Butyrate alleviates adipose mitochondrial dysfunction and inflammation in experimental model of polycystic ovarian syndrome by modulating SIRT1-dependent mechanism

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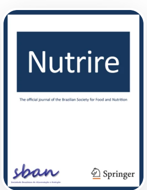

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Abstract

Purpose

Impaired adipose tissue (AT) remodeling has been suggested as a pathophysiological driver of endocrinometabolic events in polycystic ovarian syndrome (PCOS) models. Mitochondrial dysfunction, especially in the adipocyte plays a key role in AT inflammation that possibly aggravates endocrine/metabolic phenotypes in PCOS. Studies have reported short-chain fatty acids (SCFAs) as metabolic modulators that potentiate energy homeostasis. Butyrate, a unique form of SCFAs improves metabolic function by inhibition of histone deacetylase activity. The present study therefore hypothesized that butyrate would reverse adipose mitochondrial dysfunction/inflammation and endocrine/metabolic features of PCOS in experimental rats.

Methods

Eight-week-old nulliparous Wistar rats were assigned into groups ($n = 5$): control (CTL), butyrate (BUT), letrozole (LEZ), and LEZ + BUT. Induction of PCOS was by letrozole (1 mg/kg) for 21 days. After the confirmation of PCOS, rats were treated with butyrate (200 mg/kg) for 6 weeks.

Results

Animals with PCOS expressed multiple ovarian cysts and hormonal/metabolic changes characterized by hyperandrogenism/hypoestrogenism, elevated anti-Mullerian hormone and hyperinsulinemia/insulin resistance. In addition, animals also demonstrated increased plasma triglyceride, decreased adiponectin, increased leptin with corresponding decrease in adipose triglyceride, and increased inflammatory markers (NF-kB, TNF-α). A significant increase in adipose caspase-6, lipid peroxidation, and decreased GSH and mitochondrial mitofusin 2/ATP synthase were also observed in experimental PCOS rats. These alterations were accompanied by increased levels of adipose MIF. Nevertheless, the administration of butyrate alleviated these alterations in the adipose and ovarian tissues of PCOS animals.

Conclusion

The results suggest the ameliorative effect of butyrate on adipose mitochondrial dysfunction and/or inflammation in PCOS by modulating SIRT1-dependent pathway.

Data availability

The data supporting the present study will be made available on request from the corresponding author.

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Contributions

KSO conceived and designed the research. SEA conducted the experiments. KSO and SEA analyzed and interpreted the data and drafted the manuscript. KSO and SEA contributed reagents to the project. KSO and SEA read, revised, and approved the final manuscript for submission.

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Ethics declarations

Ethics approval and consent to participate

This research was carried out in adherence to guidelines from the National Institutes of Health Guide for the Care and Maintenance of Laboratory Animals, and the protocol was approved by the Ethical Review Board of Afe Babalola University and the approval number was with the approval number ABUADERC/10B/2022, Nigeria. Consent to participate is not applicable.

Competing interests

The authors declare no competing interests.

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