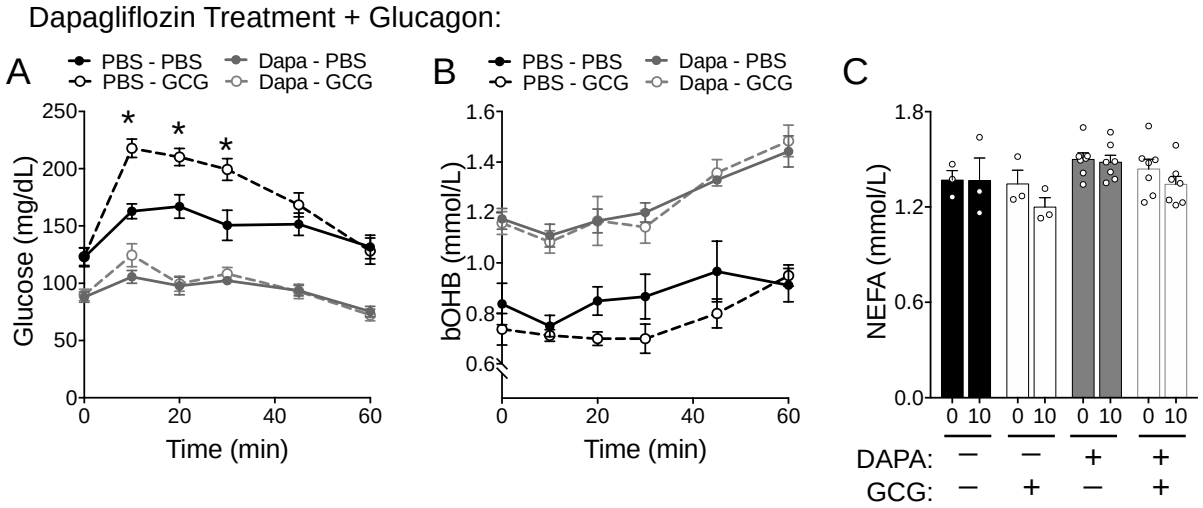


Supplementary Figure 4. 1 mg/kg glucagon induces a significant drop in circulating ketones. 5 hr fasted WT mice were administered 1mg/kg glucagon i.p. and ketones signficantly dropped by 10 min post-injecion. * - p<0.05 vs. PBS control, values are mean ± SEM.



SUPPLEMENTARY DATA

Supplementary Figure 5. Dapagliflozin-induced ketosis is not increased with exogenous addition of glucagon. (A) Glucagon (20µg/kg) significantly elevated glucose in PBS-treated mice, but not in dapagliflozin-treated mice. Glucagon had no effect on (B) βOHB levels or (C) circulating NEFA in either PBS- or dapagliflozin-treated mice. * - $p<0.05$ vs. PBS control, values are mean ± SEM.



Supplementary Figure 6. Mice with low insulin from overnight fasting maintain increased dapagliflozin-induced ketogenesis. Mice were fasted for 12hrs followed by 3hrs of dapagliflozin treatment. (A) Glycemia was similar between PBS- and dapagliflozin-treated controls. (B) βOHB was significantly elevated in dapagliflozin-treated mice, with no effect on (C) NEFA levels. * - $p<0.05$ vs. 3hr PBS control, values are mean ± SEM.