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Prolonged Intake of Luvos Healing Earth does not alter the Composition of the Gut Microbiota in Patients with Diarrhea-predominant Irritable Bowel Syndrome and Healthy Controls

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ABSTRACT

Background & Aims: The mineral compound Luvos Healing Earth (LHE) is a commercially available remedy empirically used for a variety of gastrointestinal disorders. The aim of this study was to investigate the possible effect of prolonged LHE therapy on gut microbiota in healthy individuals and in patients with diarrhea-predominant irritable bowel syndrome (IBS-D).
Methods: In this prospective exploratory study, a total of 20 participants, including 12 healthy controls and 8 patients with IBS-D, received treatment with LHE (Magenfein Granulat, 1 sachet bid) for 6 weeks. Fecal samples were collected for microbiota analysis in the morning fasting state at regular intervals at 6 different timepoints: 2 weeks before starting therapy (Screen), and every 2 weeks during LHE therapy (V0-V3). Additionally, a follow-up visit was scheduled 4 weeks after the end of treatment (V4). Microbiota analysis was performed using the GA-map® Dysbiosis Test Lx v2. Dysbiosis Index, bacterial diversity, as well as the balance or imbalance of functionally important bacteria were assessed.
Results: The microbiota analysis revealed an overlap in gut microbiota profiles between healthy controls and patients with IBS-D. Bacterial communities were consistently stable during the entire treatment period, and no significant variations in composition were observed 4 weeks after the end of the therapeutic intervention. There was a remarkable stability of microbiota profiles over time within each individual and a high inter-individual variation. The majority of fecal samples exhibited profiles, reflecting an eubiotic state, with no significant changes in dysbiosis index, functional bacteria profiles, or bacterial diversity.
Conclusion: Our findings indicate intraindividual resilience of microbiota consortia during the entire study period. Prolonged intake of LHE does not cause significant alterations in fecal microbiota profiles in healthy controls and patients with IBS-D. Luvos Healing Earth does not affect the stability of gut microbial diversity and bacterial functions.

Key words: gut microbiota – mineral loess – healing earth – microbiota modulation – diarrhea – irritable bowel syndrome.

Abbreviations: DI: dysbiosis index; DLA-M: dietary lipid adsorbent-montmorillonite; IBS: irritable bowel syndrome; IBS-D: diarrhea-predominant IBS; LVE: Luvos Healing Earth; PCA: principal component analysis.

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INTRODUCTION

Healing clays are mineral compounds of various composition used since ancient times for therapeutic and cosmetic purposes [1]. The use of edible clays as a natural remedy to control gastrointestinal symptoms has gained increasing importance over the past years in the field of traditional medicine [2]. Luvos® Healing Earth (LHE) is a specific edible mineral compound that is derived from glacial loess, which is a sedimentary deposit of windblown particles resulting from the erosion and weathering of rocks during the last ice age [3]. It consists predominantly of silicate particles in the 20–60 µm size range (60-70%), carbonates (10-30%) and other minerals and trace elements, including calcium, potassium, iron, magnesium, copper and zinc [4]. Due to its physicochemical characteristics, LHE possesses high adsorbing and absorbing capacities and acid neutralization properties, which may contribute to its beneficial effects in the digestive tract.

Luvos Healing Earth is widely used as an over-the-counter medical device in Germany and in other Western countries for a

variety of gastrointestinal disorders, including gastroesophageal reflux disease [5], functional dyspepsia, diarrhea and diarrhea-predominant irritable bowel syndrome (IBS-D) [6, 7].

Recent studies indicate that certain natural clay minerals may have antimicrobial actions and, therefore, potentially impact the composition of various microbial populations [8]. For instance, the topical application of French green clays has been successfully used in the treatment of skin infections caused by *Mycobacterium ulcerans*, which leads to a necrotizing fasciitis known as Buruli ulcer [9]. *In vitro* studies have also demonstrated that specific mineral products exhibit intrinsic, heat-stable antibacterial activity against susceptible and resistant Gram-negative pathogens, including *Escherichia*, *Salmonella*, *Pseudomonas*, and Gram-positive *Staphylococcus* (PRSA/MRSA) [10, 11]. Other compounds, such as Jordan's red soil, which is rich in montmorillonite, kaolinite, illite, vermiculite, and palygorskite, can influence microbial interactions and induce the proliferation of certain bacterial strains, including Actinomycetes, *Bacillus* spp., and *Lysobacter* spp., capable of producing antibiotic substances to compete with other bacteria [12].

No important adverse effects associated with LHE therapy have been reported so far; however, the effect of a prolonged use of LHE on bacterial communities of the human gut microbiota is not known.

The aim of this study was to investigate variations in fecal microbiota composition of healthy individuals and patients with IBS-D before, during and after consumption of LHE.

METHODS

Study Participants

Patients with IBS-D and healthy controls were prospectively recruited at the Ludwig Maximilians University Hospital in Munich, Germany from May 2021 to May 2022.

Subjects were recruited within the ARENA project (DRKS-ID: DRKS00032274), a prospective pilot study focused on research on the impact of LHE consumption on the gut microbiota profiles of healthy individuals, patients with IBS-D, as well as dyspeptic patients with liver cirrhosis and concomitant minimal hepatic encephalopathy. The study protocol was reviewed and approved by the local ethics committee and government authorities, approval number 20-0880, and was conducted in accordance with the current Good Clinical Practice guidelines and the Declaration of Helsinki [13]. All recruited subjects provided their written informed consent for participation. Healthy subjects did not report any gastrointestinal disease, tumor disease, severe metabolic or cardiovascular disease requiring therapy, or neurodegenerative disease. Patients with IBS-D were diagnosed according to Rome IV criteria after an accurate anamnesis and clinical evaluation. Presence of a mixed form of IBS (IBS-M, with changing bowel habits including diarrhea and constipation) or constipation form of IBS (IBS-C) were exclusion criteria. Other exclusion criteria included: antibiotic treatment within 4 weeks prior to study inclusion or during study period, documented underlying allergy against LHE, hospitalization, planned bowel cleansing or major surgery during the study period, pregnancy and lactation status.

Study Design and Specimen Collection

Study subjects received treatment with Luvos® Magenfein Granulat (Heilerde-Gesellschaft Luvos Just GmbH & Co., Friedrichsdorf, Germany), 1 sachet bid over a period of 6 weeks. A 2-day long pause was observed after the first 3 weeks, according to the manufacturer recommendations. Participants were instructed to maintain a daily diary, recording their consumption of LHE together with clinical symptoms and changes in bowel habits. Fecal samples were collected from each participant at 6 different timepoints: 2 weeks before starting therapy (screening visit, Screen), on day 0 (visit 0, V0), during treatment on days 14, 28 and 42 (visits V1-V3), and 4 weeks after the end of treatment on a follow-up visit (day 71, visit V4), as illustrated in Fig 1.

Fecal samples were collected using a sterile stool sample collection kit (PT26.1; Carl Roth, Karlsruhe, Germany) containing RNA-Later (Ambion, Thermo Fisher Scientific, Waltham, MA) and kept in the refrigerator at 4°C (for a maximum of 8 h) until transfer to the laboratory. After aliquoting, the samples were stored at −80°C until further analysis.

Microbiota Analysis

Microbiota analysis was performed using the GA-map® Dysbiosis Test Lx v2 (Genetic Analysis, Oslo, Norway), which characterizes the microbiota composition, and assesses the degree of deviation from that of a reference healthy population, by detection of 48 bacterial markers (DNA probes) [14]. Each bacterial marker represents a preselected target in the bacterial 16S rRNA gene, detected at various taxonomic levels (e.g., species, family, phylum). In brief, the test utilizes fecal homogenization, and mechanical and enzymatic bacterial cell disruption to isolate bacterial genomic DNA. Subsequently, 16S rRNA hypervariable regions V3-V9 were amplified by polymerase chain reaction (PCR). The amplified bacterial DNA was used in a probe-labeling reaction (single nucleotide extension) before hybridization of the probe-set to solid-phase. Finally, the abundance of bacteria was assessed by the strength

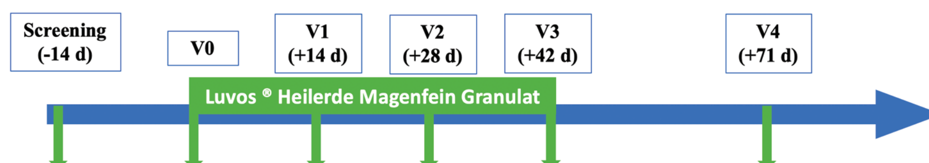

Fig. 1. Study design and sample collection schedule.

of fluorescent signal (probe intensity), detected and measured by a Luminex® L×200™ instrument (Luminex Corporation). The raw signal intensity measured of each bacterial marker was normalized using a hybridization control and a synthetic template, and background noise was removed prior to analysis. In total, the relative abundance of 48 bacteria markers targeting more than 300 bacteria species was measured.

The test algorithmically assesses fecal bacterial abundance and profile in comparison to a healthy reference population. A deviation in the microbiota from normobiosis is summarized using a dysbiosis index (DI) ranging from 1 to 5. Dysbiosis index of 1–2 indicates normobiosis, 3 indicates mild dysbiosis, and 4–5 indicates severe dysbiosis. Bacterial abundance is reported as a score within the range of –3 to +3 (0 indicates within the normal range) and is measured for all 48 bacteria markers for each sample analyzed (Supplementary file, Table S1). To estimate bacterial diversity normalized signal intensities from a set of 28 selected uncorrelated bacterial markers was utilized. Depending on the number of different species and their abundance, diversity was categorized as either expected ("balance") or lower than expected ("imbalance"). The assessment of key gut microbiota functions involved the evaluation of the abundance of selected bacterial markers consolidated into five functional bacteria profiles: butyrate-producing bacteria, gut mucosa-protective bacteria, gut health marker, gut barrier-protective and potentially harmful bacteria, and pro-inflammatory bacteria. Each profile represented a unique set of bacteria signatures linked to their specific functional properties. Based on the abundance scores of the selected markers, the profiles were categorized as either "balanced" or "imbalanced" (Supplementary file, Table S2 for summary).

Statistical Analyses

Descriptive statistical analysis was performed using IBM SPSS Statistics 21.0.0 (IBM Corporation, New York, N.Y., USA) and GraphPad Prism 7. Numerical variables were expressed as mean values ± standard deviation. The chi-square test was used for comparison of categorical data. Shapiro–Wilk test was used to assess the normality of the data. To evaluate statistical differences between two groups Mann-Whitney-U-Tests and Kruskal-Wallis tests were performed for non-normally distributed data. All tests were carried out two-sided with a level of significance set to 0.05.

Analysis of microbiota profiles was based on the normalized signal strengths from the 48 bacterial markers in the GA-map® Test, performed in R using the Stats package (version 4.0.5). Principal component analysis (PCA) with confidence ellipses was used to illustrate overall similarities and variations in the microbiota profile between samples (using scaled and log-transformed normalized signal strengths). Nonparametric statistical tests were used to assess differential expression of each bacterial marker, between and within groups. Mann-Whitney-U-test was used for comparing the groups comprising healthy or IBS-D. Wilcoxon signed-rank test (i.e., paired test) was used to compare timepoints within each of the groups. V0 was here compared with each of the remaining timepoints (Screen, V1, V2, V3 and V4). All p-values were corrected by applying Bonferroni correction. Differences were considered statistically significant if the adjusted p-value (p adj.) was <0.05.

RESULTS

Characteristics of the Study Cohort

A total of 20 subjects including 12 healthy individuals (male: 6, female: 6, mean age, 26.4±5.6 years) and 8 patients with IBS-D (male: 3, female: 5, mean age 29±10.8 years) were enrolled. No statistically significant differences were found in age distribution and gender proportions between groups. All recruited participants successfully completed the treatment with LHE according to the study protocol and provided fecal samples during the scheduled visits, except for two healthy subjects who did not provide a fecal specimen for V4. Four patients (50%) with IBS-D reported an improvement in bowel habits and/or gastrointestinal symptoms during the treatment period, whereas no changes in bowel habits were reported by the remaining patients with IBS-D and the healthy participants.

Gut Microbiota Composition during Study

The gut microbiota profiles of 118 fecal samples were analyzed using the GA-map® Dysbiosis Test Lx v2. Principal component analysis was used to visualize variation in signal strength data. The inter-individual comparison between the IBS-D and healthy groups PCA showed that the microbiota profiles were overlapping to a great degree both at baseline (V0) and at the end of LHE treatment (V3), (Fig. 2). No bacterial markers were found to display significant differences between healthy individuals and IBS-D groups (paired timepoints, p adj. >0.05).

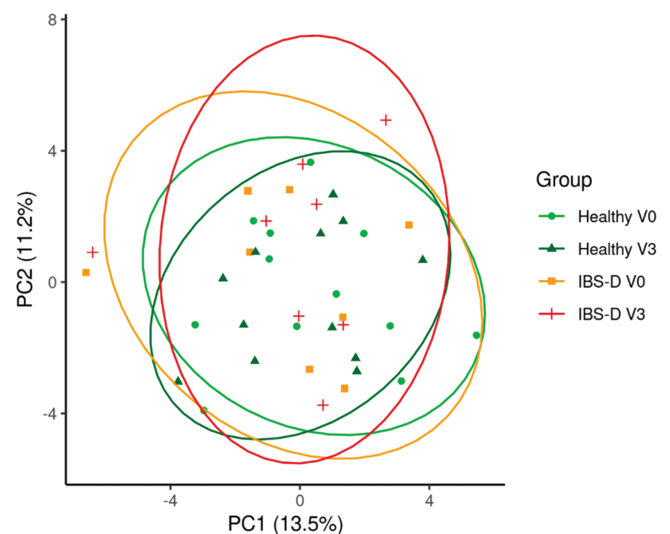

Fig. 2. PCA score plot for the between-groups comparison of healthy controls (n=12) and patients with IBS-D (n=8) at day 0/baseline (V0) and day 42/end of treatment (V3). The plot show 90% confidence ellipses and was generated using normalized signal strengths from the GA-map® Dysbiosis Test Lx.

The within-group analysis revealed a remarkable stability of bacterial communities over time. Microbiota profiles exhibited consistent similarity across different timepoints and covered a largely overlapping area in the PCA plot, demonstrating microbial stability prior to, during, and after LHE treatment in both healthy subjects and patients with IBS-D (Fig. 3 A-B). Overall, a notable inter-individual variation was observed.

The microbiota profiles showed high similarity within each individual and maintained their stability throughout the entire study period, including different timepoints, in both, healthy and IBS-D groups (see Fig. 3 C-D). No significant changes in the abundance (signal intensities) of single bacterial markers were observed in the intra-individual comparisons at different timepoints (V0 vs. Screen/V1/V2/V3/V4, p adj.>0.05).

Dysbiosis Index, Bacterial Diversity and Functional Bacteria Profiles

The large majority of fecal samples analyzed showed normobiotic bacterial profiles. Within the healthy group, the calculated DI indicated normobiosis (DI of 1-2) in 64 samples (91.4%), mild dysbiosis (DI of 3) in 4 samples (5.7%), and severe dysbiosis (DI of 4-5) in 2 samples (2.9%). For patients with IBS-D, the microbiota exhibited a DI of 1-2 in 42 samples (87.5%) and a DI of 3 in 6 samples (12.5%). No severe dysbiosis was observed in the IBS-D patient group. When comparing the different timepoints, no significant differences in the DI were observed for both patients with IBS-D and healthy controls (Fig. 4).

Most of the bacterial markers analyzed exhibited either no deviation or only a low degree of deviation from the normal abundances defined in the healthy reference population of the GA-map® Test [14] (Supplementary file, Fig. S3 and S4). There were a few exceptions that contributed to a high DI observed at certain timepoints among healthy individuals. For example, two healthy subjects had a DI of 4 or 5 at the Screen-timepoint, primarily due to elevated levels of *Bacteroides stercoris* or elevated levels of *Shigella* spp./*Escherichia* spp. and decreased levels of *Lachnospiraceae*, respectively.

Analysis of functional bacteria profiles revealed reduced abundances of butyrate-producing bacteria in 8.3-33.3% of healthy individuals and in 0-12.5% of patients with IBS-D (Fig. 5). Imbalances in the profiles of gut mucosa-protective bacteria, gut barrier-protective bacteria and potentially harmful bacteria were observed in 0-8.3% and 0-12.5% of healthy subjects and patients with IBS-D, respectively. Bacterial markers with pro-inflammatory functions were found to be more abundant only at the Screen-timepoint in 8.3% of healthy individuals. No imbalances in pro-inflammatory profiles were observed in patients with IBS-D, and no significant deviations in gut health profiles were observed in both groups. Bacterial diversity was normal in the IBS-D group, while a reduction was observed in 0-25% of healthy subjects, primarily in samples from the two subjects who presented with a high DI. Significant variations

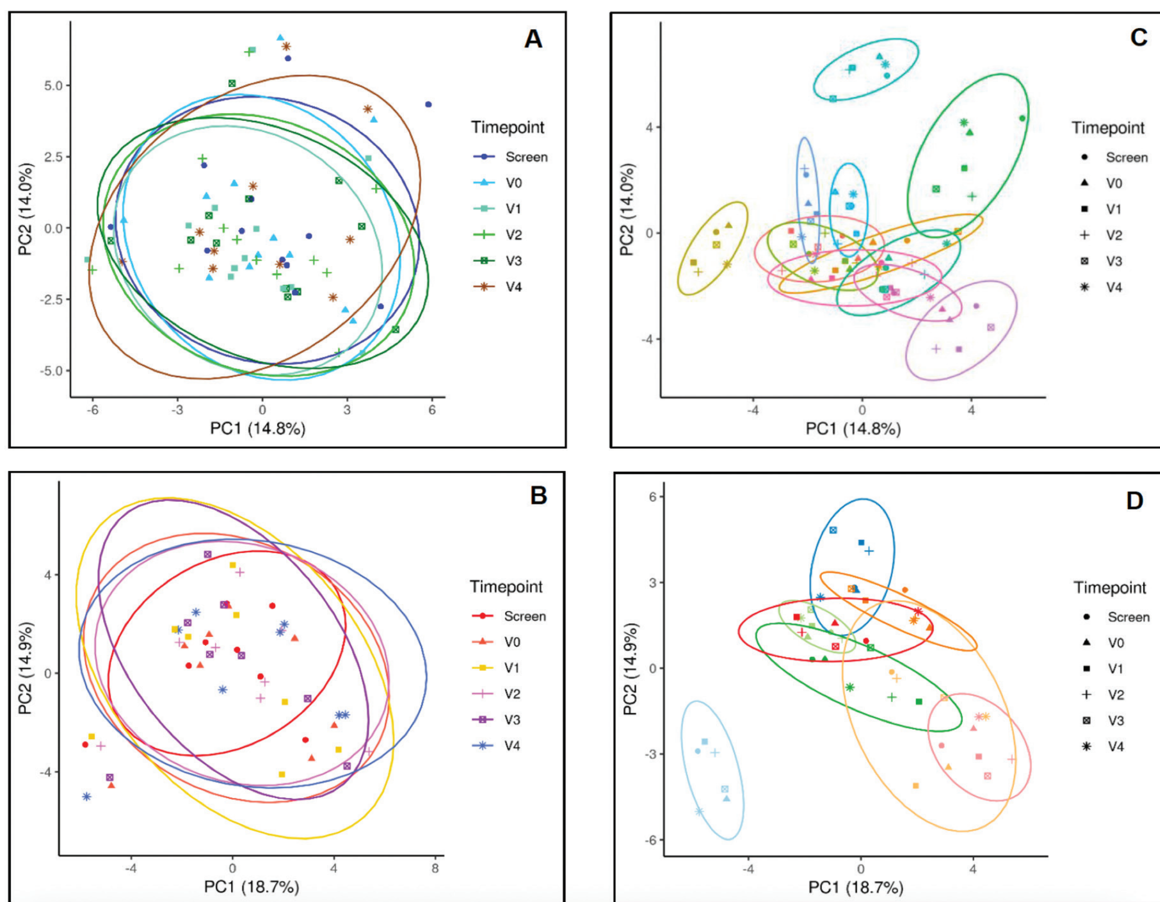

Fig. 3. PCA score plots for the within-groups comparison of healthy controls (n=12*) and patients with IBS-D (n=8). The plots are grouped by timepoints, for A) healthy group and B) IBS-D group, and by subjects, for C) healthy group and D) IBS-D group. Timepoints: -14 days (Screen), day 0/baseline (V0), day 14 (V1), day 28 (V2), day 42/end of treatment (V3), and day 71/4 weeks post-treatment (V4). *n=10 for timepoint 'V4'. The plots show 90% confidence ellipses and were generated using normalized signal strengths from the GA-map® Dysbiosis Test Lx.

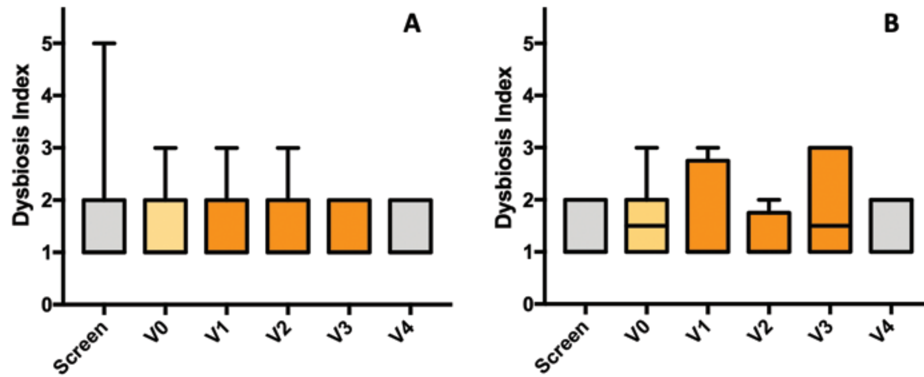

Fig. 4. Box plots showing the dysbiosis index (DI) in healthy subjects (A) and in patients with IBS-D (B) at different timepoints: -14 days (Screen), day 0/baseline (V0), day 14 (V1), day 28 (V2), day 42/end of LHE-treatment (V3), and 4 weeks post-treatment (V4).

in functional bacteria profiles and bacterial diversity were not observed during or after LHE treatment.

DISCUSSION

To our knowledge this is the first study investigating the influence of a mineral compound therapy on human gut microbiota. The most remarkable finding in our analysis was the stability of microbial profiles observed during the entire study period. Regular use of LHE for 6 weeks was not associated with major changes in microbiome composition or alterations of functionally important bacterial markers. Microbial profiles showed a marked inter-individual variation, maintaining a consistent composition within the same individual across multiple timepoints (before, during, and after LHE exposure). This indicates that treatment with LHE does not result in significant perturbation of the gut microbiota.

The gut microbiota composition is highly sensitive to changes in exogenous factors, e.g. diet or medications, which may cause significant alterations in microbial diversity and function. Several studies have previously shown that different mineral clays may have antimicrobial effects [8]. However, only a small number of these studies have assessed the effect of mineral clays on gut microbiota, and such studies were conducted in animal models. Xia et al. [15] observed that dietary supplementation with copper bearing montmorillonite was associated with reduced incidence of diarrhea and decreased total viable counts of *Clostridium* spp. and *E. coli* in small intestine and proximal colon of weanling pigs as compared to controls. In experimental studies investigating high-fat diet-induced obesity, supplementation with clay mineral preparations, specifically Korean bentonite (Bgp35b-p) and Chinese dietary lipid adsorbent-montmorillonite (DLA-M), resulted in positive alterations in gut microbiome, shown in mouse models [16, 17]. The high-fat diet resulted in microbial dysbiosis, characterized by decreased *Bacteroidetes* and increased *Firmicutes* and *Proteobacteria* abundances. Conversely, the addition of bentonite Bgp35b-p was associated with a significant increase in the relative abundance of bacteria producing short-chain fatty acids (SCFA), such

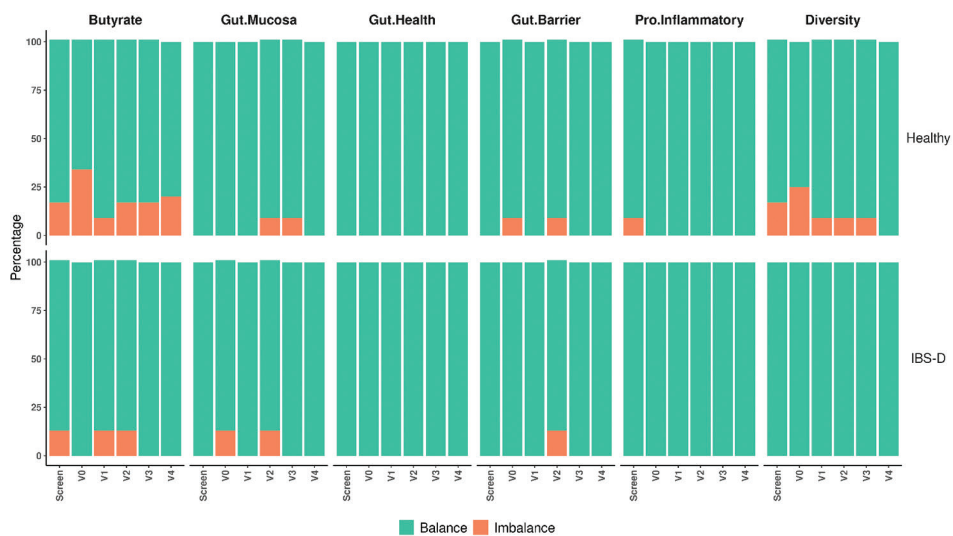

Fig. 5. Rates (percentage) of samples with „imbalance," marked in red, for each functional bacteria profile and diversity per timepoint, for healthy controls (n=12*) and patients with IBS-D (n=8). Timepoints: -14 days (screen), day 0/baseline (V0), day 14 (V1), day 28 (V2), day 42/end of treatment (V3), and 4 weeks post-treatment (V4). *n=10 for timepoint ‚V4'.

as *Ruminococcaceae*, and a decrease of *Clostridiaceae* and *Lachnospiraceae* [16]. Similarly, supplementation with DLA-M resulted in higher abundances of SCFA-producing *Blautia* bacteria and decreased levels of endotoxin-producing *Desulfovibrio* bacteria [17]. Our findings do not support an antibacterial activity of LHE, at least towards the bacterial markers selected in the GA-map® Dysbiosis Test Lx. Although the mechanisms how clay components affect bacteria are largely unknown, variations in composition and peculiar physicochemical characteristics (i.e. mineralogy, cation exchange capacity [8]) may explain different interactions with microorganisms and bacterial metabolites.

We observed a higher inter-individual variation than intra-individual variation in microbiota profiles among healthy subjects. These findings are in agreement with those of previous studies, indicating that gut microbiota composition is highly personalized as a result of continuous influences by multiple factors such as age, gender, diet, environment, lifestyle, diseases and medications [18-20]. Furthermore, bacterial assemblages exhibited remarkable stability over time within the same individual. This suggests that the inter-individual variability of gut microbiota is much stronger compared to the temporal variability, indicating that each individual possesses a unique and largely stable microbial signature over time [21, 22].

Irritable bowel syndrome is a common functional gastrointestinal disorder and alterations in microbiota composition and function are believed to play a significant role in its pathogenesis [23, 24]. While there is evidence supporting benefits of mineral clays in alleviating some IBS-related symptoms [6, 25], data on their impact on gut microbiota are currently lacking. In this study, analogously to the group of healthy subjects, microbiota profiles of patients with IBS-D were characterized by high inter-individual variability and an intra-individual stability over time. The comparison of microbiota profiles between patients with IBS-D and healthy controls revealed a large overlap, showing a certain degree of similarity in bacterial communities between the two groups. These findings are in line with a previous study conducted by our group, where we did not find significant differences between individuals with various IBS subtypes and healthy controls by employing the same methodology to compare the fecal microbiota [26]. Although an increasing number of studies highlights differences in microbial diversity and alteration in the relative abundance of specific bacteria in patients with IBS compared to healthy subjects, such findings often present conflicting results and reflect the heterogeneity of the IBS spectrum [27, 28]. Currently, no clear microbial signature that can reliably distinguish between patients with IBS and healthy individuals or discriminate different IBS subtypes has been reported.

One limitation of our study is associated with the methodology used to analyze the fecal microbiota. The GA-map® Dysbiosis Test Lx allows for the evaluation of a specific set of bacterial markers, targeting the most relevant gut bacteria in a standardized manner [14]. However, it is important to note that this analysis may not reveal potential variations in bacterial assemblages that are not covered by the predefined markers. Furthermore, the assessment of gut microbiota activity relies on functional prediction, which is based on 16S rRNA gene data and the relative abundances of bacteria included in the functional profiles.

Future studies should prioritize metabolomic analysis with direct measurements of bacterial products, such as short chain fatty acids SCFA, and comprehensive microbiota analysis encompassing all bacterial communities. This approach will provide a more precise evaluation of the impact of LHE on gut microbiota.

CONCLUSIONS

Our study indicates that short and prolonged use of LHE does not alter the composition of the microbiota in patients with IBS-D or in healthy individuals. These findings highlight the resilience properties characterizing the human gut microbiota. Additionally, our findings provide further strong support for the safety of LHE therapy in relation to gastrointestinal bacterial communities.

Conflicts of interest: P.M., M.S. are advisory board Luvos GmbH. K.G., K.H.K., C.C. are employees of Genetic Analysis AS. C.C. and K.H.K. own shares in Genetic Analysis AS. All other authors have no conflicts of interest to declare.

Authors' contribution: R.V., C.S., and P.M. designed the study. R.V., C.S., and P.M. obtained funding and supervised the study procedures. R.V., M.S., L.M., S.K. recruited suitable subjects, collected samples and registered data. K.G., K.H.K., C.C. performed laboratory workup, microbiota analysis, bioinformatic and statistical analyses. R.V., C.S., P.M., K.G., K.H.K. and C.C. interpreted the data. R.V., C.S. and P.M. drafted the manuscript. All authors critically revised the manuscript, approved the final version to be published, and agree to be accountable for all aspects of the work.

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Supplementary material: To access the supplementary material visit the online version of the *J Gastrointestin Liver Dis* at http://dx.doi.org/10.15403/jgld-5309

REFERENCES

1. Gomes CSF. Healing and edible clays: a review of basic concepts, benefits and risks. Environ Geochem Health 2018;40:1739-1765. doi:10.1007/s10653-016-9903-4

2. Carretero MI. Clay minerals and their beneficial effects upon human health. A review. Appl Clay Sci 2002;21:155-163. doi:10.1016/S0169-1317(01)00085-0
3. Smalley IJ. The properties of glacial loess and the formation of loess deposits. J Sediment Res 1966;36:669-676. doi:10.1306/74D7153C-2B21-11D7-8648000102C1865D
4. Uehleke B. Mit Heilerde natürlich behandeln – innerlich und äußerlich. Ein traditionsreiches Naturheilmittel im Fokus der Wissenschaft. Ernähr Med 2019;34:199-207. doi:10.1055/a-0979-0257
5. Orth T, Mönnikes H. PS042 Healing earth in patients with NERD is a safe and effective therapeutic option. Internist 2020;61(1 Suppl):S30. Abstracts zum 126. Kongress der Deutschen Gesellschaft für Innere Medizin e.V. doi:10.1007/s00108-020-00787-z
6. Mokhtare M, Asadipanah M, Bahardoust M, et al. Efficacy of adding Luvos® Healing Earth supplementation to mebeverine in improving symptoms and quality of life of patients with diarrhea-predominant irritable bowel syndrome: A randomized clinical trial. Biomed Res Ther 2018;5:2776-2783. doi:10.15419/bmrat.v5i10.493
7. Madisch A, Schaper S, Stange R, Uehleke B. PS04 Wirksamkeit der Luvos-Heilerde bei dyspeptischen und reizdarmtypischen Symptomen– Ergebnisse einer prospektiven nicht-interventionellen Studie. Internist 2020;61(1 Suppl):S31. Abstracts zum 126. Kongress der Deutschen Gesellschaft für Innere Medizin e.V. doi:10.1007/s00108-020-00787-z
8. Williams LB, Haydel SE. Evaluation of the medicinal use of clay minerals as antibacterial agents. Int Geol Rev 2010;52:745-770. doi:10.1080/00206811003679737
9. Williams LB, Haydel SE, Giese RF, Eberl DD. Chemical And Mineralogical Characteristics of French Green Clays Used for Healing. Clays Clay Miner 2008;56:437-452. doi:10.1346/CCMN.2008.0560405
10. Tong G, Yulong M, Peng G, Zirong X. Antibacterial effects of the Cu(II)-exchanged montmorillonite on Escherichia coli K88 and Salmonella choleraesuis. Vet Microbiol 2005;105:113-122. doi:10.1016/j.vetmic.2004.11.003
11. Haydel SE, Remenih CM, Williams LB. Broad-spectrum in vitro antibacterial activities of clay minerals against antibiotic-susceptible and antibiotic-resistant bacterial pathogens. J Antimicrob Chemother 2008;61:353-361. doi:10.1093/jac/dkm468
12. Falkinham JO 3rd, Wall TE, Tanner JR, et al. Proliferation of antibiotic-producing bacteria and concomitant antibiotic production as the basis for the antibiotic activity of Jordan's red soils. Appl Environ Microbiol 2009;75:2735-2741. doi:10.1128/AEM.00104-09
13. World Medical Association. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. JAMA 2013;310:2191-2194. doi:10.1001/jama.2013.281053
14. Casén C, Vebø HC, Sekelja M, et al. Deviations in human gut microbiota: a novel diagnostic test for determining dysbiosis in patients with IBS or IBD. Aliment Pharmacol Ther 2015;42:71-83. doi:10.1111/apt.13236
15. Xia MS, Hu CH, Xu ZR. Effects of copper bearing montmorillonite on the growth performance, intestinal microflora and morphology of weanling pigs. Anim Feed Sci Tech 2005;118:307-317. doi:10.1016/j.anifeedsci.2004.11.008
16. Lee ES, Song EJ, Lee SY, et al. Effects of bentonite Bgp35b-p on the gut microbiota of mice fed a high-fat diet. J Sci Food Agric 2018;98:4369-4373. doi:10.1002/jsfa.8934
17. Xu P, Hong F, Wang J, et al. Microbiome Remodeling via the Montmorillonite Adsorption-Excretion Axis Prevents Obesity-related Metabolic Disorders. EBioMedicine 2017;16:251-261. doi:10.1016/j.ebiom.2017.01.019
18. Human Microbiome Project Consortium. Structure, function and diversity of the healthy human microbiome. Nature 2012;486:207-214. doi:10.1038/nature11234
19. Vasapolli R, Schütte K, Schulz C, et al. Analysis of Transcriptionally Active Bacteria Throughout the Gastrointestinal Tract of Healthy Individuals. Gastroenterology 2019;157:1081-1092.e3. doi:10.1053/j.gastro.2019.05.068
20. Schloissnig S, Arumugam M, Sunagawa S, et al. Genomic variation landscape of the human gut microbiome. Nature 2013;493:45-50. doi:10.1038/nature11711
21. Costello EK, Lauber CL, Hamady M, Fierer N, Gordon JI, Knight R. Bacterial community variation in human body habitats across space and time. Science 2009;326:1694-1697. doi:10.1126/science.1177486
22. Rajilić-Stojanović M, Heilig HG, Tims S, Zoetendal EG, de Vos WM. Long-term monitoring of the human intestinal microbiota composition. Environ Microbiol 2013;15:1146-1159. doi:10.1111/1462-2920.12023
23. Han L, Zhao L, Zhou Y, et al. Altered metabolome and microbiome features provide clues in understanding irritable bowel syndrome and depression comorbidity. ISME J 2022;16:983-996. doi:10.1038/s41396-021-01123-5
24. Collins SM. A role for the gut microbiota in IBS. Nat Rev Gastroenterol Hepatol 2014;11:497-505. doi:10.1038/nrgastro.2014.40
25. Chang FY, Lu CL, Chen CY, Luo JC. Efficacy of dioctahedral smectite in treating patients of diarrhea-predominant irritable bowel syndrome. J Gastroenterol Hepatol 2007;22:2266-2272. doi:10.1111/j.1440-1746.2007.04895.x
26. Vasapolli R, Schulz C, Schweden M, et al. Gut microbiota profiles and the role of anti-CdtB and anti-vinculin antibodies in patients with functional gastrointestinal disorders (FGID). Eur J Clin Invest 2021;51:e13666. doi:10.1111/eci.13666
27. Pittayanon R, Lau JT, Yuan Y, et al. Gut Microbiota in Patients With Irritable Bowel Syndrome-A Systematic Review. Gastroenterology 2019;157:97-108. doi:10.1053/j.gastro.2019.03.049
28. Su Q, Tun HM, Liu Q, et al. Gut microbiome signatures reflect different subtypes of irritable bowel syndrome. Gut Microbes 2023;15:2157697. doi:10.1080/19490976.2022.2157697