

Lincomycin-Induced Alterations in Intestinal Nutrient Sensing, Neural Signaling, and Gastrointestinal Function in Rats

Abdelhakim E. Hrush^{1*}  | Salheen M. Salheen²  | Murad A. Belhaj³  | Warda E. Harroush⁴  |
Mohamed T. Elfouly⁵ 

¹Department of Biomedical Engineering, Faculty Medical Technology, University of Zawia, Zawia, Libya.

²Department of Physiology, Biochemistry and Nutrition, Faculty of Veterinary Medicine, University of Tripoli, Libya.

³Midwifery and Neonatal Department, The Higher Institute of Medical Sciences and Technologies, Abu Salim, Tripoli, Libya.

⁴Department of Human Cells and Tissues, Libyan Biotechnology Research Center, Tripoli, Libya.

⁵Department of Science, Centre for Environmental Sustainability and Remediation, RMIT University, Melbourne, Australia.

ABSTRACT

Purpose: This study aimed to determine whether lincomycin treatment alters mesenteric afferent responses to intraduodenal nutrient stimulation, gastrointestinal myoelectric activity, and intestinal morphology in rats.

Materials and Methods: Forty laboratory rats weighing 180–220 g were assigned to control and lincomycin-treated groups. Lincomycin was administered orally for approximately 10 days to induce antibiotic-associated intestinal dysbiosis. Mesenteric and vagal afferent nerve activity was recorded using bipolar silver–silver chloride electrodes. Nutrient-evoked responses were assessed following intraduodenal administration of 0.3 mL of 40% glucose and selected amino acid and lipid solutions. Gastrointestinal myoelectric activity was recorded from the ileum, cecum, and colon, and gross intestinal morphology was evaluated macroscopically.

Results: Intraduodenal glucose produced a marked increase in mesenteric afferent activity in control rats. In lincomycin-treated animals, basal afferent activity was reduced and the glucose-evoked response was substantially attenuated. Lincomycin treatment was also associated with altered gastrointestinal myoelectric activity, including increased colonic spike activity, together with pronounced cecal enlargement and luminal distension.

Conclusion: Lincomycin treatment was associated with impaired nutrient-evoked intestinal afferent signaling, altered gastrointestinal electrical activity, and marked cecal morphological changes. These findings suggest that antibiotic-induced disruption of the intestinal environment may affect sensory-motor regulation and nutrient-related signaling. (*Open J Biomed Res* 2026;5:139-146)

Keywords: Lincomycin; gut dysbiosis; nutrient sensing; mesenteric afferent signaling; gastrointestinal motility.

ARTICLE INFO

*Corresponding author:

Abdelhakim E. Hrush

Email: a.hrush@zu.edu.ly

Received: 27 July 2026

Accepted: 20 September 2026

Published: 22 September 2026

DOI:

<https://doi.org/10.26629/ojbr.2026.17>

Copyright: © 2026 by the authors.

Articles published in the *Open J Biomed Res* are licensed under a Creative Commons Attribution-Noncommercial 4.0 International License.

<https://creativecommons.org/licenses/by-nc/4.0/>



AUDIOABSTRACT



How to cite this article | Hrush AE, Salheen SM, Belhaj MA, Harroush WE, Elfouly MT. Lincomycin-Induced alterations in intestinal nutrient sensing, neural signaling, and gastrointestinal function in rats. *Open J Biomed Res* 2026;5:139-146.

INTRODUCTION

The gastrointestinal tract harbors a complex and dynamic microbial ecosystem that contributes to host nutrition, metabolism, immune regulation, epithelial homeostasis, and protection against pathogens.^{1,2} Although microbial density is greatest in the colon, the small intestine represents the principal site of nutrient digestion and absorption and contains specialized epithelial and enteroendocrine sensing systems that detect luminal carbohydrates, amino acids, peptides, and fatty acids.^{3,4} Activation of these nutrient-sensing pathways regulates intestinal transport, gastrointestinal hormone secretion, food intake, glucose homeostasis, and whole-body energy metabolism.^{3,4}

Increasing evidence indicates that intestinal nutrient sensing is influenced not only by dietary nutrients but also by the gut microbiota and its metabolites. Microbial products can interact directly or indirectly with epithelial and enteroendocrine signaling pathways, while microbiota-mediated changes in the luminal environment, epithelial integrity, and epithelial regeneration may further modify intestinal sensing and absorptive functions.⁴⁻⁶ Therefore, disruption of the intestinal microbial ecosystem has the potential to alter communication between luminal nutrients, microbial metabolites, and host nutrient-sensing mechanisms.

Antibiotic exposure is a major cause of perturbation of the gut microbial ecosystem. In addition to eliminating susceptible pathogens, antibiotics can reduce microbial diversity, alter the abundance of commensal taxa, modify microbial metabolic activity, and impair host-microbiota interactions.⁷⁻⁹ Antibiotic-associated dysbiosis has also been linked to disruption of intestinal barrier integrity and alterations in microbial metabolites that participate in host metabolic and immune regulation.^{8,9} However, considerably less is known about how

antibiotic-induced microbial disruption affects nutrient-sensing pathways in the small intestine. This represents an important knowledge gap because small-intestinal nutrient sensing contributes to the regulation of nutrient handling, gastrointestinal hormone secretion, and systemic metabolic homeostasis.^{4,5}

Lincomycin is a lincosamide antibiotic that has been used experimentally to induce substantial perturbations of the intestinal microbiota. Short-term lincomycin administration in young pigs produces marked temporal changes in gut microbial composition and short-chain fatty acid concentrations.¹⁰ Similarly, experimental lincomycin exposure in mice results in depletion and restructuring of the intestinal microbiota, accompanied by alterations in short-chain fatty acids, intestinal morphology, and mucosal immune parameters.¹¹ These findings establish lincomycin exposure as a useful experimental approach for investigating the physiological consequences associated with antibiotic-induced microbial disruption. Nevertheless, whether lincomycin-induced dysbiosis is accompanied by changes in nutrient-sensing receptor expression in the small intestine remains poorly understood.

Therefore, the present study aimed to investigate the effects of lincomycin treatment on intestinal nutrient-related sensory signaling and gastrointestinal function in rats. Specifically, the study sought to determine whether lincomycin exposure alters mesenteric afferent responses to intraduodenal nutrient stimulation, affects gastrointestinal myoelectric activity, and produces associated changes in intestinal morphology. By integrating electrophysiological and macroscopic assessments, the study aimed to characterize functional alterations in intestinal sensory-motor regulation following antibiotic-induced disruption of the intestinal environment and to

provide a basis for future studies examining the underlying microbiota-dependent and receptor-mediated mechanisms.

MATERIALS AND METHODS

Study Design

An experimental animal study was conducted to investigate the effects of lincomycin-induced intestinal dysbiosis on nutrient-evoked afferent signaling, gastrointestinal myoelectric activity, and intestinal morphology in rats. A total of 40 laboratory rats weighing 180–220 g were included in the study and allocated to control and lincomycin-treated groups. Animals in the experimental group received lincomycin orally for 9–14 days to induce disruption of the intestinal microbial environment. Control animals received no treatment under otherwise comparable experimental conditions. At the end of the treatment period, animals underwent electrophysiological assessment of mesenteric and vagal afferent nerve activity and gastrointestinal myoelectric activity. Nutrient solutions were administered intraduodenally to evaluate nutrient-evoked neural responses. Macroscopic changes in gastrointestinal morphology were also assessed.

Experimental Animals and Ethical Considerations

Forty laboratory rats weighing 180–220 g at the beginning of the experiment, were used. Animals were housed under controlled environmental conditions and free access to standard laboratory chow and water unless otherwise specified. All experimental procedures were performed in accordance with institutional and national guidelines for the care and use of laboratory animals.

Before electrophysiological procedures, the animals were anesthetized. The adequacy of anesthesia was monitored throughout the experiment and additional anesthetic was administered when required. At the completion of the experimental procedures, animals were euthanized according to the approved institutional

protocol. Rats assigned to the experimental group received lincomycin (Lincocin) orally at a dose of 84 + 10 mg/kg/day for consecutive days. The treatment regimen was selected to produce antibiotic-mediated perturbation of the intestinal microbial environment.

Surgical Preparation and Electrophysiological Recording

Following induction of anesthesia, animals were surgically prepared for electrophysiological recording. The abdominal cavity was accessed and the appropriate mesenteric and vagal nerve branches were carefully isolated while preserving their anatomical connections. Spontaneous and nutrient-evoked afferent nerve activity was recorded using bipolar silver–silver chloride (Ag/AgCl) electrodes. The isolated nerve was positioned on the recording electrodes, and electrical signals were recorded. A stable baseline recording was obtained before administration of each nutrient stimulus. Changes in afferent impulse activity following intraduodenal nutrient administration were subsequently monitored over time and compared with the corresponding pre-stimulation baseline.

Intraduodenal Nutrient Stimulation

Nutrient-evoked afferent responses were evaluated by administering selected nutrient solutions directly into the duodenum. A volume of 0.3 mL of the test solution was administered intraduodenally after stabilization of baseline nerve activity.

The nutrient stimuli included (1) 40% glucose solution; (2) 10% amino acid solutions containing glutamate, glycine, and γ -aminobutyric acid (GABA); and (3) a lipid emulsion. Following administration, afferent nerve activity was continuously recorded. The primary electrophysiological outcome was the change in afferent impulse frequency relative to the baseline recording period.

Recording of Gastrointestinal Myoelectric Activity

Gastrointestinal myoelectric activity was recorded using surface electrodes positioned on the serosal surface of the ileum, cecum, and colon. Electrical recordings were used to characterize basal gastrointestinal myoelectric activity, including slow-wave activity and spike potentials. Signals were recorded before and/or after nutrient stimulation and compared between control and lincomycin-treated animals.

Macroscopic Assessment of the Gastrointestinal Tract

At the completion of the electrophysiological experiments, the gastrointestinal tract was examined macroscopically. Particular attention was directed toward the cecum and colon to identify treatment-associated changes in gross morphology. Cecal size, luminal distension, intestinal wall appearance, and the presence of accumulated intestinal contents or gas were documented and compared between control and lincomycin-treated animals. Representative images were obtained for qualitative comparison.

RESULTS

Lincomycin Treatment Attenuated Glucose-Evoked Mesenteric Afferent Activity

Intraduodenal administration of 0.3 mL of 40% glucose produced a clear increase in mesenteric afferent impulse activity in control rats (Fig. 1A). Baseline activity remained relatively stable during the pre-stimulation period, ranging approximately from 22 to 26 impulses/s. Following glucose administration, afferent activity increased progressively, reaching its highest values approximately 40–60 min after stimulation. Although activity subsequently declined, it remained above baseline levels at the end of the recording period.

In lincomycin-treated rats, basal mesenteric afferent activity was markedly lower than that observed in controls, with values of approximately 3–6 impulses/s during the pre-

stimulation period (Fig. 1B). Intraduodenal glucose administration nevertheless elicited an increase in afferent firing, reaching approximately 15–20 impulses/s at peak response. The response remained elevated above baseline during the later recording period, although its overall magnitude was lower than that observed in control animals. These findings indicate that lincomycin treatment was associated with a marked reduction in basal mesenteric afferent activity and an attenuated neural response to intraduodenal glucose stimulation.

Lincomycin Treatment Produced Marked Cecal Enlargement and Distension

Macroscopic examination revealed substantial differences in cecal morphology between control and lincomycin-treated rats (Fig. 2). In control animals, the cecum showed the expected gross anatomical appearance, with normal dimensions, wall contour, and moderate luminal filling. In contrast, rats treated with lincomycin for 10 days exhibited pronounced cecal enlargement and luminal distension. The affected cecum appeared markedly expanded relative to the control specimen, with visible accumulation of luminal contents and gas. Changes in wall appearance and vascular prominence were also observed. These findings demonstrate a clear macroscopic alteration of cecal morphology following lincomycin treatment.

Lincomycin Treatment Increased Colonic Myoelectric Activity

Electrophysiological recordings of gastrointestinal myoelectric activity showed increased spike activity in the ascending colon of lincomycin-treated rats. Compared with control animals, colonic spike activity increased by approximately 300%. This increase in electrical activity indicates a marked alteration in colonic motor electrophysiology following lincomycin exposure.

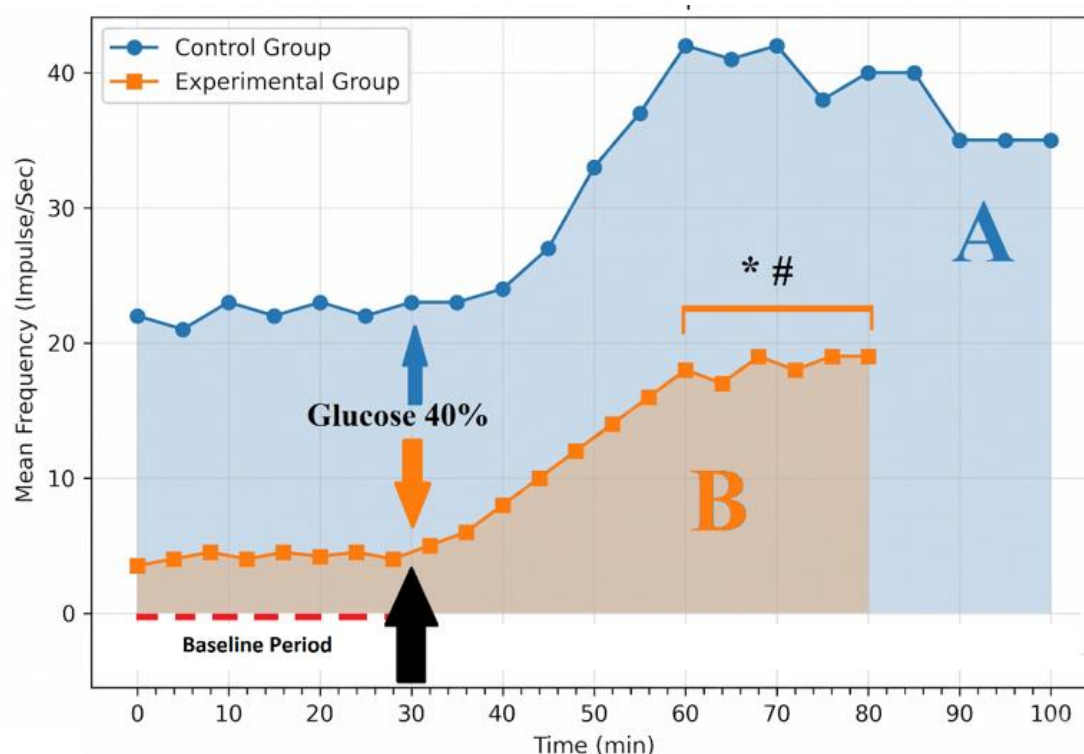


Fig 1: Effect of intraduodenal glucose administration on mesenteric afferent nerve activity in control and lincomycin-treated rats. Time-course changes in the frequency of mesenteric afferent impulses before and after intraduodenal administration of 0.3 mL of 40% glucose solution. (A) Control rats. (B) Lincomycin-treated rats. Arrows indicate the time of glucose administration.

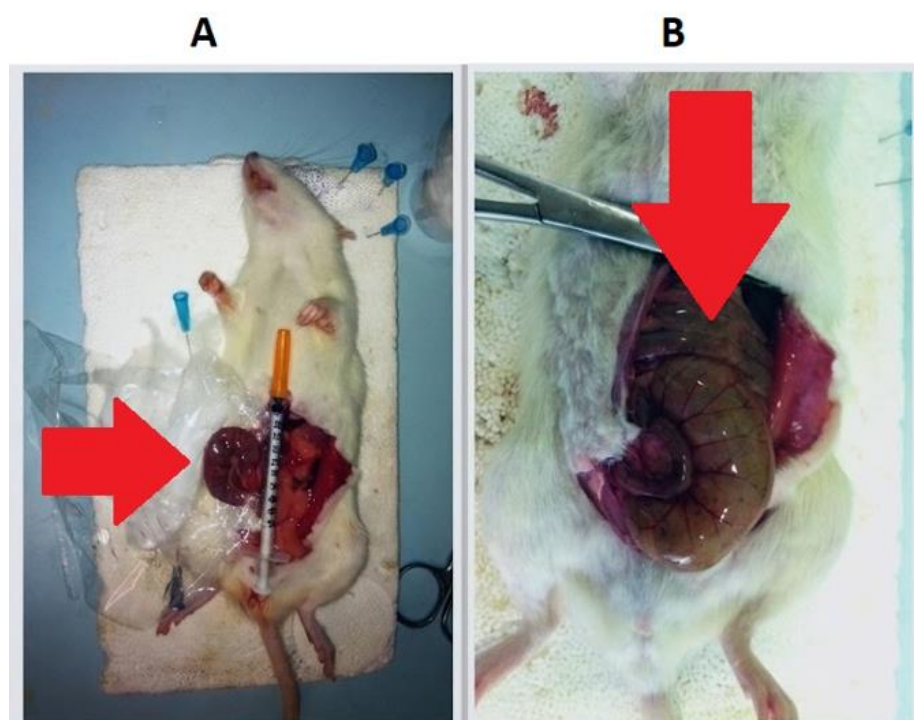


Fig 2: Macroscopic appearance of the cecum in control and lincomycin-treated rats. Representative gastrointestinal specimens showing cecal morphology in (A) a control rat and (B) a rat treated with lincomycin for 10 days. Lincomycin treatment was associated with marked cecal enlargement and luminal distension. Arrows indicate the principal regions of morphological alteration.

DISCUSSION

The present study showed that lincomycin treatment was associated with marked alterations in intestinal sensory signaling, gastrointestinal electrical activity, and cecal morphology in rats. The main functional finding was an attenuated mesenteric afferent response to intraduodenal glucose compared with control animals. This was accompanied by altered gastrointestinal myoelectric activity and pronounced cecal enlargement and distension. Together, these findings suggest that antibiotic-induced disruption of the intestinal environment may affect multiple components of gastrointestinal sensory and motor regulation.

The reduced glucose-evoked afferent response is consistent with growing evidence that intestinal nutrient sensing depends on coordinated interactions among epithelial nutrient sensors, enteroendocrine cells, microbial metabolites, and extrinsic sensory pathways. Enteroendocrine cells can communicate rapidly with sensory neurons and contribute to the transmission of luminal nutrient signals to the nervous system.^{12,13} Microbial metabolites, particularly short-chain fatty acids, may further modulate enteroendocrine activity and secretion of hormones such as glucagon-like peptide-1 (GLP-1) through receptors including FFAR2 and FFAR3.¹⁴ Previous studies have shown that lincomycin treatment can substantially alter gut microbial composition and short-chain fatty acid concentrations.^{10,11} Therefore, altered microbial signaling may contribute to the attenuated glucose response observed in the present study, although microbial metabolites and specific nutrient receptors were not directly measured.

The present findings are also compatible with previous reports demonstrating that antibiotic-induced dysbiosis can modify intestinal sensory and motor function. Aguilera et al. showed that antibiotic-induced microbial disruption produced changes in colonic sensory and motor responses in mice,¹⁵ while

an earlier study reported enhanced expression of visceral sensory-related systems following antibiotic exposure and stress.¹⁶ These findings indicate that the neural consequences of antibiotic treatment may vary according to the antibiotic used, treatment duration, intestinal region examined, and microbial populations affected. In the present study, the lower basal and glucose-evoked mesenteric afferent activity is therefore best interpreted as altered intestinal sensory responsiveness rather than complete loss of nutrient sensing.

The changes in gastrointestinal myoelectric activity provide additional evidence of disturbed intestinal neuromuscular regulation. Gastrointestinal motility depends on coordinated activity among enteric neurons, smooth muscle, interstitial cells of Cajal, epithelial mediators, and autonomic pathways.¹⁷ Experimental alteration or depletion of the gut microbiota has also been associated with changes in gastrointestinal transit, contractility, serotonin signaling, and enteric neuronal function.^{18,19} The altered colonic spike activity observed after lincomycin treatment may therefore reflect disruption of these regulatory networks, although the present study cannot distinguish microbiota-mediated effects from possible direct actions of the antibiotic.

Marked cecal enlargement and luminal distension were also observed in lincomycin-treated rats. Cecal enlargement is a recognized feature of germ-free and antibiotic-treated rodents and has been associated with substantial changes in microbial composition, luminal metabolites, intestinal transit, and intestinal physiology.²⁰ Similar alterations in intestinal microbial communities and microbial metabolites have been reported following lincomycin exposure.^{10,11} Therefore, the morphological changes observed in the present study are consistent with substantial disturbance of intestinal homeostasis, although the specific contributions of altered fermentation, gas production, fluid accumulation, or impaired transit were not directly assessed.

Several limitations should be considered. Gut microbiota composition was not directly characterized, and specific nutrient receptors, enteroendocrine hormones, inflammatory mediators, and short-chain fatty acids were not measured. Therefore, the present findings demonstrate an association between lincomycin treatment and altered intestinal sensory-motor function but do not establish the precise mechanisms involved. Future studies combining electrophysiology with microbiome profiling, metabolomic analysis, nutrient-receptor expression, and gastrointestinal hormone measurements would help determine whether the observed changes are directly mediated by antibiotic-induced microbial disruption.

CONCLUSION

Lincomycin treatment was associated with impaired glucose-evoked mesenteric afferent signaling, altered gastrointestinal myoelectric activity, and marked cecal enlargement in rats. These findings indicate that antibiotic-induced disruption of the intestinal environment can affect nutrient-related sensory signaling, gastrointestinal motor regulation, and intestinal morphology. However, because microbiota composition, microbial metabolites, nutrient receptors, and enteroendocrine mediators were not directly assessed, the underlying mechanisms remain to be clarified. Future studies combining electrophysiological measurements with microbiome, metabolomic, and receptor-expression analyses are needed to define the pathways involved and determine whether these functional alterations are reversible.

AUTHOR CONTRIBUTIONS

Abdelhakim E. Hrush: Conceptualization, methodology, writing – original draft, literature review, investigation, data curation, and manuscript preparation. **Salheen M. Salheen:** Writing – original draft, literature review, investigation, data curation, and manuscript preparation. **Murad A. Belhaj:** Validation,

critical review, writing – review & editing, and final approval of the manuscript. **Warda E. Harroush:** Writing – original draft, literature review, investigation, data curation, and manuscript preparation. **Mohamed T. Elfouly:** Validation, critical review, writing – review & editing, and final approval of the manuscript.

CONFLICT OF INTEREST

The authors declare no conflicts of interest concerning the research, authorship, and publication of this article.

FUNDING

This research received no external funding.

REFERENCES

1. Hillman ET, Lu H, Yao T, Nakatsu CH. Microbial ecology along the gastrointestinal tract. *Microbes Environ.* 2017;32(4):300-313. doi:10.1264/jsme2.ME17017.
2. Ohland CL, Jobin C. Microbial activities and intestinal homeostasis: a delicate balance between health and disease. *Cell Mol Gastroenterol Hepatol.* 2015;1(1):28-40. doi:10.1016/j.jcmgh.2014.11.004.
3. Rasoamanana R, Darcel N, Fromentin G, Tomé D. Nutrient sensing and signalling by the gut. *Proc Nutr Soc.* 2012;71(4):446-455. doi:10.1017/S0029665112000110.
4. Duca FA, Waise TMZ, Peppler WT, Lam TKT. The metabolic impact of small intestinal nutrient sensing. *Nat Commun.* 2021;12(1):903. doi:10.1038/s41467-021-21235-y.
5. Dontamsetti KD, Pedrosa-Suarez LC, Aktar R, Peiris M. Sensing of luminal contents and downstream modulation of GI function. *JGH Open.* 2024;8(5). doi:10.1002/jgh3.13083.
6. Arenas-Gómez CM, Garcia-Gutierrez E, Escobar JS, Cotter PD. Human gut homeostasis and regeneration: the role of the gut microbiota and its metabolites. *Crit Rev Microbiol.* 2023;49(6):764-785. doi:10.1080/1040841X.2022.2142088.
7. Willing BP, Russell SL, Finlay BB. Shifting the balance: antibiotic effects on host-microbiota mutualism. *Nat Rev Microbiol.*

- 2011;9(4):233-243.
doi:10.1038/nrmicro2536.
8. Dahiya D, Nigam PS. Antibiotic-therapy-induced gut dysbiosis affecting gut microbiota-brain axis and cognition: restoration by intake of probiotics and synbiotics. *Int J Mol Sci.* 2023;24(4):3074. doi:10.3390/ijms24043074.
9. Duan H, Yu L, Tian F, Zhai Q, Fan L, Chen W. Antibiotic-induced gut dysbiosis and barrier disruption and the potential protective strategies. *Crit Rev Food Sci Nutr.* 2022;62(6):1427-1452. doi:10.1080/10408398.2020.1843396.
10. Tang S, Zhang S, Zhong R, Su D, Xia B, Liu L, et al. Time-course alterations of gut microbiota and short-chain fatty acids after short-term lincomycin exposure in young swine. *Appl Microbiol Biotechnol.* 2021;105(21-22):8441-8456. doi:10.1007/s00253-021-11627-x.
11. Zhang S, Zhong R, Han H, Yi B, Yin J, Chen L, et al. Short-term lincomycin exposure depletion of murine microbiota affects short-chain fatty acids and intestinal morphology and immunity. *Antibiotics (Basel).* 2020;9(12):907. doi:10.3390/antibiotics9120907.
12. Kaelberer MM, Buchanan KL, Klein ME, Barth BB, Montoya MM, Shen X, et al. A gut-brain neural circuit for nutrient sensory transduction. *Science.* 2018;361(6408). doi:10.1126/science.aat5236.
13. Bellono NW, Bayrer JR, Leitch DB, Castro J, Zhang C, O'Donnell TA, et al. Enterochromaffin cells are gut chemosensors that couple to sensory neural pathways. *Cell.* 2017;170(1):185-198.e16. doi:10.1016/j.cell.2017.05.034.
14. Tolhurst G, Heffron H, Lam YS, Parker HE, Habib AM, Diakogiannaki E, et al. Short-chain fatty acids stimulate glucagon-like peptide-1 secretion via the G-protein-coupled receptor FFAR2. *Diabetes.* 2012;61(2):364-371. doi:10.2337/db11-1019.
15. Aguilera M, Cerdà-Cuéllar M, Martínez V. Antibiotic-induced dysbiosis alters host-bacterial interactions and leads to colonic sensory and motor changes in mice. *Gut Microbes.* 2015;6(1):10-23. doi:10.4161/19490976.2014.990790.
16. Aguilera M, Vergara P, Martínez V. Stress and antibiotics alter luminal and wall-adhered microbiota and enhance the local expression of visceral sensory-related systems in mice. *Neurogastroenterol Motil.* 2013;25(8). doi:10.1111/nmo.12154.
17. López-Pingarrón L, Almeida H, Soria-Aznar M, Reyes-Gonzales MC, Rodríguez-Moratinos AB, Muñoz-Hoyos A, et al. Interstitial cells of Cajal and enteric nervous system in gastrointestinal and neurological pathology, relation to oxidative stress. *Curr Issues Mol Biol.* 2023;45(4):3552-3572. doi:10.3390/cimb45040232.
18. Bernabè G, Shalata MEM, Zatta V, Bellato M, Porzionato A, Castagliuolo I, et al. Antibiotic treatment induces long-lasting effects on gut microbiota and the enteric nervous system in mice. *Antibiotics (Basel).* 2023;12(6):1000. doi:10.3390/antibiotics12061000.
19. Ge X, Ding C, Zhao W, Xu L, Tian H, Gong J, et al. Antibiotics-induced depletion of mice microbiota induces changes in host serotonin biosynthesis and intestinal motility. *J Transl Med.* 2017;15(1):13. doi:10.1186/s12967-016-1105-4.
20. Kennedy EA, King KY, Baldrige MT. Mouse microbiota models: comparing germ-free mice and antibiotics treatment as tools for modifying gut bacteria. *Front Physiol.* 2018;9:1534. doi:10.3389/fphys.2018.01534