

Walls, K. M., Hong, K. U., & Hein, D. W. (2023). Heterocyclic amines reduce insulin-induced AKT phosphorylation and induce gluconeogenic gene expression in human hepatocytes. *Archives of Toxicology*, 97(6), 1613-1626. <https://doi.org/10.1007/s00204-023-03488-2>

## **Definitions**

- **Heterocyclic Amines (HCAs):** Chemicals that form when meat is cooked at high temperatures. They can cause changes in DNA and have been linked to cancer.
- **Insulin Resistance:** A condition where the body's cells don't respond properly to insulin, making it hard to control blood sugar levels.
- **Gluconeogenesis:** The process by which the liver makes glucose (sugar) from non-carbohydrate sources.
- **AKT Phosphorylation:** A process that activates the AKT protein, which plays a role in glucose uptake and metabolism in the body.
- **HepG2 Cells:** A type of human liver cancer cell used in scientific research to study liver functions and diseases.

## **Key Findings**

- HCAs reduce the ability of insulin to activate the AKT protein in liver cells.
- HCAs increase the production of glucose in liver cells.
- These effects suggest that HCAs could contribute to insulin resistance and the development of type II diabetes.

## **Introduction**

The study investigates how heterocyclic amines (HCAs), which are chemicals found in cooked meats, affect insulin signaling and glucose production in human liver cells. The focus is on understanding if HCAs can lead to insulin resistance, a precursor to type II diabetes.

## **Main Content**

### **Background**

HCAs are chemicals formed when meat is cooked at high temperatures, like grilling or frying. These chemicals are known to damage DNA and have been linked to cancer. This study explores if HCAs also affect insulin signaling and glucose production, potentially leading to insulin resistance and type II diabetes.

### **Methods**

- **Cell Culture:** Human liver cancer cells (HepG2) and cryopreserved human liver cells were treated with different concentrations of HCAs (MeIQ, MeIQx, and PhIP) for three days.
- **Insulin Signaling:** The cells were then tested for insulin-induced AKT phosphorylation using Western blot analysis.
- **Gene Expression:** The levels of genes involved in glucose production were measured using RT-qPCR.
- **Glucose Production:** The amount of glucose produced by the cells was measured after treating them with HCAs.

## **Results**

- **Insulin Signaling:** Treatment with HCAs significantly reduced insulin-induced AKT phosphorylation in both HepG2 and cryopreserved human liver cells.
- **Gene Expression:** HCAs increased the expression of gluconeogenic genes (G6PC and PCK1) in the liver cells.
- **Glucose Production:** HCAs increased the amount of glucose produced by the liver cells, indicating enhanced gluconeogenesis.

## **Conclusion**

The study shows that HCAs found in cooked meats can impair insulin signaling and increase glucose production in liver cells. This suggests that regular consumption of HCAs could contribute to insulin resistance and the development of type II diabetes. Reducing intake of cooked meats high in HCAs might help prevent these metabolic disorders.

Word Count: 415

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