# Enterolactone as a Potential Therapeutic Agent for the Treatment of Type-two Diabetes

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# Introductory Context

- Type-two Diabetes
- Enterolactone (ENL)
- Previous studies establish the foundation
  - Positive effects of coffee
  - Specific compounds and pathway: unknown

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# Type-two Diabetes

- Healthy Glucose Management:
  - We eat a meal → digestive system breaks down sugar → blood glucose increases → we use and then store the glucose (insulin)
- Type-two Diabetes:
  - blood glucose increases → insulin is released, but does not contribute to glucose utilization or stored (insulin resistance)

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# Coffee Metabolites

- Coffee → digestive tract → metabolites absorbed → compounds distributed to tissues to have their effect
- Our study:
  - Lignin (ENL) → fat cells → increase glucose uptake

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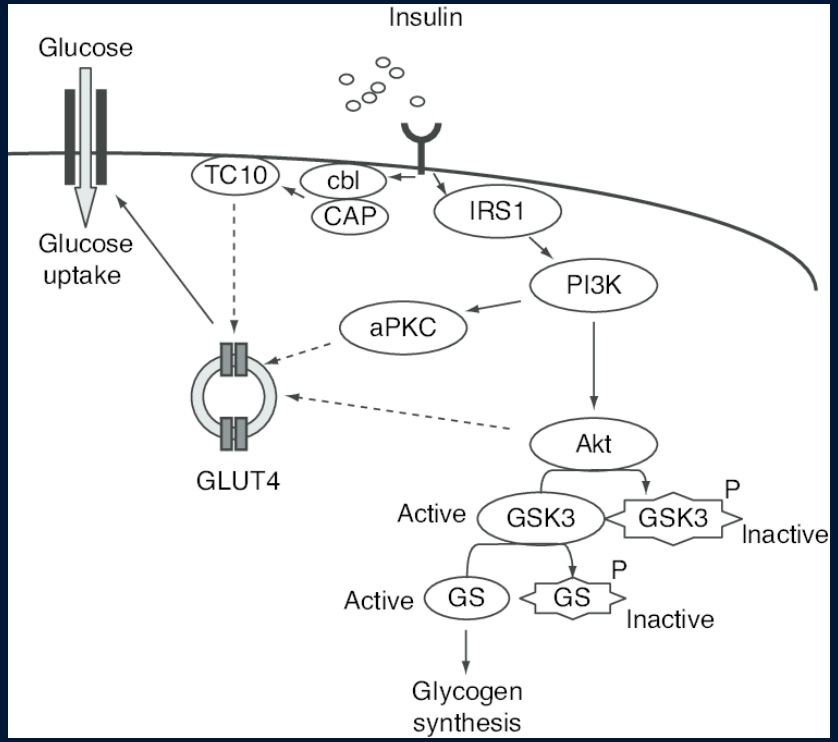
# Insulin-Stimulated Glucose Uptake




Bachmann, Rebecca & Chen, Jie. (2009). Chapter 21 Interleukin-6 and Insulin Resistance. Vitamins and Hormones Series - VITAMIN HORMONE-ADVAN RES APP. 80. 613-633.

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# Research Objectives

- Determine the effect of ENL on glucose uptake in 3T3-L1 differentiated adipocytes
- Determine the optimal ENL dose
- Characterize the mechanism by which the effect is elicited

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# Methodology

- Cells are differentiated and treated with ENL , controls, and Glut4 inhibitors
  - Glucose uptake is measured and compared to controls
  - Glucose uptake is measured in the presence of a Glut4 inhibitor
- Akt and IRS-1 phosphorylation is measured following ENL treatment

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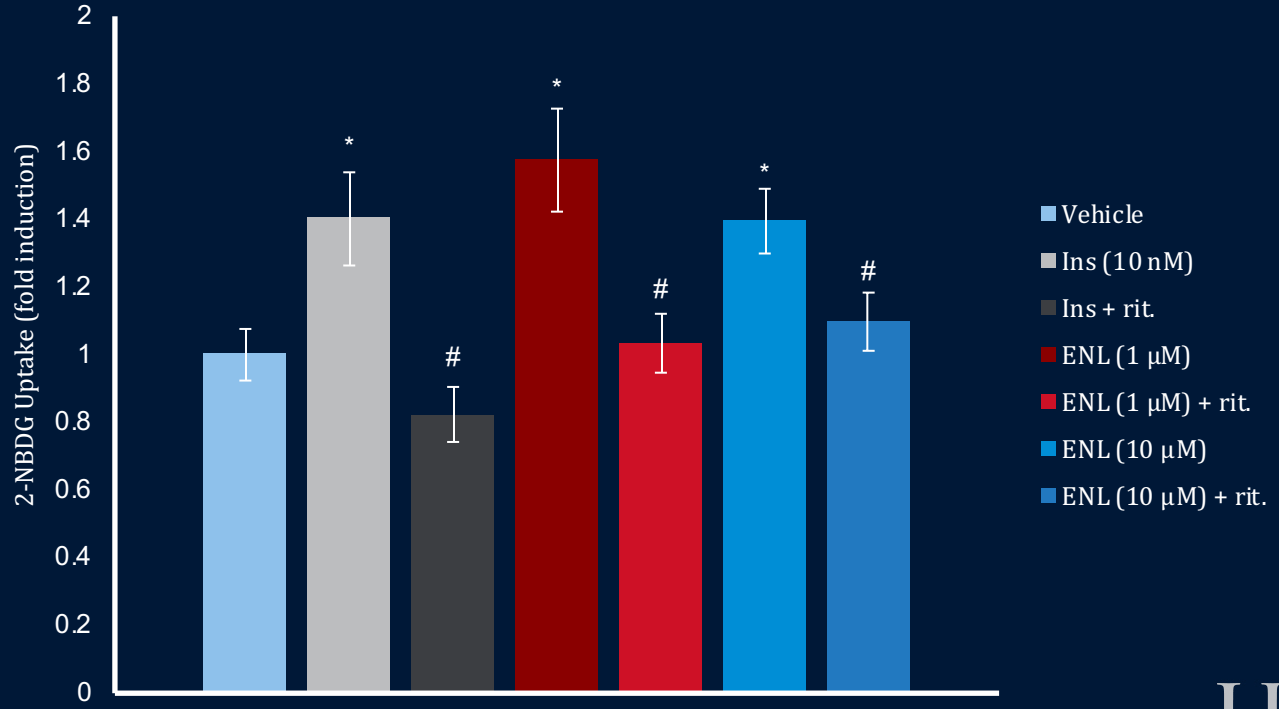
# Glucose Uptake with ENL Treatment and Ritonavir GLUT4 Inhibition

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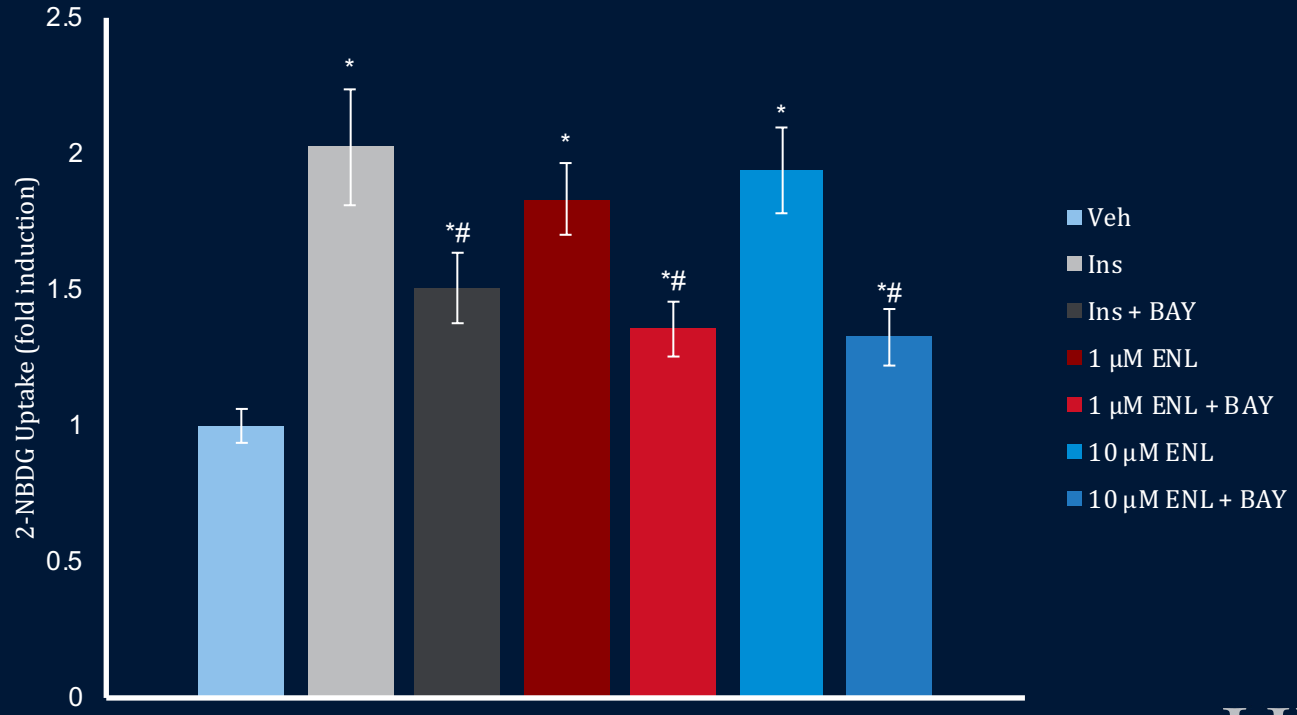
## ENL Dependent Glucose Uptake and BAY 876 GLUT4 Inhibition

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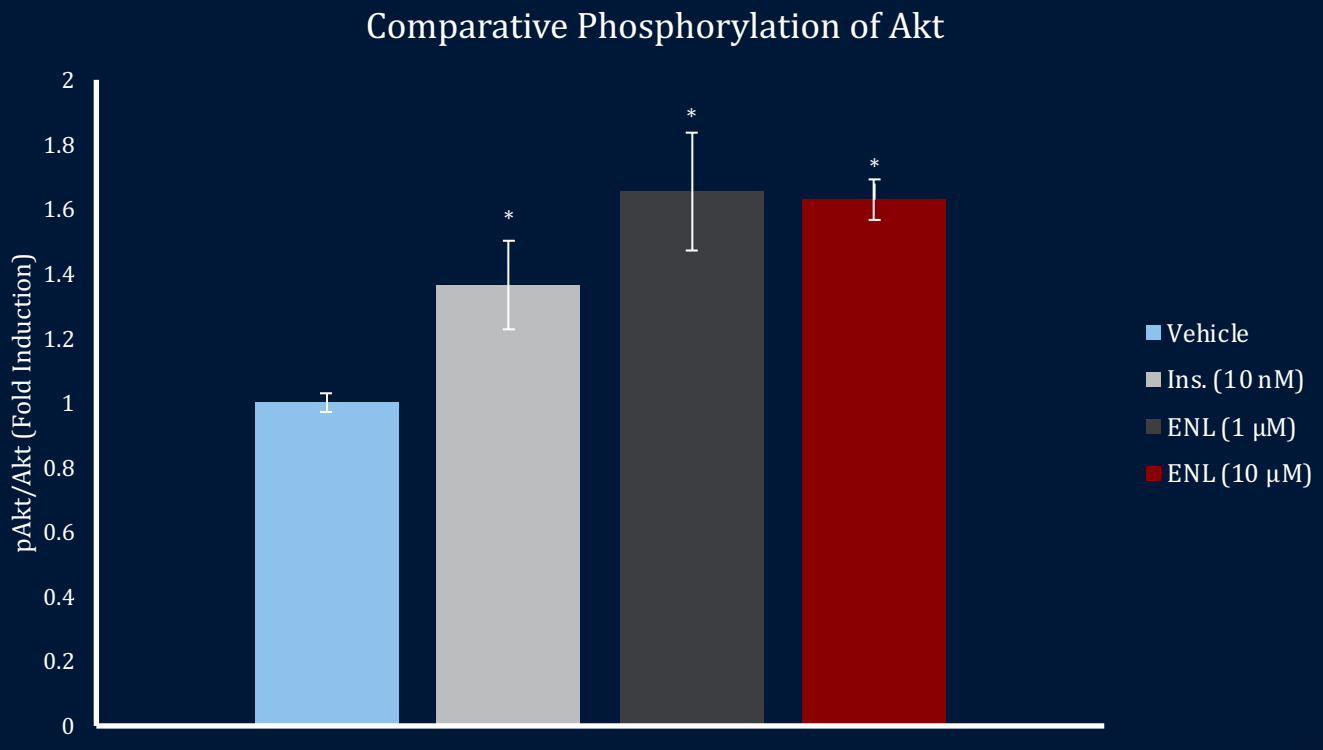


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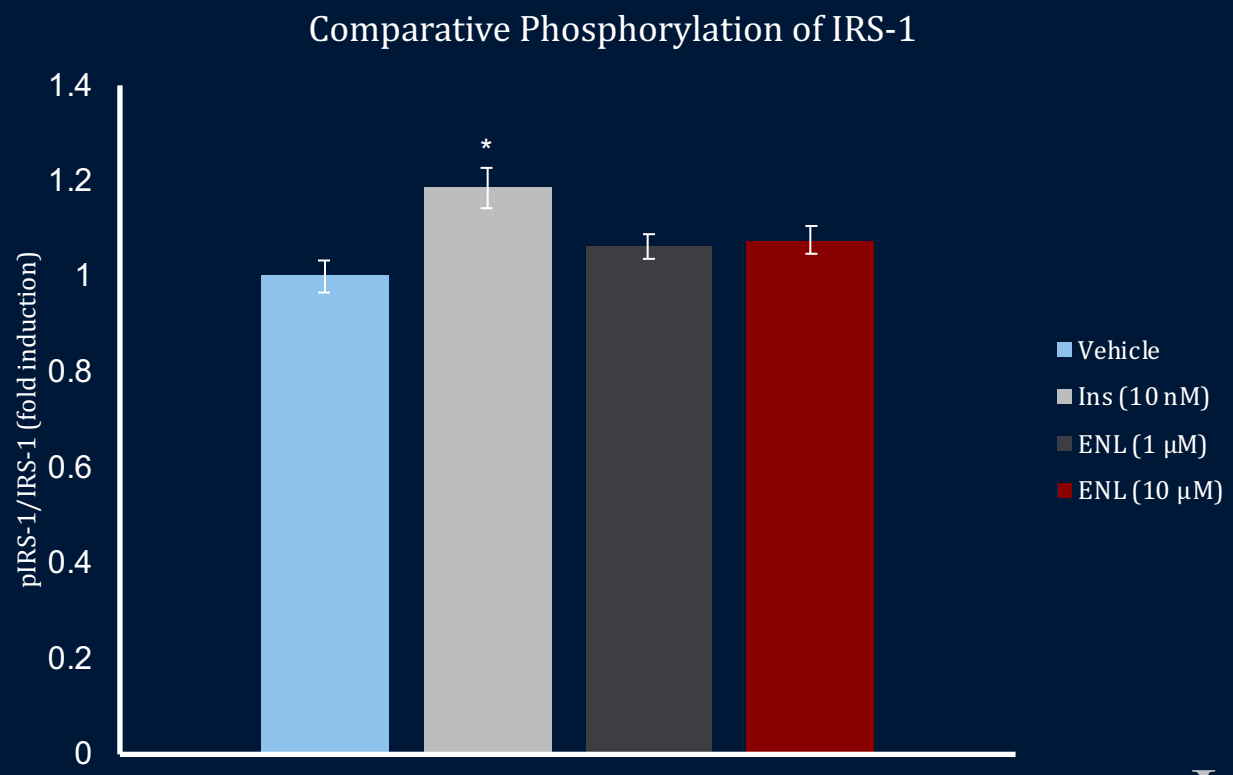


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# Interpretation of Data

- ENL increases glucose uptake
  - ENL-stimulated glucose uptake is dependent on Akt phosphorylation and GLUT4 translocation
- IRS-1 phosphorylation indicates a pathway for glucose uptake that is divergent from insulin's
- Further studies are needed to confirm the rest of the pathway and the viability of animal model experiments

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# Contributions to the Field

- Foundational data to advise future translational studies: provide a natural, inexpensive treatment for Type-two diabetes

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# Questions?

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