In Overweight Adults Elderberry Juice Boosts Key Genes for Metabolic Flexibility

Researchers examined how elderberry juice (EBJ) alters transcriptional response to feeding and fasting.

Metabolic flexibility is defined as efficiently switching between fuel sources in response to changing energy demands and nutrient availability. It is a key determinant of metabolic health. Metabolic flexibility enables healthy individuals to use glucose in the fed state and switch to fatty acid oxidation during fasting. Loss of metabolic flexibility drives several metabolic disorders.

Anthocyanins are increasingly studied for their role in metabolic flexibility. American black elderberries have the highest levels of anthocyanins and have been reported to improve metabolic health. The authors previously showed that EBJ intake improved several indices of metabolic flexibility in overweight adults, although the underlying molecular mechanisms were unknown.

Study

The present study explored how EBJ alters transcriptional response to feeding and fasting. Obese and overweight adults completed a randomized, placebo-controlled crossover trial, which compared daily intake of EBJ to a placebo. Each study arm lasted seven days, including four days of a fully controlled diet and a washout period of three weeks between arms.

On day eight of each arm, a meal tolerance test was administered, which included a high-carbohydrate breakfast plus EBJ or placebo. Transcriptomic responses were assessed using RNA sequencing of peripheral blood mononuclear cells from 10 participants. Fasting and postprandial samples were used for RNA sequencing. Further, the team performed a differential gene expression analysis.

Gene expression changes relevant to metabolic regulation were identified using a pathway-driven filtering strategy based on literature-defined and Kyoto Encyclopedia of Genes and Genomes (KEGG) metabolic functions. Gene ontology (GO) enrichment analysis was performed to identify coordinated cellular responses. Pathways relevant to metabolic flexibility altered by EBJ or placebo were identified using gene set enrichment analysis (GSEA).

Results

The team identified 1,512 differentially expressed genes (DEGs) in the EBJ group and 350 DEGs in the placebo group during the transition from fasted to fed states. Comparisons between placebo and EBJ identified two DEGs in the fed state but none in the fasted state. Mapping DEGs to

literature-defined and KEGG pathways identified 234 and 59 metabolic genes in the EBJ and placebo groups, respectively.

Both groups significantly enriched various pathways, although the EBJ group showed higher gene-level representation. Three among the top five significantly regulated genes in both groups were shared: leukocyte immunoglobulin-like receptor A4 (LILRA4), pyruvate dehydrogenase kinase 4 (PDK4), and perilipin 2 (PLIN2); each exhibited stronger (down)regulation in the EBJ group.

In addition, EBJ-fed samples showed unique upregulation of solute carrier family 2 member 3 (SLC2A3) and PPARG coactivator 1 beta (PPARGC1B). Multiple GO biological process terms showed significant enrichment among upregulated genes in the EBJ group; these included cellular response to nitrogen compounds, regulation of target of rapamycin (TOR) signaling, insulin receptor signaling, response to growth factors, and cellular response to insulin stimulus.

Immune-related pathways, including pattern recognition receptor and innate immune response-activating signaling pathways, also showed significant upregulation in the EBJ group. Downregulated processes included protein-RNA complex assembly, protein-RNA complex organization, and ribonucleoprotein complex biogenesis. Within the cellular component category, the immunological synapse was significantly enriched among upregulated genes in the EBJ group.

Multiple ribosome-related genes were significantly enriched among downregulated genes in the EBJ group, alongside reduced expression of oxidative phosphorylation and TCA cycle genes, which the authors interpret as part of adaptive responses to feeding. In the molecular function category, various kinase-related activities were significantly enriched among upregulated genes in the EBJ group; these included protein kinase activity, protein serine/threonine kinase activity, histone kinase activity, histone-modifying activity, and guanosine 5'-diphosphate (GDP) binding.

The structural ribosome constituent was enriched among downregulated genes in the EBJ group. In the placebo group, there were significant changes in biological process terms in response to feeding. The negative regulation of the regulated secretory pathway and the negative regulation of exocytosis were the upregulated biological processes. GDP binding was significantly enriched among upregulated genes within the molecular function category.

The placebo group had no significant changes within the cellular component category. GSEA showed that 27 pathways were significantly related to metabolic flexibility in the EBJ group compared to seven in the placebo group. Pathways in the EBJ group included autophagy, oxidative phosphorylation, fatty acid degradation, and insulin, forkhead box O (FoxO), AMP-activated protein kinase (AMPK), mechanistic TOR (mTOR), and adipocytokine signaling pathways, among others.

Conclusion

The study provided a comprehensive transcriptomic analysis of EBJ's effects on metabolic flexibility in response to a meal tolerance test. The findings indicate that EBJ intake may enhance transcriptional response to feeding, with about four times more DEGs during the fasted-to-fed state transition than placebo.

However, the authors stress that peripheral blood mononuclear cells are immune-derived and serve as surrogates of systemic responses, not direct measures of metabolic tissues. They also

note that transcriptomic findings sometimes contrasted with their prior clinical results showing EBJ improved glucose tolerance and fat oxidation, highlighting the complexity of integrating molecular and physiological outcomes.

Given the small size of the RNA sequencing cohort, these findings may be deemed exploratory; larger studies are required to corroborate these results.

Source:

https://www.news-medical.net/news/20251003/Elderberry-juice-boosts-key-genes-for-metabolic-flexibility-in-overweight-adults.aspx