

EFFECT OF MIKROBIÓM+® ON DIGESTIVE SYMPTOMS, MENTAL WELL-BEING, SLEEP QUALITY, AND SKIN QUALITY

The microbiome affects not only digestive tract health but also extra-digestive organs such as the brain and skin.



CONSUMER STUDY

- 3-month
- consumer study
- on the effects of Mikrobióm+® on digestion, mood, sleep, and skin.

The aim of our study was to investigate the effects of a 3-month supplementation with Mikrobióm+® (500 mg/day) on self-assessed digestive health, sleep quality, psychological well-being, and skin appearance in healthy adult participants. Participants took Mikrobióm+® twice daily for a period of three months. At three different time points during supplementation, they completed an online questionnaire evaluating their subjective perception of the above-mentioned parameters. After three months, we observed significant improvements in digestive discomfort (particularly bloating), increased energy levels, enhanced psychological well-being, and better skin and sleep quality. These findings confirm the potential of Mikrobióm+® as a natural supplement that supports overall health through modulation of the gut microbiome.

Communication between the gut and other organs is bidirectional, with short-chain fatty acids (SCFAs) playing an important role as signaling molecules. Flavonoids such as hesperidin and naringin, present in Mikrobióm+®, may positively influence skin appearance, sleep quality, and overall mental well-being through their effects on SCFA production and gut health.



Introduction

It is increasingly clear that gut function affects not only digestive tract health but also extra-digestive health. Changes in the gut microbiota — a dynamic population of microorganisms — can influence other organs as well. The gut microbiota mediates these connections through neural, endocrine, immune, and metabolic pathways. In recent years, the gut-brain and gut-skin axes have received significant attention (1).

The gut-brain axis refers to the bidirectional communication between the central nervous system and the gut microbiota. Altered microbiota composition and intestinal inflammation are associated with stress, the development of anxiety and depression, and reduced sleep quality, thereby affecting mental well-being (2).

The gut-skin axis represents a bidirectional communication system between gut health and skin condition. Increased intestinal permeability can contribute to systemic inflammation, which may lead to skin inflammation, such as acne. Additionally, disrupted microbiota may reduce immune tolerance, potentially contributing to allergic skin reactions associated with eczema (3, 4).

Gut health can be improved in various ways. Intake of prebiotics and probiotics helps maintain a healthy and balanced microbiota. Probiotics are live microorganisms that reduce the number of harmful gut bacteria. Prebiotics are indigestible food components that selectively support the growth and activity of specific gut bacteria and the production of short-chain fatty acids (5, 6).

Another way to support gut health is through flavonoids. Flavonoids are a group of polyphenols found in various fruits and vegetables. They have numerous beneficial effects, including combating oxidative stress and reducing chronic inflammation (7, 8).

Mikrobióm+® is a natural blend extracted from *Citrus sinensis* (unripe oranges) and *Citrus paradisi* (grapefruit), designed to positively modulate the composition of the gut microbiota. The active components in Mikrobióm+® are the citrus flavonoids hesperidin and naringin. Mikrobióm+® is non-fermentable, and its flavonoids are activated through deglycosylation.

It has already been shown that the gut microbiota is associated with sleep quality and mental well-being (9, 10). Mikrobióm+® induces a positive shift in microbiota composition, enabling higher production of short-chain fatty acids (SCFAs), particularly butyrate and propionate. SCFAs are the main metabolites produced by the microbiota in the colon, acting as signaling molecules with a range of health effects, including on the gut-brain and gut-skin axes (11).

Therefore, we aimed to investigate whether Mikrobióm+® could improve skin condition, sleep, mental well-being, and digestive health.

The objective of this consumer study was to evaluate the effect of Mikrobióm+® supplementation at a dose of 500 mg for three months on self-assessed skin quality, sleep quality, mental well-being, and gastrointestinal health in healthy individuals.

Methods

1) Participants

The study participants were individuals who purchased the product under investigation without specifying a particular reason. Commonly reported reasons for using the product included addressing issues such as inflammatory bowel conditions, bloating, diarrhea, constipation, and skin problems like eczema and dermatitis. At the time of purchase, consumers were invited to participate in the study. Those who agreed were subsequently enrolled.

2) Investigational Product and Supplementation Protocol

Each participant received a total of 180 capsules containing Mikrobióm+® and was instructed to take two capsules daily for the three-month supplementation period. The daily dose provided 400 mg of hesperidin and 25 mg of naringin.

3) Study Design

After providing consent to participate, each participant was asked to complete three questionnaires: the first at baseline (before starting supplementation), the second after one month of supplementation, and the third at the end of the three-month supplementation period. An overview of the study design is shown in Figure 1.

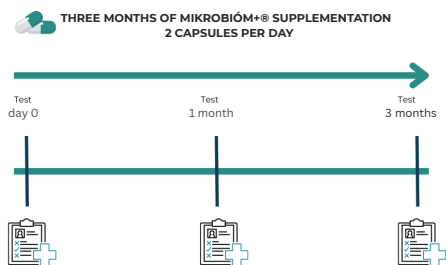


Figure 1. Overview of the study design

4) Measurements

The first two questionnaires were identical and included questions assessing digestive symptoms, skin quality, mental well-being, energy levels, and

sleep quality. The final questionnaire included additional questions to evaluate adherence to the supplementation protocol and overall satisfaction with the product used in the study (Appendix 1).

5) Statistical Analysis

The collected data were analyzed using IBM SPSS Statistics software. Due to the non-normal distribution of the data, the Friedman test was used to evaluate whether questionnaire scores differed significantly across the three time points. When the Friedman test indicated statistical significance ($p = 0.05$), post-hoc analyses were conducted using the Wilcoxon signed-rank test to identify pairwise differences between time points (e.g., baseline vs. 1 month, baseline vs. 3 months, and 1 month vs. 3 months). To account for multiple comparisons, the significance threshold for the Wilcoxon tests was adjusted to $p = 0.017$.

Results

1) Baseline Characteristics

The baseline characteristics of the study participants are presented in Table 1.

Questionnaires were collected from a total of 97 participants; however, only data from those who completed all three questionnaires within the specified timeframe were included in the analysis, resulting in a final sample of 56 participants.

	MEAN VALUES	SD
AGE (YEARS)	43	11.5
WEIGHT (KG)	70.9	14.3
HEIGHT (CM)	170.8	10.7
BMI	24.2	3.8

Table 1. Baseline characteristics of participants ($n = 56$)

2) Digestive Symptoms

The results related to digestive symptoms are shown in Figure 2. One month after starting supplementation, there was a significant improvement in digestive symptom scores compared to baseline ($p < 0.017$), and these improvements remained stable after three months

of supplementation.

Bloating symptoms, however, continued to improve between the first and third months ($p = 0.002$).

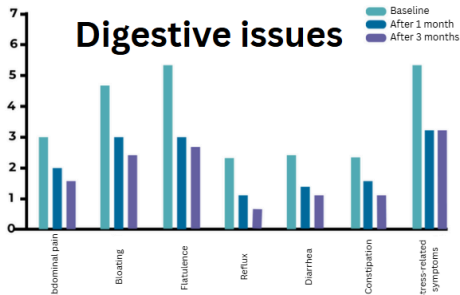


Figure 2: Results related to digestive issues

3) Mental Well-Being

Scores for mental well-being and energy levels are shown in Figure 3.

Results demonstrated a significant improvement compared to baseline after just one month of supplementation ($p < 0.017$), and these improvements remained stable at the three-month assessment ($p < 0.017$).

Notably, the emotional well-being score increased significantly only between baseline and the first month ($p < 0.001$), with no further significant changes observed between baseline and the third month ($p = 0.058$).

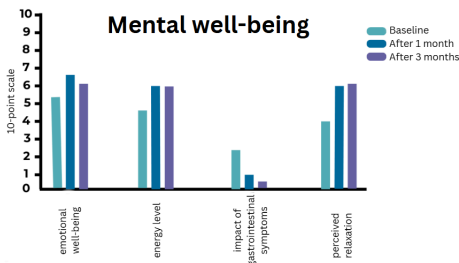


Figure 3: Results related to mental well-being

4) Sleep Quality

The overall sleep quality score showed a significant improvement from baseline after one month of supplementation, with further significant improvements observed between baseline and the third month, as well as between the first and third months ($p < 0.001$) (Figure 4).

Sleep quality level

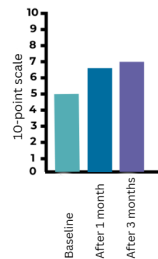


Figure 4: Results Related to Sleep Quality

5) Skin Quality

The results related to skin quality are shown in Figure 5.

Scores for skin hydration, itching, and overall skin quality showed significant improvement from baseline after one month of supplementation ($p < 0.017$) and remained stable throughout the three-month period ($p < 0.017$).

Skin elasticity improved significantly between baseline and the first month, with further improvement observed between the first and third months ($p < 0.001$).

No statistically significant changes were observed in skin redness scores ($p = 0.056$).

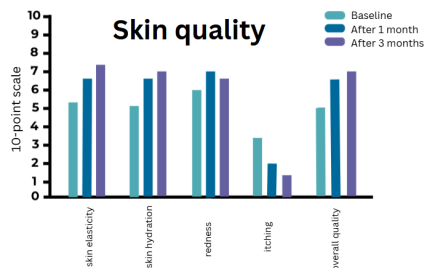


Figure 5: Results Related to Skin Quality

6) Overall Product Satisfaction

A total of 53.6% of participants rated the product 9 or higher, while 33.9% gave it a rating between 6 and 8. Another 12.5% rated the product between 3 and 5, and no participant gave a score lower than 3 (Figure 6).

Overall satisfaction

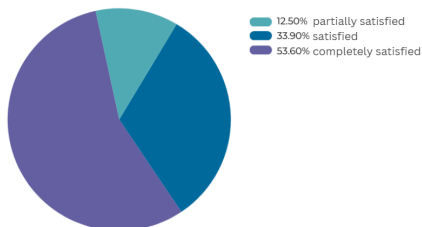


Figure 6: Overall product satisfaction

Discussion

The aim of this study was to assess the effects of three months of daily supplementation with Mikrobióm+® (400 mg hesperidin, 25 mg naringin) on self-perceived gastrointestinal health, mental well-being, skin quality, and sleep quality in healthy men and women. Significant positive changes were observed in digestive symptoms, mental well-being and energy levels, skin quality, and overall sleep quality. Noticeable improvements appeared after just one month of daily supplementation and generally persisted throughout the three-month period. However, emotional well-being scores showed a decreasing trend between the first and third months compared to baseline, and no significant changes were observed in skin redness scores. Conversely, certain parameters, such as reduced bloating and increased skin elasticity, continued to improve even after the first month.

Mikrobióm+® is a natural blend extracted from *Citrus sinensis* (unripe oranges) and *Citrus paradisi* (grapefruit), designed to positively modulate the composition of the gut microbiome. The active compounds in this product—hesperidin (400 mg) and naringin (25 mg)—are non-fermentable

flavonoids that, after metabolism by the gut microbiota into the aglycones hesperetin and naringenin, have been shown to benefit intestinal barrier function and inflammation (12, 13).

Previous data specifically demonstrated that in vitro supplementation with Mikrobióm+® led to a significant increase in *Roseburia spp.*, butyrate-producing bacteria that contribute to maintaining gut homeostasis and inhibiting inflammatory responses (12). Conversely, low levels of *Roseburia* are associated with various intestinal issues, such as bloating, abdominal pain, and inflammatory bowel diseases (14). The findings of the present study further support the ability of Mikrobióm+® to positively influence the gut microbiome (GM) and overall intestinal health.

Imbalance in the gut microbiome (GM), also known as dysbiosis, can lead to increased intestinal permeability (“leaky gut syndrome”), allowing bacterial metabolites or pro-inflammatory compounds to enter the bloodstream. This can negatively affect mental health through increased inflammation and disruption of neurotransmitter systems (2). Hesperidin and naringin help maintain intestinal barrier integrity by strengthening tight junctions between gut epithelial cells, thereby reducing gut permeability. Together with their anti-inflammatory and antioxidant properties, they contribute to restoring a healthy gut barrier, reducing inflammation, and limiting reactive oxygen species (ROS) circulation, which may positively influence mental well-being (9, 15). Increased gut permeability can also contribute to skin inflammation, such as acne or dermatitis (3, 4). In line with these findings, our study demonstrated significant improvements in mental well-being and subjective skin quality, suggesting a potential modulatory effect of the tested supplement on the gut-brain and gut-skin axes.

It is important to note that, despite the apparent downward trend in emotional well-being scores between the first and third months, stress-related

digestive symptoms were not negatively affected. This trend warrants further research to understand possible confounding factors, such as individual variability, adaptation to supplementation, or external influences unrelated to the intervention. Butyrate positively influences intestinal barrier function and reduces gut inflammation, which is reflected in lower calprotectin levels. Therefore, Flavobiotic is a premium solution for strengthening the intestinal barrier and enhancing immunity.

We have already demonstrated that a four-week supplementation with 500 mg of Mikrobióm+® improved subjectively perceived sleep quality (unpublished data). The current study further supports these findings. Butyrate-producing genera appear to be positively associated with better sleep quality through the reduction of inflammation and support of metabolic health (16). The gut microbiome communicates with the brain via neuroimmune, neuroendocrine, and sensory-neural pathways, which influence mental health and behavior, including sleep patterns. Poor sleep is associated with increased markers of inflammation and a less favorable microbiome profile, highlighting the role of the gut-brain axis in sleep regulation (9, 16).

In conclusion, the results of this study suggest that three months of daily supplementation with Mikrobióm+® significantly improved gastrointestinal health, mental well-being, skin quality, and sleep quality in healthy individuals, with benefits appearing after just one month and persisting throughout the study period. Specific parameters, such as reduced bloating and increased skin elasticity, showed further improvements even after the first month. These findings indicate the potential of Mikrobióm+® to positively modulate the gut microbiome and its downstream effects on the gut-brain and gut-skin axes. Future research should aim to clarify factors contributing to variability in outcomes, including individual responses to supplementation. Overall, these results provide

strong evidence for the potential of Mikrobióm+® as a natural supplement supporting holistic health through targeted modulation of the gut microbiome.

References

1. Ahlawat, Asha, K.K. Sharma, Gut-organ axis: a microbial outreach and networking. *Lett Appl Microbiol*. 2021 Jun; 72(6):636-668.
2. Clapp M, Aurora N, Herrera L, Bhatia M, Wilen E, Wakefield S. Gut microbiota's effect on mental health: The gut-brain axis. *Clin Pract*. 2017 Sep 15;7(4):987.
3. Makrantonaki E, Ganceviciene R, Zouboulis C. An update on the role of the sebaceous gland in the pathogenesis of acne. *Dermatoendocrinol*. 2011 Jan;3(1):41-9.
4. Bjerre RD, Bandier J, Skov L, Engstrand L, Johansen JD. The role of the skin microbiome in atopic dermatitis: a systematic review. *Br J Dermatol*. 2017 Nov;177(5):1272-1278.
5. Food and Agriculture Organization of the United Nations (FAO), World Health Organization (WHO). Health and nutritional properties of probiotics in food including powder milk with live lactic acid bacteria: Report of a joint FAO/WHO expert consultation. Córdoba, Argentina: FAO/WHO; 2001.
6. Bounhik Y, Raskine L, Simoneau G, Vicaut E, Neut C, Flourie B, Brous F, Borset FR. The capacity of nondigestible carbohydrates to stimulate fecal bifidobacteria in healthy humans: a double-blind, randomized, placebo controlled, parallel-group, dose-response relation study. *Am J Clin Nutr*. 2004 Dec;80(6):1658-64.
7. Wen K, Fang X, Yang J, Yao Y, Nandakumar KS, Salem ML, Cheng K. Recent Research on Flavonoids and their Biomedical Applications. *Curr Med Chem*. 2021;28(5):1042-1066.
8. Ullah, A.; Munir, S.; Badshah, S.L.; Khan, N.; Ghani, L.; Poulson, B.G.; Emwas, A.-H.; Jaremkoo, M. Important Flavonoids and Their Role as a Therapeutic Agent. *Molecules* 2020, 25, 5243.
9. Limbana T, Khan F, Eskander N. Gut Microbiome and Depression: How Microbes Affect the Way We Think. *Cureus*. 2020;12(8):e9966.
10. Grosicki GJ, Riemann BL, Flatt AA, Valentino TR, Lustgarten MS. Self reported sleep quality is associated with gut microbiome composition in young, healthy individuals: a pilot study. *Sleep medicine*. 2020;73:76-81.
11. Blaak EE, Canfora EE, Theis S, Frost G, Groen AK, Mithieux G, et al. Short chain fatty acids in human gut and metabolic health. *Benef Microbes*. 2020;11(5):411-55.
12. Sost MM, Ahles S, Verhoeven J, Verbruggen S, Stevens Y, Venema K. A Citrus Fruit Extract High in Polyphenols Beneficially Modulates the Gut Microbiota of Healthy Human Volunteers in a Validated In Vitro Model of the Colon. *Nutrients*. 2021 Nov 1;13(11):3915.
13. Stevens Y, Rymenant EV, Grootaert C, Camp JV, Possemiers S, Masclee A, Jonkers D. The Intestinal Fate of Citrus Flavanones and Their Effects on Gastrointestinal Health. *Nutrients*. 2019 Jun 27;11(7):1464.
14. Banaszak M, Górna I, Woźniak D, Przysławski J, Drzymała-Czyż S. Association between Gut Dysbiosis and the Occurrence of SIBO, LIBO, SIFO and IMO. *Microorganisms*. 2023 Feb 24;11(3):573.
15. Madureira MB, Concato VM, Cruz EMS, Bitencourt de Moraes JM, Inoue FSR, Concino Santos N, Gonçalves MD, Cremer de Souza M, Basso Scandolara T, Fontana Mezonni M, Galvani M, Rodrigues Ferreira Seiva F, Panis C, Miranda Sapla MM, Pavanelli WR. Naringenin and Hesperidin as Promising Alternatives for Prevention and Co-Adjuvant Therapy for Breast Cancer. *Antioxidants (Basel)*. 2023 Feb 27;12(3):586.
16. Grosicki GJ, Riemann BL, Flatt AA, Valentino T, Lustgarten MS. Self-reported sleep quality is associated with gut microbiome composition in young, healthy individuals: a pilot study. *Sleep Med*. 2020 Sep;73:76-81.