Protective Effects of Curcumin in High Fat Diet (HFD)-Induced Obesity Include Anti-Inflammatory Effects in Adipose Tissue and Changes in Gut Microbiome

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1. Abstract

Objective: Curcumin, a traditionally used spice in Asia has several health-protecting effects. However, its role on gut microbiota and obesity-associated inflammation is still poorly understood. The objective of this study was to determine whether the protective effects of curcumin in high fat diet (HFD)-induced obesity are mediated by reduced white adipose tissue (WAT) inflammation and changes in gut bacteria.

Methods: Male B6 mice were fed a HFD (45% kcal fat) or HFD supplemented with 0.4% (w/w) curcumin (HFC) for thirteen weeks. Body weight, adiposity, glucose and insulin tolerances, as well as serum triglycerides, insulin, leptin and resistin levels were measured. Gut microbiome composition was determined by 16S RNA metagenomics sequencing. Expression of inflammation-related genes in WAT was measured by qRT-PCR. Macrophage counts in WAT were evaluated by galectin-3 immunohistochemical staining.

Results: Pro-inflammatory transcription factor NF-kappa-B p65 subunit (p65) and toll-like receptor-4 (TLR-4) gene expression were downregulated in HFC group compared to HFD mice. Furthermore, curcumin reduced total macrophage infiltration in WAT in HFC mice compared to HFD group. Expression of both M1 (CD80, CD86) and M2 (Arginase-1) associated genes was decreased. The relative abundance of bacteria representing the Lactococcus (anti-inflammatory), Sutterella, and Turicibacter (implicated in short-chain fatty acid (SCFA) production) genera, was increased by the curcumin supplement.

Conclusion: Curcumin exerts protective effects against dietary obesity, in part through downregulation of adipose tissue inflammation which may be due to the production of SCFA, and possibly other curcumin metabolites by gut microbiota.

2. Background

Curcumin exerts protective effects against obesity-related inflammation in adipose tissue by regulating macrophage infiltration and changing gut microbiota. As a result, the protective effects of curcumin on obesity may be mediated by its anti-inflammatory properties.

3. Hypothesis and Study Design

Figure 1. Protective effects of curcumin in HFD-induced obesity may be partially mediated by gut microbiota-derived short-chain fatty acid (Hypothesis)

3.1 Curcumin reduced adipocyte size, but not the body weight (N = 9 – 10)

3.2 Curcumin reduced adipose tissue inflammation and macrophage infiltration (N = 6 – 9)

4. Results (Adipose Tissue Analysis)

4.1 Curcumin reduced adipocyte size, but not the body weight (N = 9 – 10)

4.2 Curcumin reduced adipose tissue inflammation and macrophage infiltration (N = 6 – 9)

5. Results (Gut Microbiota Analysis)

5.1 Curcumin can effectively reduce adipose tissue inflammation

5.2 Curcumin can modulate the composition of gut microbiota, and increase expression of SCFA-producing bacteria

5.3 Evaluation of SCFA, LBP, IL-6 and IL-17 levels in blood and tissues will provide more insights into mechanisms linking curcumin, obesity & gut microbiota

6. Conclusion

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7. Acknowledgement

8. Abbreviations

CD = Cluster of differentiation, HF = High fat, HFC = High fat curcumin, LPS = Lipopolysaccharide, LBP = LPS binding protein, p65 = NF-kappa-B p65 subunit, SCFA = short-chain fatty acid, WAT = White adipose tissue, *P< 0.05, **P< 0.01, ***P< 0.001

9. References


Figure 2. Protective effects of curcumin in HFD-induced obesity may be partially mediated by gut microbiota-derived short-chain fatty acid

Figure 3. Study design

Figure 4. PCA of gut microbiota profiles in HF vs. HFC groups: HF-induced alterations in gut microbiota are modified by curcumin. PC1= Diet-induced variation, PC2= Intra-group variation

Figure 5. Curcumin increases the relative abundance of Sutterella, Turicibacter and Lactococcus bacterial genera.

Figure 1. High-fat diet can induce adipose tissue inflammation by altering gut microbiota composition

- Obesity is associated with chronic low-grade inflammation, compromised intestinal barrier function, and abnormal gut microbiota composition [1,2]
- High fat (HF) or western diet change the composition of gut microbiota, also known as gut dysbiosis, and increases adipose tissue inflammation [2]
- SCFA-producing bacteria, boosted by curcumin, might exert beneficial effects in obesity [3]